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# Red blood cell transfusion for critically ill patients admitted through the emergency department in South Korea

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**Background:** Red blood cells (RBCs) are a limited resource, and the adverse effects of transfusion must be considered. Multiple randomized controlled trials on transfusion thresholds have been conducted, leading to the establishment of a restrictive transfusion strategy. This study aimed to investigate the status of RBC transfusions in critically ill patients.

**Methods:** This cohort study was conducted at five university hospitals in South Korea. From December 18, 2022, to November 30, 2023, 307 nontraumatic, anemic patients admitted to intensive care units through the emergency departments were enrolled. We determined whether patients received RBC transfusion, transfusion triggers, and the clinical results.

**Results:** Of the 154 patients who received RBC transfusions, 71 (46.1%) had a hemoglobin level of 7 or higher. Triggers other than hemoglobin level included increased lactate levels in 75 patients (48.7%), tachycardia in 47 patients (30.5%), and hypotension in 46 patients (29.9%). The 28-day mortality rate was not significantly reduced in the group that received transfusions compared to the non-transfusion group (21.4% vs. 26.8%, P=0.288). There was no difference in the intensive care unit and hospital length of stay or the proportion of survival to discharge between the two groups. The prognosis showed the same pattern in various subgroups.

**Conclusions:** Despite the large number of RBC transfusions used in contradiction to the restrictive strategy, there was no notable difference in the prognosis of critically ill patients. To minimize unnecessary RBC transfusions, the promotion of transfusion guidelines and research on transfusion criteria that reflect individual patient conditions are required.

Key Words: critical illness; emergency department; erythrocyte transfusion; intensive care unit

# INTRODUCTION

Red blood cell (RBC) transfusion is an important treatment strategy for improving tissue oxygenation and perfusion. However, blood transfusions can cause adverse effects including transfusion-associated circulatory overload or transfusion-related immunomodulation [1,2].

# **Original Article**

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Additionally, blood is a limited medical resource requiring appropriate transfusion [3]. In clinical practice, many patients receive unnecessary blood transfusions [4,5].

Recent guidelines recommend a restrictive transfusion strategy with a low hemoglobin (Hb) level of 7 g/dl as the RBC threshold in critically ill patients [6-8]. These guidelines also suggest that Hb thresholds, clinical judgment, and other physiological parameters should be considered. However, evidence for the physiological criteria for RBC transfusion is not clear; therefore, it is performed according to the subjective judgment of the clinicians. According to a survey published in the Korean Journal of Blood Transfusion in 2016, most RBC transfusion decisions in Korea are based on clinical judgment rather than the Hb threshold [9]. In a review article published in 2023, the RBC transfusion rate in Korea was higher than that in other countries and continues to increase [10]. A recent international prospective cohort study of 3,643 critically ill patients reported that pre-transfusion Hb levels varied widely from 5.2 g/dl to 13.1 g/dl [11]. However, studies reporting on RBC transfusion practices and triggers in critically ill patients are rare.

This multicenter cohort study investigated the practice of RBC transfusions in critically ill patients admitted to intensive care units (ICUs) through emergency departments (EDs) in Korea. This study aimed to identify the current status of RBC transfusions, triggers for transfusions, and differences in prognosis depending on whether RBC transfusions were administered. Our hypothesis is that, even in clinical situations where there is no clear evidence that RBC transfusions improve outcomes, they are still being administered to critically ill patients.

#### MATERIALS AND METHODS

This research study was conducted with approval from the Institutional Review Boards of each of the five hospitals in a metropolitan area of South Korea (No. HYUH 2022-08-013-001, GURI 2022-09-008-003, SCHUH 2022-08-005-001, HKS 2022-08-002-001, 2208-016-519). Written informed consent was obtained from all patients.

