The Implementation of a Red Blood Cell Transfusion Guideline in Critically Ill Surgical Patients at Siriraj Hospital

Anticha Siritongtaworn, M.D., Puriwat To-adithep, M.D., Onuma Chaiwat, M.D.

Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To compare the RBC transfusion rate and clinical outcomes before and after the implementation of a transfusion guideline and to determine the adherence rate to the guideline.

Methods: This is a prospective experimental study in adult patients (≥18 years) admitted to surgical intensive care units. After developing and implementing a transfusion guideline, the data including patients' characteristics, transfusion and outcomes were collected prospectively (post-educational group). Data in pre-educational group was retrieved retrospectively from medical records.

Results: There were 197 patients in pre-educational group and 188 patients in post-educational group. The incidence of RBC transfusion significantly decreased significantly in post-educational group (37.2% vs. 48.7%, p = 0.02). The hemoglobin threshold for RBC transfusion was significantly lower in post-education group (8.16±1.43 vs. 8.97±1.57, p=0.001). The 28-day mortality rate was significantly decreased after the implementation of the guideline. (3.2 % vs. 11.2 %, p = 0.007). The adherence rate to transfusion guideline was reported as 47.1%.

Conclusion: The incidence of RBC transfusion was lower after the implementation of a transfusion guideline.

Keywords: Red Blood cell; transfusion; surgical patients; intensive care; guidelines (Siriraj Med J 2019;71: 66-73)

BACKGROUND

Anemia has been associated with poor clinical outcomes including higher mortality in patients who underwent non-cardiac surgery.[1] Red blood cell transfusions (RBCs) is one of the available methods that is frequently used to treat anemia or hemorrhage in order to improve oxygen delivery to tissues. Nevertheless, it is well established that RBC transfusion is an independent predictor of death, nosocomial infection, multi-organ dysfunction syndrome (MODS) and acute respiratory distress syndrome (ARDS) in critically ill patients.[2] Transfusion related immunomodulation (TRIM) is accounted to be the underlying cause.[3]

However, many studies from diverse locations in North America and Western Europe have demonstrated that 30-40% of the patients admitted to intensive care unit (ICU) still received RBC transfusion.[4-6] In addition, it was increasing up to 73% in patients with an ICU-stay longer than 7 days.[4] The pre-transfusion hemoglobin (Hb) was reported around 8.5 g/dl. Surgical patients have shown to receive more blood transfusions than medical patients, particularly in those with emergency surgery.[4] A retrospective study from Siriraj Hospital in critically ill surgical patients who had been on mechanical ventilation for greater than 24 hours reported an incidence of RBC transfusion was as high as 83 % and the mean RBC

Corresponding author: Onuma Chaiwat
E-mail: onuma.cha@mahidol.ac.th
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ORCID ID: 0000-0003-4464-9226
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transfusion threshold was at Hb level of 8.7±1.2 g/dL.[7] The morbidity and mortality were higher in transfused patients.[7] Although recent data suggested that restrictive transfusion strategy with the a Hb threshold of 7.0 g/dl was well tolerated in general critically ill patients[8,9], trauma patients[10], sepsis patients[11,12] and in cardiac surgery patients[13,14] concerns have been raised regarding the actual practices and the remaining high incidence of RBC transfusion.

In addition, there has been lack of high quality data regarding the optimal Hb threshold in certain critically ill populations such as those with preexisting coronary disease, cerebrovascular disease and renal failure. The implementation of a guideline with specifies indication for transfusion might help to reduce the unnecessary transfusion. Although a number of previous guidelines[12,15,25] have been published, the adherence to the guideline might be problematic. Educational program including training course and posters related to the specific guideline for transfusion probably improves the adherence rate to the guideline. As a result, lower RBCs transfusion rate and better clinical outcomes are anticipated. This study aims to compare the RBC transfusion rate before and after the implementation of a guideline and the adherence rate to the guideline in critically ill surgical patients.

MATERIALS AND METHODS

The study was approved by Siriraj Institutional Review Board (Si 602/2013) with the waiver of informed consent. It was a prospective experimental study. All surgical patients admitted to SICU with age of equal to or more than 18 years during the study period were included. Patients with brain death or imminent death required withholding or withdrawing the treatment or had demonstrated an active blood loss (defined as blood loss of more than 30% of blood volume) were excluded.

