ORIGINAL INVESTIGATION

J Crit Intensive Care 2022;13:43–47
https://doi.org/10.37678/dcybd.2022.3111

Anemia and Red Blood Cell Transfusion Practices in a Medical Intensive Care Unit

Turkay AKBAS[1], Oner Abidin BALBAY[2]

[1]University of Düzce School of Medicine , Internal Medicine Department, Section of Intensive Care Unit, Düzce, Turkey

[2]University of Düzce School of Medicine, Pulmonary and Critical Care Medicine, Düzce, Turkey

Cite this article as: Akbas T, Balbay OA. Anemia and Red Blood Cell Transfusion Practices in a Medical Intensive Care Unit. J Crit Intensive Care 2022;13:43–47

Corresponding Author: Turkay Akbas
E mail: turkayakbas@yahoo.com

Received: May 16, 2022
Accepted: May 26, 2022
Available online: Jun 13, 2022

ABSTRACT

Objective: The study was aimed to describe red blood cell (RBC) transfusion practices in a medical intensive care unit (ICU).

Material and Method: This retrospective study involved patients admitted to the ICU between September 2015 and February 2020. A restrictive transfusion strategy was applied during the study period, in which hemoglobin levels were kept between 7.0 and 9.0 g/dL, and the recommended threshold for RBC transfusion was <7 g/dL, except for patients with acute coronary disease, acute cerebrovascular event, heart failure, severe hypoxemia, or undergoing hip fracture surgery, for whom hemoglobin levels were kept at ≥8 g/dL.

Results: Six hundred seventeen patients were included in the study (age 70±16 years, 51.7% male), with a mean hemoglobin level of 11.1±2.3 g/dL on admission. RBC transfusion was performed on 204 (33.1%) patients, and admission hemoglobin levels were significantly lower in the transfused than the non-transfused patients (9.4±1.9 vs. 11.9±2.1 g/dL; p<0.001). An average of 3.5 units per patient was transfused. Transfused patients had high disease severity scores, required high rates of invasive mechanical ventilation, renal replacement therapy and vasopressor use, and had longer ICU and hospital stays. ICU, in-hospital, 28-day, and 90-day mortality rates were significantly high among transfused patients. Logistic regression analysis identified RBC transfusion as an important predictor of 28-day (OR, 2.51; 95% CI, 1.49-4.23, p=0.001) and 90-day (OR, 1.69; 95% CI, 1.25-2.28; p=0.001) mortality.

Conclusion: Patients receiving RBC transfusion have high disease severity scores, exhibit low admission hemoglobin levels, require more organ support therapies, and have high mortality rates. The presence of RBC transfusion is a significant predictor of mortality.

Keywords: Critical illness, anemia, blood transfusion, mortality

Introduction

Anemia, defined as hemoglobin levels of <12 g/dL, is reported in between 40% and 85% of patients on admission to the intensive care unit (ICU) (1-3), and 25% to 37% of patients have admission hemoglobin levels of <9 g/dL (1,4). The prevalence of anemia can rise to 97% by ICU day 8 and to 100% by ICU day 13 (2). There are three main causes of anemia development in severely ill patients. Iron metabolism dysregulation and a blunted erythropoietin response are considered reasons for RBC underproduction where the host inflammatory response to critical illness is implicated (5). A second important cause of anemia is phlebotomy for diagnostic testing, with an average of 40 ml of blood being collected for a 24-hour period (6). Phlebotomized blood can rise to 70 ml/day with disease severity (3). The third cause of anemia is hemodilution from large-volume resuscitation in critically ill patients (7). Since anemia is commonly encountered in critically ill patients, red blood cell (RBC) transfusion is frequently performed. Approximately 30% to 50% of critically ill patients receive a transfusion during their ICU stay (1,2,6,8). The incidence of RBC transfusion can increase to 85% in patients with an ICU length of stay (LOS) >7 days (3). Anemia is the main indication for transfusion in up to 90% of patients (2,8). A restrictive blood transfusion strategy is applied for stable critically ill patients, the recommended target hemoglobin level being between 7.0 and 9.0 g/dL, while the recommended hemoglobin threshold for RBC transfusion is <7 g/dL (9). The purpose of the present study was to determine RBC transfusion practices in a tertiary medical ICU and to investigate the impact of RBC transfusion on the clinical outcomes of critically ill patients.