# **Study Setting and Population**

This cohort study focused on patients admitted to the ICU after visiting the EDs of five university hospitals in a metropolitan area of South Korea. Among these, patients aged  $\geq 18$  years, without trauma, and with Hb  $\leq 10$  g/dl were included in the cohort. Liberal transfusion strategies involve administering blood transfusions when the Hb level is below 9–10 g/dl, whereas

#### **KEY MESSAGES**

- Transfusions that do not follow a restrictive transfusion strategy are frequently observed.
- Triggers other than hemoglobin levels are associated with red blood cells (RBCs) transfusions.
- RBC transfusions that do not follow a restrictive transfusion strategy does not improve prognosis in critically ill patients.

restrictive transfusion strategies involve transfusing when the Hb level is below 7–8 g/dl. We hypothesized that transfusion thresholds may differ among clinicians in real-world practice. Accordingly, we designed our cohort to include patients with an Hb level of  $10\,\text{g/dl}$  or less to examine the variability in transfusion criteria.

Patients with diseases requiring surgery, with do-not-resuscitate orders, or who received massive blood transfusions were excluded from the study. The criteria for massive transfusion are defined as receiving more than 10 units of RBC within 24 hours or more than 6 units within 6 hours. Therefore, this study includes non-massively bleeding and non-bleeding critically ill patients. Among the 312 patients enrolled between December 18, 2022, and November 30, 2023, 307 patients were

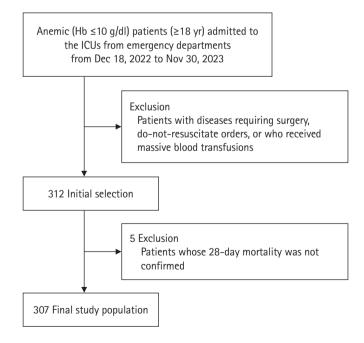


Figure 1. Study flowchart. Hb: hemoglobin; ICU: intensive care unit.



included as study subjects, excluding five patients whose 28-day mortality was not confirmed (Figure 1). In this cohort, there were no predetermined criteria for transfusion, and transfusion decisions were made by clinicians.

#### **Data Collection and Variables**

We confirmed whether the patient received an RBC transfusion in the EDs or ICUs within 24 hours of visiting the EDs. Age, sex, body mass index, vital signs, and comorbidities were identified as baseline characteristics. Acute Physiology and Chronic Health Evaluation (APACHE) II scores and Sequential Organ Failure Assessment (SOFA) scores were confirmed as indicators of patient severity. We identified sepsis, gastrointestinal (GI) bleeding, out-of-hospital cardiac arrest, in-hospital cardiac arrest, and receipt of ventilator care or continuous renal replacement therapy as the representative reasons for ICU admission.

The proportion of patients with Hb levels of <7 g/dl corresponding to restrictive transfusion was identified. Conversely, we confirmed the proportion of patients who received blood transfusions despite their Hb being  $\geq 7$ . This study did not directly ask clinicians why they decided to administer transfusions. However, this was indirectly confirmed by the proportion of patients who met the previously known triggers for RBC transfusion: low Hb level, increased lactate level, tachycardia, and hypotension.

The primary outcome variable for the patients' clinical course was set as the 28-day mortality rate. In addition, the duration of ICU and hospital admissions, and the proportions of patients with survival discharge were also identified. We aimed to confirm the hypothesis that these outcomes would not show significant differences based on whether RBC transfusions were administered. Study outcomes were confirmed in subgroups based on Hb level 7 g/dl. Furthermore, considering that outcomes for critically ill patients may vary depending on the conditions precipitating their admission, we evaluated these outcomes across various subgroups. These subgroups included patients with GI bleeding, sepsis, those on mechanical ventilation, and those undergoing continuous renal replacement therapy.

#### **Statistical Analyses**

Continuous variables were tested for normality using the Shapiro-Wilk test and none showed normal distribution. Therefore, continuous variables are expressed as median (interquartile range [IQR]). Categorical variables are expressed

as numbers (%). The two groups were compared using the Mann-Whitney U-test for continuous variables and Fisher's exact test for categorical variables. Statistical significance was determined using two-sided tests with a P-value  $\leq 0.05$ . All analyses were conducted using R software (version 4.2.0) with the R Studio interface.