The study consisted of 5 periods

- 1 month for developing a transfusion guideline and distributing a guideline to ICU physicians and surgeons by setting the meeting and official letters to the head of department
- After an approval from SIRB, 4 months pre-guideline data collection (April to August 2011) from the previous medical records were obtained (pre-educational group)
- 1 month (February 2014) for providing educational programs to the anesthesia attending staff who were the same group in both pre- and post-educational period and anesthesia resident trainees who were working in ICU during the study period. Programs included formal lecture at the beginning, poster presentation, reminder card and reminder about transfusion guideline once a month
- 4 months prospective observational period with data collection after providing educational programs between March and July 2014 (post-educational group)
- 2 months of follow up period

Data collection were 1) patient profiles including age, gender, weight, height, primary diagnosis, co-morbid disease (diabetes mellitus, hypertension, cardiovascular disease, chronic lung disease, chronic kidney disease, hematologic disease), smoking, alcohol drinking, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, type and duration of surgery, type and duration of anesthesia and the presence of sepsis on ICU admission; 2) transfusion data (post-educational group) including Hb/hematocrit (Hct) level before RBC transfusion. In case, the patients were transfused more than one time, we collected the transfusion information at the first transfusion), indication for RBC transfusion and the number, type and storage time of the transfused RBC; 3) clinical outcomes including nosocomial infection, cardiovascular events, acute lung injury (ALI)/ARDS, and MODS, ventilator days, ICU and hospital length of stay and 28-day mortality rate

Guideline for transfusion of RBC in critically ill surgical patients, Siriraj Hospital[15, 16]

Preface

1. World Health Organization (WHO) defines anemia as hemoglobin concentration (cHb) < 13.0 g/dl in men and < 12.0 g/dl in women.

2. Except dramatic emergency events with exsanguinating patients, transfusion of RBC should be generally performed as single-unit transfusion, which means one unit a time; the next unit, if necessary is given after actual Hb recording.

3. Any varyiation from the standards described below should be explained by the decision maker and documented in the patients file.

Indications for red cell transfusion **(Fig 1)**

Patients with prolonged hemorrhagic shock or acute hemorrhage (> 30% blood volume) that is difficult to estimate and not manageable by colloid/crystalloid infusion, and signs of oxygen deficiency, such as drop in central venous oxygen saturation ($ScvO_2$), increase in arterio-venous differences of oxygen ($AVDO_2$), elevated plasma lactate level and increase in base excess (BE).

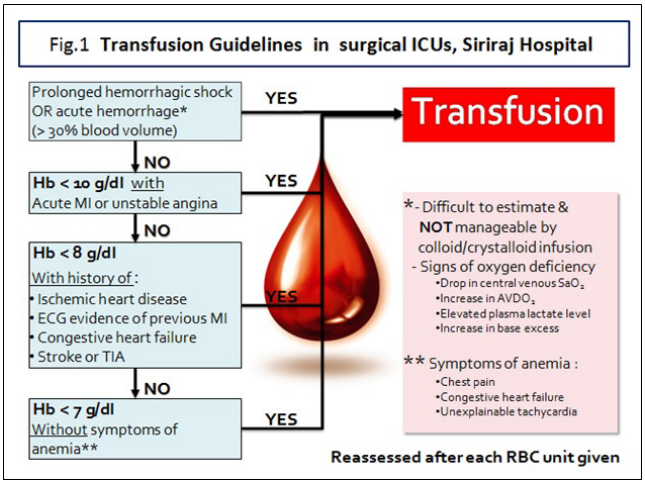

Fig 1. Transfusion Guidelines in surgical ICUs, Siriraj Hospital.

Additional indications

A. Hemoglobin concentration (cHb) < 7 g/dl in normovolemic anemia without pathologic symptoms related to anemia.

A. 1 Symptoms of anemia

I. Chest pain (deemed to be cardiac in origin)

II. Congestive heart failure

III. Otherwise unexplainable tachycardia

Situation has to be reassessed after each RBC unit given.