Materials and Methods

The study was conducted retrospectively in a nine-bed medical ICU in a university hospital in Turkey between September 2015 and February 2020. All patients aged ≥18 years with length of ICU stay >24 hours were included. None of the patients had coronavirus disease-2019. Exclusion criteria were age <18 years, multi-trauma, pregnancy, brain death, and length of ICU stay ≤24 hours. Patients who have terminal cancer diseases that considered as palliative care patient also excluded. First admission records were used in case of patients with multiple ICU admissions. A restrictive strategy for RBC transfusion was applied in the ICU during the study period. Hemoglobin concentrations were kept in the range of 7.0-9.0 g/dL, and one unit of RBC was transfused every time that hemoglobin levels decreased below 7 g/dL, unless patients had acute coronary disease, acute cerebrovascular event, heart failure, or severe hypoxemia, or had undergone hip fracture surgery, in which cases hemoglobin levels were kept at ≥8 g/dL (9). Another unit of RBC was given when hemoglobin concentrations after transfusion were below the predetermined threshold. Leukocyte-depleted RBC transfusion was carried out in the hospital throughout the study period. The study protocol was approved by the University of Düzce Institutional Review Board (Number: 2022/36; Date: 07.03.2022).

Data collected on admission to the ICU included demographics, comorbidities, admission diagnosis, and laboratory results. Clinical and laboratory data for sequential organ failure assessment (SOFA) and acute physiology and chronic health evaluation (APACHE) II scores were reported using the worst values within the first 24 hours after admission. Hemoglobin levels measured on admission to the ICU (within 6 hours), 24, 48 and 72 hours after admission, and the last hemoglobin level measured before discharge from the ICU were included. Data collected during ICU stay included the number of transfused RBC units, invasive mechanical ventilation (IMV), renal replacement therapy (RRT), and vasopressor use. Length of stay (LOS) in the ICU and hospital, and mortality rates were also recorded.

Admission diagnoses were defined as follows (1): infectious diagnosis included primarily sepsis-related diagnoses involving the central nervous system, lung, gastrointestinal system, soft tissue, urinary tract, and device-related infections. Cardiac diagnosis encompassed rhythm problems, acute coronary syndrome, heart failure, and cardiac arrest not precipitated by an underlying disease, such as sepsis or respiratory failure. Neurological diagnosis included intracranial bleeding, ischemic cerebrovascular accident, neuromuscular disease, and status epilepticus. Diagnosis of respiratory disease included chronic obstructive pulmonary diseases and asthma exacerbation, pulmonary embolism, and pneumothorax. Surgery encompassed any planned or unplanned surgeries. Gastrointestinal diseases included acute/chronic liver failure, ileus, bleeding, and pancreatitis.

Data were expressed as mean and standard deviation after the Kolmogorov-Smirnov test showed normal distribution, except for LOS, which was expressed as median and interquartile range. Continuous variables with normal distribution were compared using Student's T test. The Mann-Whitney U test was used for the comparison of non-normally distributed variables. Categorical variables were expressed as percentages, and statistical comparisons were performed using the X^2 test. Hemoglobin levels over time were compared using analysis of variance with repeated measures. Forward stepwise logistic regression analysis was performed in order to determine adjusted relative risks of 28- and 90-day mortality in patients receiving RBC transfusion during the ICU stay. Variables with potential confounders considered for the logistic regression analysis included age, sex, SOFA and APACHE II scores, medical history, admission diagnosis, admission hemoglobin, RBC transfusion, and the requirement of IMV, RRT, and vasopressors during ICU stay. Multicollinearity between variables was checked before modeling, and all variables were included in the models thereafter. Kaplan-Meier survival curves, describing 28-day survival distributions for transfused and non-transfused patients, were compared with the use of a Log-Rank test. A p value <0.05 was regarded as statistically significant. Statistical analysis was performed on Statistical Package for the Social Science 23 version software (IBM Corp., Armonk, NY, USA).

Results

Six hundred seventeen patients were included in the study (mean age 70±16 years; male 51.7%). The mean hemoglobin level on admission was 11.1±2.3 g/dL. Hemoglobin levels were <12 g/dL in 66% of the patients and <9 g/dL in 18.6% on admission. RBC transfusion was performed on 204 (33.1%) patients, and the mean admission hemoglobin level was significantly lower in transfused patients than in non-transfused patients (9.4±1.9 vs. 11.9±2.1 g/dL; p<0.001). The rate of hemoglobin levels of <12 g/dL on admission was higher in transfused patients than in non-transfused patients (179 [87.7%] vs. 230 [55.7%]; p<0.001). Additionally, transfused patients had a higher rate of hemoglobin levels of <9 g/dL compared to non-transfused patients (89 [43.6%] vs. 26 [6.3%]; p<0.001) on admission. The mean hemoglobin level immediately before RBC transfusion was 7.0±0.7 g/dL in the transfused patients. An average of 3.5 units of RBC was transfused per patient (718 units in 204 patients). The patients with gastrointestinal bleeding on admission received more RBC units than those without gastrointestinal bleeding (83 units in 16 patients with gastrointestinal bleeding, 5.2 units per patient; 635 units in 188 patients without gastrointestinal bleeding, 3.4 units per patient; p=0.002).