# **RESULTS**

#### **Characteristics of the Study Population**

A total of 307 patients were identified from five university hospitals in South Korea from December 18, 2022, to November 30, 2023 (Figure 1). Table 1 shows the baseline characteristics of the study population. Of 307 patients, 154 (50.2%) received one or more RBC transfusions in the first 24 hours. The median age was 68 years (IQR, 57-80 years) in the transfusion group and 76 years (IQR, 68-83 years) in the non-transfusion group. The proportion of men in the group that received and did not receive blood transfusions was 53.9% and 45.1%, respectively. Vital signs, APACHE II, and SOFA scores, which indicate initial clinical severity, were not significantly different between the two groups. The proportion of patients with chronic liver disease was higher in the transfusion group than that of the non-transfusion group (20.8% vs. 9.2%, P=0.006). The most common reason for ICU admission were sepsis (n=55, 35.9%) in the non-transfusion group and GI bleeding (n=68, 44.2%) in the transfusion group.

We identified the lowest Hb levels among patients in the ED. The median Hb level in the transfusion group was 6.8 g/dl (IQR, 5.5-8.0 g/dl), which was significantly lower than the non-transfused group, with a median Hb of 9.2 g/dl (IQR, 8.4-9.5 g/dl). Among patients who received transfusions, the proportion of patients with Hb levels <7 g/dl was 53.9%, which was significantly higher than that of non-transfusion patients (5.9%) (Table 1). Conversely, 71 patients (46.1%) received RBC transfusion despite Hb ≥7 g/dl based on criteria that did not follow the restrictive transfusion threshold (Figure 2). Patients who received transfusions received a median of 2 units (1-4) of RBCs in the first 24 hours. Of the 154 patients who received RBC transfusion in the first 24 hours, 55 (35.7%) did not undergo Hb testing after one unit of RBC transfusion. The median Hb value after receiving one unit of RBC was 7.4 g/dl (IQR, 6.6-8.8 g/dl; n=99 patients).

#### **Presumed Triggers for RBC Transfusion**

Table 2 shows the presumed triggers for RBC transfusion.



**Table 1.** Baseline characteristics of study population

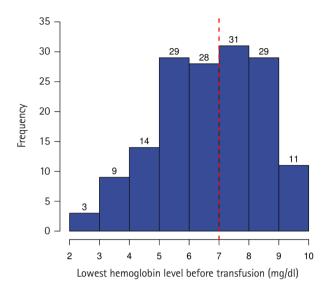
Variable	No transfusion (n=153)	Transfusion (n=154)	P-value
Age (yr)	76 (68–83)	68 (57–80)	<0.001
- bex			0.138
Male	69 (45.1)	83 (53.9)	
Female	84 (54.9)	71 (46.1)	
BMI (kg/m²)	21.5 (18.4–24.1)	21.6 (19.1–24.9)	0.343
Systolic BP (mm Hg)	112.0 (93.0–144.0)	111.0 (92.5–137.0)	0.789
Diastolic BP (mm Hg)	63.0 (50.0–78.0)	62.0 (51.0-78.0)	0.853
Heart rate (beats/min)	93.0 (76.0–110.0)	98.0 (82.0-110.0)	0.377
Respiratory rate (breaths/min)	18.0 (16.0–22.0)	20.0 (18.0–22.0)	0.238
5pO <sub>2</sub> (%)	97.0 (95.0–99.0)	98.0 (94.0-99.0)	0.487
Body temperature (°C)	36.7 (36.1–37.3)	36.5 (36.0-37.3)	0.185
Mental			0.189
Alert	100 (66.7)	117 (76.0)	
Verbal	13 (8.5)	14 (9.1)	
Pain	27 (17.6)	17 (11.0)	
Unresponsive	11 (7.2)	6 (3.9)	
APACHE II score	19.0 (15.0–24.0)	19.0 (14.0–24.0)	0.777
SOFA score	6.0 (4.0-9.0)	6.0 (3.0-8.0)	0.177
Comorbidity			
Hypertension	96 (63.4)	75 (48.7)	0.011
Diabetic mellitus	87 (56.9)	66 (42.9)	0.017
Myocardial infarction	13 (8.5)	8 (5.2)	0.268
Heart failure	19 (12.4)	12 (7.8)	0.191
Cerebrovascular disease	21 (13.7)	21 (13.6)	1.000
Chronic lung disease	10 (6.5)	5 (3.2)	0.198
Chronic liver disease	14 (9.2)	32 (20.8)	0.006
Chronic kidney disease	39 (25.5)	27 (17.5)	0.097
Solid tumor	18 (11.8)	21 (13.6)	0.732
Chronic anemia	15 (9.8)	20 (13.0)	0.473
Reason for ICU admission			
Sepsis	55 (35.9)	31 (20.1)	0.003
Ventilator care	29 (19.0)	24 (15.6)	0.529
GI bleeding	5 (3.3)	68 (44.2)	< 0.001
OHCA	9 (5.9)	4 (2.6)	0.252
IHCA	2 (1.3)	2 (1.3)	1.000
CRRT	28 (18.3)	26 (16.9)	0.860
reatment in ED			
Vasopressors	64 (41.8)	53 (34.4)	0.197
High flow nasal cannula	20 (13.1)	14 (9.1)	0.281
Noninvasive ventilation	1 (0.7)	1 (0.7)	1.000
aboratory value	. ,	. ,	
Hb (g/dl)	9.2 (8.4–9.5)	6.8 (5.5–8.0)	<0.001
Hb <7 g/dl	9 (5.9)	83 (53.9)	<0.001
Hematocrit (%)	28.4 (26.7–30.0)	21.6 (17.4–24.9)	<0.001