B. Hemoglobin concentration (cHb) < 8 g/dl in normovolemic anemia with history of:

I. Ischemic heart disease

II. Electrocardiographic evidence of previous myocardial infarction

III. Presence of congestive heart failure

IV. Stroke or transient ischemic attack

C. Hemoglobin concentration (cHb) < 10 g/dl in patients with acute myocardial infarction or unstable angina.

Statistical analysis

The primary outcome was the incidence of RBC transfusion after the guideline implementation and the secondary outcomes included the adherence to the guidelines (Hb threshold of RBC transfusion), ICU and hospital length of stay (LOS), in-hospital and 28-day mortality. The sample size was calculated by predicting the transfusion rate before the implementation using a guideline about 50% and reduced to 35% during the post-implementation period, at test significant level 0.05 and power of 80%. After adding up 20% for possible missing data, the sample size of 200 patients in each group was required.

Continuous data were presented as median with interquartile range (IQR) or mean with standard deviation (SD) with 95% confidential interval (CI). Categorical data were presented as numbers and percentages. Non-parametric Mann-Whitney U test or unpaired t-test for continuous data and Chi-Square or Fisher's exact test for numbers of events were used for comparison between pre- and post- educational program. P-value < 0.05 was considered as statistically significant. Data analysis was performed using SPSS 15.0 (SPSS Inc., Chicago, IL).

RESULTS

The overall population was 400 patients, 200 in a pre-educational group and 200 in a post-educational group. Three patients from pre-educational group were excluded due to massive hemorrhage and twelve patients in post-educational group were excluded due to massive hemorrhage (10) and incomplete data (2). These left 197 and 188 patients in pre- and post-educational groups for analysis. (Fig 2)

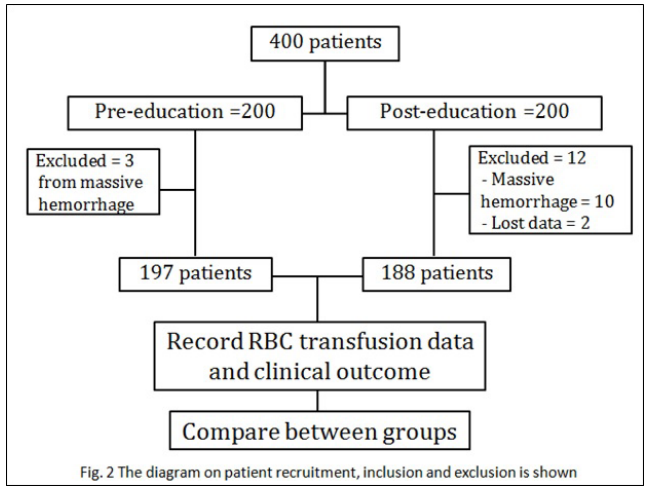

Fig 2. The diagram on patient recruitment, inclusion and exclusion is shown.

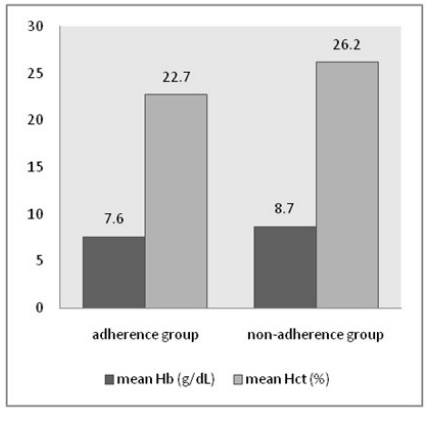

Fig 3. The mean Hb and Hct in adherence and non-adherence group in post-educational patients.

Patient characteristics and intra-operative data were shown in Table 1. There was no significant difference in patient characteristics, underlying medical diseases,

TABLE 1. Characteristic of patients on admission to surgical intensive care unit.