Transfused patients had high APACHE II and SOFA scores, and high rates of IMV, RRT, and vasopressor requirement (Table 1). Transfused patients stayed longer in the ICU (14 [6-28] vs. 4 [2-7] days; p<0.001) and in the hospital (19 [9-38] vs. 9 [5-15] days; p <0.001) than non-transfused patients. The transfusion rate increased from 12.8% with ICU stays of ≤3 days to 68.3% with ICU stays of >14 days, and the mean units of transfused RBC also rose from two with ICU stays of ≤3 days to five with ICU stays of >14 days (Table 2). Hemoglobin concentrations over time analyzed by analysis of variance with repeated measures exhibited significant diminution in both transfused and non-transfused patients (Figure 1). Hemoglobin levels were <12 g/dL in 85.3% of the patients and <9 g/dL in 36.8% on the last day of ICU stay. The transfused group included more patients with hemoglobin levels <12 g/dL than the non-transfused group on the last day of ICU stay (203 [99.6%] vs. 323 [78.6%]; p <0.001). Moreover, the rate of hemoglobin levels of <9 g/dL was higher in transfused patients compared to non-transfused patients (150 [73.5%] vs. 88 [21.3%]; p <0.001).

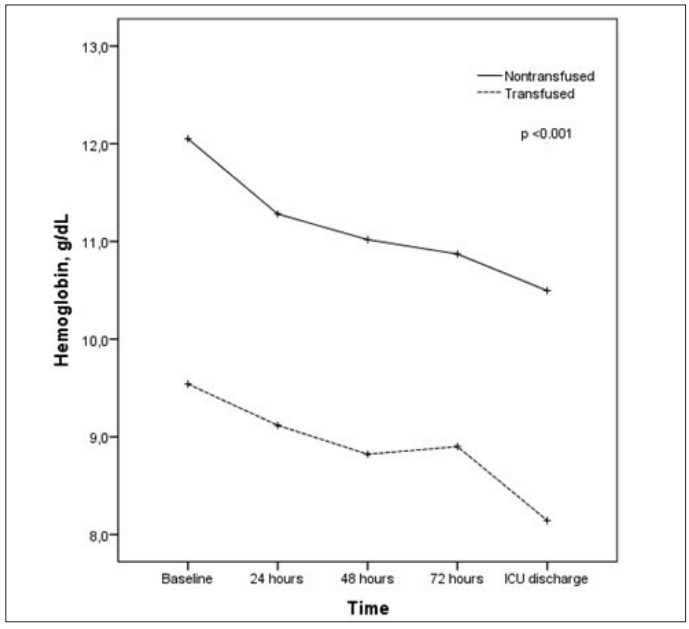

Figure 1. Courses of hemoglobin patterns in transfused and non-transfused patients. Transfused patients had significantly lower mean hemoglobin levels than non-transfused patients from the first day of admission to the ICU to the last day of ICU stay

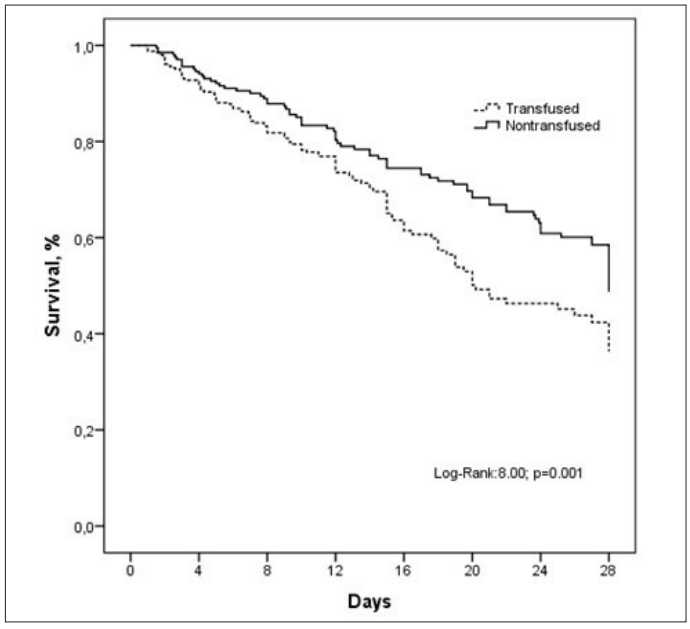

Figure 2. 28-day survival analysis by transfusion status. Transfused patients had significantly lower survival rates than non-transfused patients