Values are presented as median (interquartile range) or number (%).

BMI: body mass index; BP: blood pressure; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit; GI: gastrointestinal; OHCA: out of hospital cardiac arrest; IHCA: in hospital cardiac arrest; CRRT: continuous renal replacement therapy; ED: emergent department; Hb: hemoglobin.



Among patients who received RBC transfusions, the proportion of patients with Hb  $\geq$ 7 g/dl was 55.8% (48/86) in patients with non-GI bleeding, which was higher than the 33.8% (23/68) in patients with GI bleeding. In particular, 64.5% of



**Figure 2.** The lowest hemoglobin level before red blood cell transfusion in patients undergoing transfusion during the first 24 hours after emergency department visit (n=154).

sepsis patients who received RBC transfusions had Hb  $\geq$ 7 g/dl and did not follow the restrictive transfusion threshold. The leading trigger for initiating RBC transfusion was Hb <7 g/dl (53.9%), followed by lactate  $\geq$ 2 mmol/L (48.7%). Among patients who received RBC transfusion, the proportion with lactate  $\geq$ 2 mmol/L was 66.7%, 55.9%, and 51.6% in patients with mechanical ventilation, GI bleeding, and sepsis, respectively. Triggers other than Hb and lactate level included tachycardia in 47 patients (30.5%) and hypotension in 46 patients (29.9%). In patients with Hb  $\geq$ 7 g/dl, the proportions of those with lactate  $\geq$  4 mmol/L, tachycardia, and hypotension were 25.4%, 28.2%, and 23.9%, respectively. Additionally, in patients with Hb <7 g/dl, the proportions of those exhibiting these conditions were higher, at 32.5%, 32.5%, and 34.9%, respectively.

# **Prognosis**

The 28-day mortality rate was 26.8% (41/153) and 21.4% (33/154) in the non-transfusion and transfusion groups, respectively, with no significant difference between the two groups (P=0.288) (Table 3). Additionally, no significant differences were found between the two groups in the length of ICU stay (6.0 vs. 5.0 days, P=0.404) and the length of hospital stay (13.0 vs. 11.0 days, P=0.367). The proportion of patients discharged alive from the hospital was 74.5% and 77.3%