	Pre-education N=197	Post-education N=188	P-value
Age (year)	64.49 ± 17.86	61.59 ± 19.49	0.13
Gender (male) N (%)	103 (52.3)	105 (55.85)	0.54
Weight (kg)	60.66 ± 15.12	60.28 ± 16.08	0.82
Height (cm)	159.78 ± 8.95	160.55 ± 9.06	0.41
Surgical patients N (%)	180 (91.37)	176 (93.62)	0.44
Medical patients N (%)	17 (8.63)	12 (6.83)	
Postoperative day, Median (IQR)	0 (0-6)	0 (0-8)	0.53
Underlying medical diseases N (%)			
Coronary artery disease	31 (15.74)	23 (12.34)	0.4
Vascular disease	34 (17.26)	44 (23.4)	0.16
Respiratory disease	61 (30.96)	62 (32.98)	0.53
End stage renal disease	8 (4.06)	6 (3.19)	0.54
Endocrine disease	57 (28.93)	65 (35.57)	0.27
Stroke	26 (13.2%)	26 (13.8)	0.88
Anemia N (%)	163 (82.74)	146 (77.66)	0.25
Coagulopathy N (%)	40 (20.3)	43 (22.87)	0.62
Immunocompromised N (%)	7 (3.55)	15 (7.98)	0.08
Malignancy N (%)	70 (35.53)	61 (32.45)	0.59
Surgical data N (%)			
Elective surgery	124 (62.94)	114 (60.64)	0.28
Emergency surgery	52 (26.4)	63 (33.51)	
General surgery	77 (39.1)	73 (38.83)	0.81
Vascular surgery	38 (19.29)	41 (21.8)	
Orthopedic surgery	28 (14.21)	22 (11.7)	
Obstetric & gynecological surgery	11 (5.58)	13 (6.91)	
Type of anesthesia N (%)	135 (68.53)	134 (71.28)	0.05
- General anesthesia	11 (5.58)	3 (1.6)	
- Regional anesthesia			
ASA class > 2 N (%)	105 (58.33)	119 (63.3)	0.14
Volume of RBC transfusion in operating room (ml), Median (IQR)	565.5 (324.8, 924.8)	706.5 (350.8,1217.8)	0.11
APACHE II score	9.67 ± 6.62	8.66 ± 5.5	0.1
SOFA score ,Median (IQR)	2 (0,5)	2 (0,3)	0.07
Indication for SICU admission			
Hemodynamic monitoring	196 (99.5)	188 (100)	1.0
Respiratory support	100 (50.76)	120 (63.83)	0.01
Shock			
Septic shock	25 (12.7)	18 (9.57)	0.35
Cardiogenic shock	6 (3.05)	2 (1.06)	
Hypovolemic shock	11 (5.58)	14 (7.45)	
Laboratory on admission			
Hb (g/dl)	10.53 ± 2.05	11.57 ± 7.64	0.71
Hct (%)	31.73 ± 6.28	33.24 ± 6.42	0.21
Creatinine (mg/dl)	1.45 ± 1.6	1.32 ± 1.32	0.39
Albumin (g/dl)	2.84 ± 0.69	2.93 ± 2.61	0.66
PaO_2 (mmHg)	177.25 ± 69.06	164.79 ± 79.80	0.2
PaO_2/FIO_2 ratio	345.05 ± 196.24	359.16 ± 178.33	0.56

Abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II score; ASA = American Society of Anesthesiology Physical Status; CI = confidence interval; FiO2 = fraction of inspired oxygen; Hb = hemoglobin; Hct = hematocrit; ;IQR = interquartile range; PaO_2 = partial pressure of arterial oxygenation; RBC = red blood cell; SOFA = Sequential Organ Failure Assessment; SICU = surgical intensive care unit

surgical data and patient conditions on ICU admission between the pre and post- education groups except for the indication for SICU admission. Respiratory support as an indication for SICU admission was higher in post-educational group, than in pre-educational group (63.83% vs. 50.76%, p = 0.01).

Patients in post-educational group had significantly lower RBC transfusion rate (37% vs. 48%, p = 0.02) and the adherence rate to the guideline was 47% .The mean Hb level before RBC transfusion was significantly lower in post-educational group (8.16 ± 1.43 vs. 8.97 ± 1.57g/dL, p = 0.001). The 28-day mortality and ICU mortality were also significantly lower in post-educational group. Patients in pre-educational group had significantly higher incidence of acute respiratory distress syndrome (ARDS) (2.5% vs. 0%, p = 0.05) and acute kidney injury (AKI) (8.1% vs. 2.1%, p = 0.01) than those in post-educational group (Table 2).

TABLE 2. Transfusion data and outcomes.

