

Incidence of Red Blood Cell Transfusion in Mechanically Ventilated Surgical Patients at Siriraj Hospital

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Background: Anemia is commonly encountered in surgical critically ill patients. The incidence of red blood cell (RBC) transfusion and transfusion trigger in this population has not been previously reported in a large tertiary care center in Thailand.

Objective: To describe the incidence of RBC transfusion and transfusion trigger and to determine the factors and outcomes associated with RBC transfusion.

Material and Method: Data of 288 adult surgical patients requiring mechanical ventilation for >24 hours was retrospectively reviewed. Patient characteristics, outcomes, and transfusion data were collected.

Results: The incidence of RBC transfusion was 83.0% (95% confidence interval (CI) 78.0-87.0%). The mean hemoglobin level before RBC transfusion was 8.7±1.2 g/dL. Patients who received RBC transfusion had significantly higher morbidity and mortality when compared with those who did not. Independent factors associated with RBC transfusion were low body weight, high Sequential Organ Failure Assessment (SOFA) score, and low hemoglobin level on admission (adjusted odds ratio 0.97, 1.19, and 0.60, respectively).

Conclusion: In critically ill adult surgical patients, the incidence of RBC transfusion and transfusion trigger remained within high threshold. Large randomized controlled studies are warranted to confirm potential benefit of RBC transfusion in surgical critically ill patients.

Keywords: Anemia, Blood transfusion, Critically ill, Surgical patients

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Anemia has been one of the most common problems encountered in critically ill patients^(1,2); accounted for 29% of patients admitted to intensive care unit (ICU)⁽³⁾; and also considered as a predictor of increased mortality in such patients^(4,5). It is resulted from multiple factors, such as acute blood loss, chronic disorders, inflammation, infection, nutrition, and metabolic disorders⁽⁶⁻⁸⁾. Anemia contributes to a decrease in global oxygen delivery and red blood cell (RBC) transfusion is considered as a rapid tool to correct oxygen debt caused by anemia. On the other hand, RBC transfusion has been found to be an independent predictor of death, nosocomial infection and increased risk of developing multi-organ dysfunction syndrome (MODS) and acute respiratory distress syndrome (ARDS)⁽⁹⁾. Despite of these, 30%

to 40% of patients admitted to ICU still received RBC transfusion^(3,5,10-12) and might be higher in patients with length of stay (LOS) in ICU for longer than seven days⁽³⁾ or in surgical critically ill patients^(3,5). In addition, "low hemoglobin (Hb)" was accounted for 90% of reasons for RBC transfusion⁽⁵⁾ despite of the mean Hb level prior to transfusion was 8.2 to 8.6 g/dL^(3,5,11).

In Siriraj Hospital, which is one of the largest tertiary medical centers in Thailand, there has been high volume of critically ill patients undergoing surgery admitted to surgical intensive care unit (SICU) annually. Regarding culture, demographic, and socioeconomic differences, the information about the incidence of RBC transfusion and transfusion trigger in this population has not been previously reported. The aims of this present study were (i) to determine the incidence of RBC transfusion as well as transfusion trigger and (ii) to identify factors and clinical outcomes associated with RBC transfusion in the adult surgical critically ill patients at Siriraj Hospital.

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Material and Method

The present study was approved by Siriraj Institutional Review Board (Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand) with the waiver of informed consent. Data from the previous prospective cohort study in adult surgical patients admitted to SICU at Siriraj Hospital were retrospectively reviewed (“Incidence and Outcome of Acute Lung Injury in Surgical Intensive Care Unit Siriraj Hospital”). All surgical patients admitted to SICU with age of equal or more than 18 years and required mechanical ventilatory support for more than 24 hours were included in this study. Neurosurgical, cardiothoracic and trauma patients; patients who were terminal illness; patients who needed permanent ventilator assistance prior to SICU admission; or patients with documented active bleeding were excluded from this study. Demographic data, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, and Hb level at SICU admission were recorded. All included patients were classified into two groups according to whether they received RBC transfusion during their stay in SICU or not and named “transfusion” and “no transfusion group”, respectively. During the present study period, there was no implemented blood transfusion protocol in SICU. The decision of RBC administration was depended on patient’s conditions and physician’s discretion. Clinical outcome data including all adverse events in SICU, duration of mechanical ventilation, LOS in SICU and in hospital, as well as SICU, hospital and 28-day mortality were also recorded in both groups. In the transfusion group, transfusion data including date of the first RBC transfusion, Hb level before RBC transfusion, and the amount of transfused RBC unit during SICU stay were recorded.

The primary end point of the present study was to determine the incidence of RBC transfusion and the secondary end point was to describe the Hb levels before each RBC transfusion as a surrogate of transfusion trigger, factors associated with RBC transfusion, all adverse events, duration of mechanical ventilation, LOS in SICU and in hospital, as well as SICU, hospital and 28-day mortality. The sample size of 285 patients was based on the estimation of 75% incidence of RBC transfusion in this population from a one-month survey with a specification of 95% confidence interval (CI) of true incidence and a margin of error of 0.05. Data analysis was performed using SPSS Statistics 17.0 software (IBM Corporation,

New York, United States). Categorical variables were presented as number with percentage and were compared between the transfusion and no transfusion group using Pearson’s Chi-square or Fisher’s exact test when appropriated. Continuous variables were presented as mean with standard deviation (SD) or median with interquartile range (IQR) and were compared between groups using unpaired t-test or Mann-Whitney U test when appropriated. Variables from the univariate analysis were further analyzed with multiple logistic regression analysis to identified independent variables associated with RBC transfusion in SICU and were presented as adjusted odds ratios (OR) with 95% CI. A p-value of less than 0.05 was considered statistically significant.