**Table 2.** Presumed triggers for RBC transfusion

Variable	Hb <7 g/dl	Lactate ≥2 mmol/L	Lactate ≥4 mmol/L	Tachycardia	Hypotension
All patients (n=154)	83 (53.9)	75 (48.7)	45 (29.2)	47 (30.5)	46 (29.9)
Hb $< 7 \text{ g/dl (n=83)}$	-	44 (53.0)	27 (32.5)	27 (32.5)	29 (34.9)
Hb ≥7 g/dl (n=71)	-	31 (43.7)	18 (25.4)	20 (28.2)	17 (23.9)
GI bleeding (n=68)	45 (66.2)	38 (55.9)	25 (36.8)	25 (36.8)	21 (30.9)
Non-GI bleeding (n=86)	38 (44.2)	37 (43.0)	20 (23.3)	22 (25.6)	25 (29.1)
Sepsis (n=31)	11 (35.5)	16 (51.6)	9 (29.0)	9 (29.0)	14 (45.2)
Mechanical ventilator (n=24)	10 (41.7)	16 (66.7)	12 (50.0)	11 (45.8)	11 (45.8)
CRRT (n=26)	12 (46.2)	10 (38.5)	7 (26.9)	4 (15.4)	2 (7.7)

Values are presented as number (%).

RBC: red blood cell; Hb: hemoglobin; Gl: gastrointestinal; CRRT: continuous renal replacement therapy.

**Table 3.** Outcomes in transfusion and non-transfusion groups

Variable	Non-transfusion (n=153)	Transfusion (n=154)	P-value
28-Day mortality	41 (26.8)	33 (21.4)	0.288
Duration of ICU admission (day)	6.0 (4.0-12.0)	5.0 (3.0-11.0)	0.404
Duration of hospital admission (day)	13.0 (8.0–20.0)	11.0 (7.0–21.0)	0.367
Survival discharge	114 (74.5)	119 (77.3)	0.596

Values are presented as number (%) or median (interquartile range).

ICU: intensive care unit.



Table 4. Subgroup analysis of study outcomes in transfusion and non-transfusion groups

Variable	No transfusion (n=153)	Transfusion (n=154)	P-value
Hb <7 g/dl	n=9	n=83	
28-Day mortality	1 (11.1)	13 (15.7)	1.000
Duration of ICU admission (day)	6.0 (3.0–16.0)	5.0 (3.0–10.5)	0.711
Duration of hospital admission (day)	16.0 (9.0–22.0)	12.0 (6.0–21.5)	0.473
Survival discharge	8 (88.9)	69 (83.1)	1.000
Hb ≥7 g/dl	n=144	n=71	
28-Day mortality	40 (27.8)	20 (28.2)	1.000
Duration of ICU admission (day)	6.0 (4.0-12.0)	6.0 (3.0-11.0)	0.539
Duration of hospital admission (day)	13.0 (7.0–20.0)	11.0 (7.0–20.5)	0.414
Survival discharge	106 (73.6)	50 (70.4)	0.629
GI bleeding	n=5	n=68	
28-Day mortality	2 (40.0)	7 (10.3)	0.112
Duration of ICU admission (day)	5.0 (4.0-12.0)	5.0 (3.0-7.5)	0.454
Duration of hospital admission (day)	12.0 (8.0–15.0)	9.0 (6.0-13.0)	0.405
Survival discharge	3 (60.0)	61 (89.7)	0.112
No GI bleeding	n=148	n=86	
28-Day mortality	39 (26.4)	26 (30.2)	0.547
Duration of ICU admission (day)	6.0 (3.5–12.0)	7.0 (3.0–13.0)	0.534
Duration of hospital admission (day)	13.0 (7.5–20.5)	15.5 (8.0–23.0)	0.343
Survival discharge	111 (75.0)	58 (67.4)	0.228
Sepsis	n=55	n=31	
28-Day mortality	17 (30.9)	11 (35.5)	0.811
Duration of ICU admission (day)	7.0 (4.0–13.5)	6.0 (4.0–12.0)	0.921
Duration of hospital admission (day)	14.0 (9.0–23.0)	16.0 (9.0–26.0)	0.871
Survival discharge	37 (67.3)	21 (67.7)	1.000
Mechanical ventilator	n=29	n=24	
28-Day mortality	13 (44.8)	13 (54.2)	0.586
Duration of ICU admission (day)	11.0 (4.0–16.0)	5.5 (3.0-11.0)	0.066
Duration of hospital admission (day)	15.0 (6.0–25.0)	9.5 (3.0-18.0)	0.060
Survival discharge	16 (55.2)	10 (41.7)	0.412
CRRT	n=28	n=26	
28-Day mortality	9 (32.1)	6 (23.1)	0.550
Duration of ICU admission (day)	5.0 (4.0–14.0)	9.5 (5.0–15.0)	0.366
Duration of hospital admission (day)	16.0 (8.5–21.5)	19.0 (12.0–26.0)	0.298
Survival discharge	19 (67.9)	19 (73.1)	0.770