	Pre-education N=197	Post-education N=188	P-value
Transfusion in SICU, N (%)	96 (48.7)	70 (37.2)	0.02
Threshold			
Hb threshold	8.97 ± 1.57	8.16 ± 1.43	0.001
Hct threshold	27.14 ± 4.76	24.54 ± 4.12	< 0.001
RBC volume transfused in SICU, Median (IQR)	627.5 (316.25, 1030.25)	650 (342.5, 904.0)	0.95
Outcomes			
Ventilator days, Median (IQR)	1 (0,2)	1 (0,2)	0.18
28-day mortality N (%)	22 (11.12)	6 (3.19)	0.007
SICU mortality N (%)	15 (7.61)	3 (1.56)	0.009
SICU LOS, Median (IQR)	2 (1,3)	2 (1,3)	0.73
Hospital LOS, Median (IQR)	15 (9,28)	13 (9,27)	0.37
Complication in SICU,N (%)			
Delirium	5 (2.54)	6 (3.2)	0.55
Stroke	0 (0)	4 (2.1)	0.07
Acute myocardial infarction	2 (1.0)	4 (2.1)	0.4
Pulmonary edema	3 (1.52)	2 (1.1)	0.55
ARDS	5 (2.5)	0 (0)	0.05
Acute kidney injury	16 (8.1)	4 (2.1)	0.01
Pneumonia	4 (2.0)	5 (2.7)	0.54
CRBSI	0 (0)	1 (0.5)	0.35
Severe sepsis	6 (3.1)	8 (4.3)	0.48
Septic shock	10 (5.1)	5 (2.7)	0.28

Abbreviations: ARDS = acute respiratory distress syndrome; CRBSI = catheter-related bloodstream infection; Hb = hemoglobin; Hct = hematocrit; LOS = length of stay; RBC = red blood cell; SICU = surgical intensive care unit; IQR = interquartile range

TABLE 3. Indications for red blood cell transfusion in post-educational group (N = 70).

Indication	N (%)
Low Hb	33 (47.1%)
Suspected anemic symptoms	14 (20%)
Keep Hct > 30 %	10 (14.3%)
History of coronary artery disease	8 (11.43%)
MI/Unstable angina	4 (5.7%)
Undefined indication	1 (1.4%)

Abbreviations: Hb = hemoglobin; Hct = hematocrit; MI = myocardial infarction

TABLE 4. Laboratory result before red blood cell transfusion in transfused patients of post-educational group (N = 70).

Laboratory	Mean ± SD
Serum lactate (mg/dL)	3.22 ± 2.58
ScvO2 (%)	67 ± 4.24
Base excess (mEq/L)	-5.12 ± 5.53

Abbreviation: $ScvO_2$ = central venous oxygen saturation

DISCUSSION

In this study, the implementation of a RBC transfusion guideline using the educational program can reduce the RBC transfusion rate and decrease the hemoglobin threshold for RBC transfusion. In addition the clinical outcomes regarding the complication (ARDS, AKI) and the mortality rate were improved after the educational program. Previous study had reported the high incidence of RBC transfusion up to 83 % in general surgical ICU, Siriraj hospital.[7] The rate of transfusion is considerably high in critically ill surgical patients who have been on mechanical ventilation longer than 48 hours.[7] Therefore, the implementation of a strategy that can reduce the number of transfusions should be considered. As a result, this study regarding the implementation of the RBC transfusion guideline was performed with the aim to decrease the rate of RBC transfusion. The educational program was a tool selected to implement the guideline in this study. Previous study demonstrated that an educational program coupled with the institution policy for RBC transfusion could reduce the total RBC units transfused.[17] In this study, we found that after the implementation of the RBC transfusion guideline, the rate of RBC transfusion was significantly decreased from nearly 50 % to 37 % which was comparable to other regions.[15] In addition, the Hb threshold for RBC transfusion was significantly decreased from 9 to 8 g/dL.