Table 1. Characteristics and outcomes of RBC transfused and non-transfused patients

Parameters	RBC transfusion (-) n = 413	RBC transfusion (+) n = 204	p
Age, years†	69.7 ± 15.9	71.6 ± 15.2	0.148
Male, n (%)	222 (53.8)	97 (47.5)	0.185
Comorbidity, n (%)			
Hypertension	275 (66.6)	150 (73.5)	0.080
Ischemic heart disease	115 (27.8)	55 (27.0)	0.817
Heart failure	153 (37.0)	70 (34.3)	0.506
Cerebrovascular disease	72 (17.4)	52 (25.5)	0.019
Diabetes mellitus	141 (34.1)	81 (39.7)	0.175
COPD	97 (23.5)	34 (16.7)	0.051
Chronic renal failure (Stage 2-5D)	77 (18.6)	50 (24.5)	0.090
Admission diagnosis, n (%)			
Infection	169 (40.9)	97 (48)	0.098
Postoperative follow-up	82 (19.9)	39 (19.1)	0.828
Neurological disease	58 (14.0)	15 (7.4)	0.015
Lung disease	51 (12.3)	13 (6.4)	0.022
Cardiovascular disease	29 (7.0)	14 (6.9)	0.942
Gastrointestinal disease‡	5 (1.2)	19 (9.3)	<0.001
Other	19 (4.6)	7 (3.4)	0.497
APACHE II†	21.6 ± 9.3	25.8 ± 8.5	<0.001
SOFA†	5.9 ± 4.2	7.7 ±3.8	<0.001
Hemoglobin, g/dL†	11.9 ± 2.1	9.4 ± 1.9	<0.001
IMV, n (%)	176 (42.6)	139 (68.1)	<0.001
RRT, n (%)	66 (16.0)	65 (31.9)	<0.001
Vasopressor, n (%)	171 (41.6)	150 (73.5)	<0.001
ICU stay, days‖	4 (2-7)	14 (6-28)	<0.001
In-hospital mortality, n (%)	125 (30.3)	113 (55.4)	<0.001
28-day mortality, n (%)	127 (30.8)	80 (39.2)	0.036
90-day mortality, n (%)	163 (39.5)	126 (61.8)	<0.001

†Values were expressed as mean ±standard deviation.
‡Gastrointestinal diseases included 18 patients with acute gastrointestinal bleeding (two in the non-transfused group and 16 in the transfused group).
‖Values were expressed as median and interquartile range (25p-75p).
APACHE: acute physiology and chronic health evaluation; **COPD:** chronic obstructive pulmonary disease; **D:** dialysis; **ICU:** intensive care unit; **IMV:** invasive mechanical ventilation; **N:** number; **RBC:** red blood cell; **RRT:** renal replacement therapy; **SOFA:** sequential organ failure assessment.

ICU, in-hospital, 28-day, and 90-day mortality rates were significantly high among transfused patients (Table 1). Since multicollinearity was detected between admission hemoglobin levels and RBC transfusion, the admission hemoglobin variable was excluded from the adjusted logistic regression analysis. That analysis identified RBC transfusion as an important predictor of 28- and 90-day mortality, together with age, disease severity scores, and vasopressor, RRT and IMV use (Table 3). Kaplan-Meier survival curves, describing the 28-day survival distributions for transfused and non-transfused patients, revealed significant differences in survival patterns (p=0.005) (Figure 2).