Values are presented as number (%) or median (interquartile range).

Hb: hemoglobin; ICU: intensive care unit; GI: gastrointestinal; CRRT: continuous renal replacement therapy.

(P=0.596), respectively. These results were consistent regardless of whether the Hb level was above or below 7 mg/dl (Table 4). There was no significant difference in 28-day mortality, duration of ICU and hospital admission, and proportions of patients who survived to discharge according to RBC transfusion in both groups with and without GI bleeding (Table 4). The same pattern was observed in the subgroups of patients with sepsis, those who received mechanical ventilation or continu-

ous renal replacement therapy.

# **DISCUSSION**

For several decades, RBCs have been transfused to maintain Hb levels above 10 g/dl [12]. However, the 1999 Transfusion Requirements in Critical Care study showed that limited and liberal transfusion strategies were equally effective in critical-



ly ill patients [13]. Recent guidelines have recommended a restrictive transfusion strategy in critically ill patients. Several studies have been conducted on the optimal Hb target, and the number of RBC transfusions is decreasing worldwide [14]. However, it is reported that RBCs are still excessively transfused to critically ill patients. In an international multicenter study (International Point Prevalence Study of Intensive Care Unit Transfusion Practices [InPUT]) in 2023, RBC transfusions beyond the restrictive transfusion strategy were performed in 51.5% of the critically ill patients [11]. Korean studies have explored the RBC transfusion amounts based on disease or surgery, however, none have specifically addressed the practical status of RBC transfusion in critically ill patients [10,15,16]. In our study, 47.4% of critically ill emergency patients received RBC transfusions with Hb levels ≥7 g/dl. Approximately 50% of critically ill patients are still receiving RBC transfusions that are inadequate for their restrictive Hb levels. These results indicate that factors other than Hb level play a role in clinicians' decisions regarding RBC transfusion.

The purpose of RBC transfusion is to meet tissue oxygen demand. Hb levels are easy to measure and have a clear cut-off value. However, even with the same Hb level, a patient's RBC requirement can vary depending on the individual's conditions and tissue oxygen consumption [17]. Recent guidelines recommend the consideration of not only the Hb level but also other parameters, such as blood pressure, heart rate, electrocardiogram, oxygen partial pressure, central venous oxygen saturation, arteriovenous oxygen difference, lactate, and others [6,7]. The InPUT study identified tachycardia, hypotension, and elevated lactate levels as important triggering factors for RBC transfusion. In our study, approximately half of patients who underwent transfusions had exhibited elevated lactate levels. Until now, studies of non-Hb parameters as a determinant of transfusion have been limited [18-23]. The PASPORT (patient-specific cerebral oxygentation monitoring as part of an algorithm to reduce transfusion) trial included 204 heart surgery patients who underwent transfusions using the existing restrictive transfusion strategy and the patient-specific near-infrared spectroscopy (NIRS) strategy and compared cognitive function 3 months after surgery. The results of this study do not support the use of the NIRS-based algorithm [23]. Additional research is needed to determine whether outcomes differ based on physiological transfusion criteria other than Hb, which were observed at a high proportion in our study.