Interestingly, the primary and secondary outcomes were improved, and even the adherence rate to the transfusion guideline was less than 50%. Several issues were concerned including 1) physician might accept the transfusion trigger of Hb around 8-9 g/dL even though evidences from previous randomized controlled trials[8,11,14] have addressed the safety of restrictive transfusion. A survey of physician's attitudes to transfusion practice in critically ill patients in the United Kingdom[18] reported that there was significant variation in transfusion threshold among physicians. It depended on the scenario and the severity of patients. The majority of respondents selected a baseline Hb threshold between 9 and 10 g/dL. In addition, previous studies from different locations reported the average pre-transfusion Hb at 8.5 g/dL.[15] 2) the educational program regarding the transfusion guideline might not be frequently provided or reminded. Previous literatures showed that the implementation of education program has significantly decreased RBC transfusion, increased transfusion safety and helped to prevent the occurrence of transfusion-related adverse effects.[17,19,20] However, only the educational program might not be adequate to improve the outcomes. The combination of the educational program and the support from medical board in terms of integration of the guideline recommendation into RBC transfusion order including the guideline recommendation can result in the better adherence rate and outcomes[17] 3) the plastic surgeon required maintaining the hematocrit level at least 30 % in the operations which involved flap procedures, and 5 out of 37 patients (14 %) of non-adherence were in this category. The researcher did not argue against this concept, although there were studies which reported that transfusion trigger of hematocrit < 25 % can decrease blood transfusion rates without increasing rates of flap-related complications.[21]; and 4) half of the patients in non-adherence group had sepsis, and the recent sepsis guideline implemented by Siriraj hospital recommended the Hb threshold for RBC transfusion at 10 g/dL.[22] However, this recommendation was based on the protocol of "early goal-directed therapy (EGDT)"[23] in sepsis patients that targeted an increase in mixed venous oxygen saturation to ≥ 70%. This was achieved by the administration of fluid resuscitation, then RBC transfusion to keep a hematocrit ≥ 30 % and then administering inotropes (dobutamine). The EGDT group received more fluid and RBC transfusion in the first 6 hours. The EGDT group demonstrated the improvement in survival, although it was not possible to separate the impact of only RBC transfusion strategy on outcome. Moreover, the recent multicenter RCT[11], which compared restrictive and liberal RBC transfusion in patients with

septic shock, did not demonstrate significant difference in terms of mortality between the two groups. Finally, the recent edition of Sepsis ad septic shock guidelines was published in 2016. It recommended to reserve RBC transfusion for patients with a Hb level less than 7 g/dl.[24] Moreover, the updated clinical practice guidelines from the American Association of Blood Banks (AABB) recommended that RBC transfusion is not indicated until the Hb level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients rather than when the Hb is 10 g/dL.[12]

Although the adherence rate was not high, the RBC transfusion rate significantly decreased after the implementation of the guideline. It might not be the guidelines itself that improved the outcomes, but the advancement in knowledge regarding the adverse effects of blood transfusion or the new recommendation from clinical practice guidelines might be accountable. Nevertheless, some limitation should be addressed. Twelve patients (6%) were excluded from the post-educational group which might alter the adherence rate and outcomes. The different in duration of data collection between pre and post-educational program should be concerned. The data of pre-educational group was collected in 2011 whereas the post-educational information was prospectively collected during 2014. The difference in time frame might result in the variety of treatment modalities especially the RBC transfusion. The lower incidence of RBC transfusion and the improvement in mortality rate may result from the better knowledge from recent publications rather than the implementation of the guideline. The frequency and efficacy of educational program as mentioned earlier might be insufficient to change attitude of transfusion. Other limitation should be addressed including there was no information regarding detail of transfusion in pre-educational group especially the indication of RBC transfusion which might help to interpret the high transfusion rate. In addition the information regarding the RBC transfusion in the operating theaters was not available in both groups, although the hemoglobin at SICUs admission was not significantly different between pre and post educational groups.

In conclusion, the implementation of educational program regarding RBC transfusion guideline can decrease the RBC transfusion rate.

What is already known on this topic?

Although RBC transfusion is an independent predictor of death, nosocomial infection, multi-organ dysfunction syndrome (MODS) and acute respiratory distress syndrome (ARDS) in critically ill patients, the majority of the patients admitted to intensive care unit (ICU) still received RBC transfusion. A pre-transfusion hemoglobin (Hb) was reported around 8.5 g/dl.

What does this study adds?

The implementation of educational program regarding RBC transfusion guideline can reduce RBC transfusion rate, complications and the mortality rates. The Hb threshold for RBC transfusion was significantly decreased from 9 g/dL in the pre-educational group to 8 g/dL in the post-educational group.

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