Discussion

Sixty-six percent of the patients in the present study had hemoglobin levels <12 g/dl on admission to the ICU, and this rate rose to 85.3% on the last day of ICU stay. Totally, 33.1% of the patients received one or more units of RBC transfusion during their ICU stay. These results were comparable with the previous literature. A large multicenter study, by Corwin et al., involving 4892 patients reported that two-thirds of the patients had a hemoglobin level of <12 g/dL on admission (8). Another multicenter study including 1136 patients reported a mean admission hemoglobin level of 11.3 ±2.3 g/dL, and that 63% of

Table 2. Transfusion rates, mean numbers of units transfused, and mortality rates according to ICU length of stay

ICU LOS	n	RBC transfused n (%)	Mean units transfused ± SD†	Mortality,n (%)
All patients	617	204 (33.1)	3.5 ± 3.2	95 (46.6)
≤3 days	188	24 (12.8)	2.0 ± 1.0	9 (37.5)
>3 days	429	180 (42.0)	3.7 ± 3.3	86 (47.8)
>7 days	236	137 (58.1)	4.1 ± 3.6	74 (54.0)
>14 days	145	99 (68.3)	4.8 ± 3.9	55 (56.0)

†Values were expressed as mean ±standard deviation.
ICU: intensive care unit; **LOS:** length of stay; **N:** number; **RBC:** red blood cell; **SD:** standard deviation.

Table 3. Logistic regression analysis for 28- and 90-day mortality

	28-day mortality†			90-day mortality‡		
Parameters	p	OR	95% CI	p	OR	95% CI
Age	0.002	1.01	1.01-1.02	0.001	1.02	1.01-1.03
SOFA	<0.001	1.10	1.06-1.15	<0.001	1.10	1.05-1.15
APACHE II	0.002	1.01	1.01-1.05	<0.001	1.04	1.02-1.06
RBC transfusion	0.001	2.51	1.49-4.23	0.001	1.69	1.25-2.28
IMV	<0.001	4.04	2.43-6.72	0.005	1.95	1.22-3.12
Vasopressor	<0.001	3.00	1.72-5.23	<0.001	2.83	1.75-4.58
RRT	0.008	1.96	1.19-3.21	0.089	1.57	0.93-2.64

†Hosmer-Lemeshow:X^2, 8.506; df, 8; p=0.386.
‡Hosmer-Lemeshow:X^2, 7.773; df, 8; p=0.456.
APACHE: acute physiology and chronic health evaluation; **CI:** confidence interval; **IMV:** invasive mechanical ventilation; **OR:** odds ratio; **RBC:** red blood cell; **RRT:** renal replacement therapy; **SOFA:** sequential organ failure assessment.

the patients had an admission hemoglobin level <12 g/dL (6). The incidence of anemia increases in line with LOS in the ICU, irrespective of admission hemoglobin levels, as in the present study (6,8). Thomas et al. reported that the rate of anemia rose from 71% on admission to the ICU to 100% by ICU day 13 (2). The percentage of RBC transfusions also increases in line with LOS in the ICU. Vincent et al. reported RBC transfusion rates of 24.5% with ICU stays of ≤2 days and 73% with ICU stays of >7 days (6). Corwin et al. determined a transfusion rate of 85% in patients with ICU stays >7 days (3). Another study, by Thomas et al., reported RBC transfusion rates of 40% during the total ICU stay, rising to 70% with ICU stays of >7 days (2). In addition to the transfusion rate, mean units of RBC transfusion also increase in line with ICU stay (3,6,8). Vincent et al. reported mean units of RBC transfusion of three in patients with ICU stays of ≤2 days, but of seven in those with ICU stays of >7 days in two multicenter studies (6,10). Similarly to the previous literature, we observed that the transfusion rate increased from 12.8% with ICU stays of ≤3 days to 68.3% with ICU stays of >14 days, and that mean units of transfused RBC rose from two with ICU stays of ≤3 days to five with ICU stays of >14 days.

The mean unit of RBC transfused in the present research is lower than that in previous studies, which have reported ranges from 4.8 to 9.5 (3,6,8,10). This is most probably due to the application of the restrictive-blood transfusion strategy in our ICU, where the mean hemoglobin level immediately before RBC transfusion was 7.0±0.7 g/dL. Studies have shown that fewer average units of RBC were used in the restrictive transfusion strategy (2.6±4.1 units per patient) in which the target hemoglobin level was kept at between 7.0 and 9.0 g/dL than in the liberal transfusion strategy (5.6±5.3 units per patient) in which the target hemoglobin level was maintained between 10.0 and 12.0 g/dL (11).

The results of this study showed that patients who received RBC transfusion at any time during their ICU stay had high admission APACHE II and SOFA scores, and low admission hemoglobin levels. These results were similar to those in the previous literature. Corwin et al. showed high APACHE II and SOFA scores along with low admission hemoglobin levels in transfused patients (8). Another study, by Vincent et al., reported high admission APACHE II and SOFA scores together with low admission hemoglobin levels in transfused patients (6). Low admission hemoglobin levels have been linked to high disease severity scores (4,8). Since transfused patients are more severely ill, life support therapies, such as IMV, RRT, and vasopressor use, are frequently required in these cases (12). Mortality rates in transfused patients are therefore generally high (4,6,8,10). There is a direct relationship between the number of units transfused and mortality rates, and RBC transfusion is an important mortality predictor in critically ill patients, as demonstrated in the present study (6,8,10).