Many randomized controlled trials have reported that the restrictive transfusion strategy showed no difference in clinical outcomes compared to the liberal strategy in critically ill patients [24-27]. However, the restrictive transfusion group underwent significantly fewer RBC transfusions. In 2021, a systematic review of 48 studies and 21,433 people analyzed the 30-day mortality and adverse events of restrictive transfusion compared to liberal transfusion [28]. According to the Cochrane review, the restrictive transfusion strategy reduced the RBC transfusion rate by 41%. Our study did not compare restrictive and liberal transfusion strategies. However, there was no significant difference in the prognosis between the transfusion and the non-transfusion groups in the various subgroups. Future research is needed to investigate the impact of Hb thresholds lower than Hb <7 g/dl, such as Hb <6 g/dl or Hb <5 g/dl, on outcomes in critically ill patients.

RBC transfusion can improve tissue oxygenation but may cause adverse effects such as transfusion-related acute lung injury, transfusion-associated circulatory overload, and immune-modulating effects resulting in nosocomial infections [29]. Additionally, in an aging society where blood product shortages are expected, Korea needs to discuss appropriate RBC transfusions. The 2018 Frankfurt Conference emphasized the significance of patient blood management in reducing unnecessary blood transfusions [30]. In 2020, the Health Insurance Review and Assessment Service in Korea evaluated the adequacy of blood transfusion for total knee replacement. The blood transfusion rate was lowered from 62.1% to 41.0% just by conducting the evaluation. ICUs are also frequent settings for blood transfusions, underscoring the importance of initiatives aimed at minimizing unnecessary blood transfusions in critically ill patients.

This study had several limitations. First, this was a multicenter study conducted in five academic hospitals in the capital region. Therefore, the characteristics of the patient group in this study may differ from those in regional or non-academic hospitals. However, given the nature of the Korean medical system, most critically ill patients are transferred to academic hospitals, therefore, there may not be a significant difference in the characteristics of these patients compared to those in general critical care. Second, we did not directly ask clinicians about the specific factors that influenced their decision to administer transfusions. Instead, we used an indirect approach by analyzing blood test results and vital signs to infer the possible triggers for RBC transfusions. The physiological transfusion criteria we identified only represent the proportions of patients presenting these conditions. We could not precisely determine how frequently these criteria were actually used by clinicians



as transfusion triggers. Nevertheless, our indirect analysis aims to hypothesize whether factors beyond Hb levels might have influenced transfusion decisions. Third, our study has limited statistical power due to insufficient sample sizes within subgroups. Specifically, the GI bleeding subgroup consisted mostly of transfused individuals (n=68), while the non-transfused group was relatively small (n=5). This disparity complicates outcome comparisons and constrains the strength of our conclusions. Nevertheless, our study aimed to demonstrate that despite transfusions being administered more frequently than restrictive Hb thresholds suggest, transfused patients did not show a clear improvement in outcomes.

In conclusion, despite the common use of RBC transfusions in critically ill patients contrary to guideline recommendations, they do not significantly improve outcomes. In this multicenter study, 50.2% of the 307 ICU patients with Hb  $\leq$ 10 g/dl, admitted through the ED, received RBC transfusions. Among the 154 patients who received transfusions, 46.1% had Hb levels  $\geq$ 7 g/dl, exceeding the restrictive threshold. This practice was notably prevalent among patients with non-GI bleeding such as sepsis. Regardless of the patient subgroups, the 28-day mortality did not differ with or without RBC transfusion. Further research on transfusion thresholds, along with institutional efforts to enforce them, is needed to prevent unnecessary transfusions.

## **CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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## **AUTHOR CONTRIBUTIONS**

Conceptualization: YC. Data curation: YC, HJC, JP, WK, CA. Formal analysis: TSK, YC, JYK. Funding acquisition: YC. Methodology: TSK, YC. Project administration: YC. Visualization: YC. Writing – original draft: TSK, YC, JYK. Writing – review & editing: YC, HJC, JP, WK, CA. All authors read and agreed to the published version of the manuscript.

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