There are a number of limitations to this study. First, it was retrospective in nature and conducted at a single center. The results cannot therefore be extrapolated to the general population. Second, we did not measure phlebotomized blood quantities, a well-known cause of anemia in critically ill patients. Third, complications associated with RBC transfusion, such as transfusion-related acute lung injury, transfusion-associated circulatory overload, transfusion reactions, and development of nosocomial infection were not investigated, and these may cause severe morbidity and even mortality. Finally, acute blood loss (surgery or active bleedings) during ICU stay, an important indication for RBC transfusion in critically ill patients, was also not investigated (3,11).

Conclusion

Transfused critically ill patients had high disease severity scores, low admission hemoglobin levels, longer ICU and hospital stays, greater organ support therapy requirements, and high mortality rates. RBC transfusion emerged as an important mortality predictor, along with age, SOFA and APACHE II scores, and life support therapies. Physicians should therefore consider RBC transfusion as a sign of disease severity in critically ill patients.

AUTHOR CONTRIBUTIONS:

Concept: TA; **Design:** TA, ÖAB; **Supervision**: TA, ÖAB; **Resources:** TA, ÖAB; **Materials:** TA, ÖAB; **Data Collection and/or Processing:** TA, ÖAB; **Analysis and/or Interpretation:** TA, ÖAB; **Literature Search:** TA, ÖAB; **Writing the Manuscript:** TA, ÖAB; **Critical Review:** TA, ÖAB

Ethics Committee Approval: The study protocol was approved by the ethics review board of Düzce University under approval number of 2022/36 at the date of 07.03.2022.

Informed Consent: Since the study was retrospective, informed consent was waived.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Presentation: Part of this study was presented at the 18th Congress of The Turkish Society of Medical and Surgical Intensive Care Medicine - 10th Euro-Asian Critical Care Meeting, December 6-9, Turkey, 2021.

References

1. Akbaş T. Long length of stay in the ICU associates with a high erythrocyte transfusion rate in critically ill patients. J Int Med Res. 2019;47(5):1948–57. [CrossRef]
2. Thomas J, Jensen L, Nahirniak S, et al. Anemia and blood transfusion practices in the critically ill: a prospective cohort review. Hurt Lung. 2010;39(3):217–25. [CrossRef]
3. Corwin L, Parsonnet KC, Gettinger A. RBC transfusion in the ICU. Is there a reason? Chest. 1995;108:767–71. [CrossRef]
4. Vincent JL, Jaschinski U, Wittebole X, et al. Worldwide audit of blood transfusion practice in critically ill patients. Crit Care. 2018;22(1):102. [CrossRef]
5. Shander A. Anemia in the critically ill. Crit Care Clin. 2004;20(2):159–78. [CrossRef]
6. Vincent JL, Baron J-F, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. JAMA. 2002;288(12):1499–507. [CrossRef]
7. Perel A. Iatrogenic hemodilution: a possible cause for avoidable blood transfusion. Crit Care. 2017;21(1):291. [CrossRef]
8. Corwin HL, Gettinger A, Pearl RG, et al. The CRIT Study: Anemia and blood transfusion in the critically ill –current clinical practice in the United States. Crit Care Med. 2004;32(1):39–52. [CrossRef]
9. Mueller MM, Van Remoortel H, Meybohm P, et al. Patient blood management recommendations from the 2018 Frankfurt consensus conference. JAMA. 2019;321(10):983–97. [CrossRef]
10. Vincent J-L, Sakr Y, Sprung C, et al. Are blood transfusions associated with greater mortality. Results of the sepsis occurrence in acutely ill patients study. Anesthesiology. 2008;108(1):31–9. [CrossRef]
11. Hébert PC, Wells G, Blajchman MA, et al. A multicenter randomized controlled clinical trial of transfusion requirement in critical care. N Engl J Med. 1999;340(6):409–17. [CrossRef]
12. Chant C, Wilson G, Friedrich JO. Anemia, transfusion, and phlebotomy practices in critically ill patients with prolonged ICU length of stay: A cohort study. Crit Care. 2006;10(5):R140. [CrossRef]