Results

Between June 2010 and September 2011, 305 patients were included in the present study. Of these, 16 patients were excluded due to documented active bleeding, leaving 288 patients for analysis. Two hundred and thirty nine (83.0%; 95% CI 78.0-87.0%) patients were transfused at least one unit of RBC during their stay in SICU. Patients who received RBC transfusion, when compared with those who did not had significantly lower weight (59.1 ± 13.0 versus 64.3 ± 16.8 kg; $p = 0.015$), higher APACHE II score (17.9 ± 6.4 versus 14.4 ± 4.0 ; $p < 0.001$), higher SOFA score (7.2 ± 3.4 versus 5.6 ± 2.9 ; $p = 0.001$), and lower Hb level at SICU admission (10.05 ± 1.88 versus

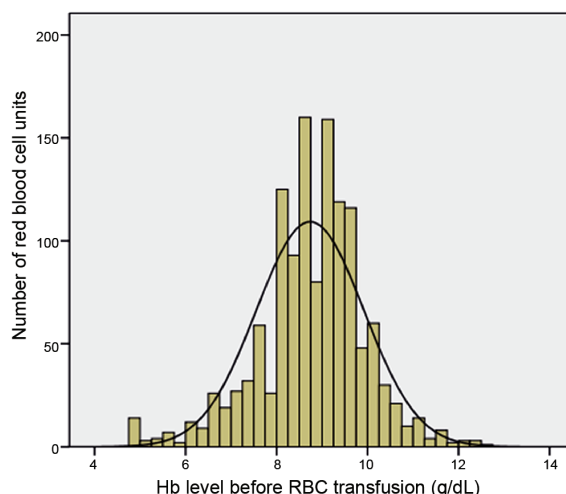


Fig. 1 represented the distribution of pre-transfusion Hb levels of the total 1,296 RBC units that were transfused in 239 patients in the transfusion group. The overall mean value was 8.7 ± 1.2 g/dL.

11.88±1.66 g/dL; p<0.001) (Table 1). The overall mean Hb level before RBC transfusion was 8.7±1.2 g/dL (Fig. 1). Patients in the transfusion group received the first RBC transfusion on average 1.4±2.9 days after SICU admission and were transfused average 4.6±4.4 units during their stay in SICU. The independent variables associated with RBC transfusion in SICU were low body weight (adjusted OR 0.97, 95% CI

0.95 to 0.99, p = 0.010), high SOFA score (adjusted OR 1.19, 95% CI 1.03 to 1.37, p = 0.020) and low Hb level at SICU admission (adjusted OR 0.60, 95% CI 0.49 to 0.73, p<0.001) (Table 2).

Patients who received RBC transfusion had significantly higher rate of all adverse events, especially the rate of pneumonia and acute kidney injury (AKI) required renal replacement therapy (RRT), than those

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

	All (n = 288)	No transfusion group (n = 49)	Transfusion group (n = 239)	p-value
Age (year)	65.7±16.4	61.8±19.7	66.5±15.6	0.070
Body weight (kg)	59.9±13.8	64.3±16.8	59.1±13.0	0.015
Height (cm)	160.1±7.9	161.0±9.8	159.9±7.5	0.378
BMI (kg/m ²)	23.3±4.8	24.8±5.8	23.0±4.5	0.054
Sex (male)	152 (52.8%)	29 (59.18%)	123 (51.46%)	0.324
Underlying disease				
Hypertension	174 (60.4%)	32 (65.31%)	142 (59.41%)	0.442
Coronary artery disease	35 (12.2%)	6 (12.24%)	29 (12.13%)	0.983
Pulmonary disease	35 (12.2%)	6 (12.24%)	29 (12.13%)	0.983
Stroke or TIA	20 (6.9%)	4 (8.20%)	16 (6.70%)	0.757
History of anemia	72 (25.0%)	7 (14.29%)	65 (27.20%)	0.057
Diabetes mellitus	93 (32.3%)	14 (28.57%)	79 (33.05%)	0.541
CRF or ESRD	52 (18.1%)	7 (14.30%)	45 (18.80%)	0.451
Type of SICU admission				
No surgery	103 (35.8%)	15 (30.60%)	88 (36.80%)	0.409
After elective surgery	64 (22.2%)	10 (20.40%)	54 (22.60%)	0.737
After emergency surgery	121 (42.0%)	24 (49.00%)	97 (40.60%)	0.278
ASA of equal or more than 3	138/185 (74.6%)	24/34 (70.6%)	114/151 (75.5%)	0.640
Anesthetic time (min)	235 (145, 408)	192.5 (114, 341)	260 (150, 420)	0.095
Surgical time (min)	170 (100, 333)	150 (84, 283)	185 (100, 350)	0.167
Estimated blood loss (ml)	400 (100, 1,100)	300 (100, 600)	499 (100, 1,200)	0.207
APACHE II score at admission	17.3±6.2	14.4±4.0	17.9±6.4	<0.001
SOFA score at admission	6.7±3.4	5.6±2.9	7.24±3.4	0.001
Hb level at admission (g/dL)	10.4±2.0	11.9±1.7	10.1±1.9	<0.001

Data were presented as mean ± standard deviation or median (interquartile range)

APACHE II = Acute Physiology and Chronic Health Evaluation II score; ASA = American Society of Anesthesiology Physical Status; BMI = body mass index; CI = confidence interval; CRF = chronic renal failure; ESRD = end-stage renal disease; Hb = hemoglobin; OR = odds ratio; SOFA = Sequential Organ Failure Assessment; TIA = transient ischemic attack; SICU = surgical intensive care unit

Table 2. Factors associated with transfusion in surgical intensive care unit

	Adjusted OR	95% CI	p-value
Body weight (kg)	0.97	0.95-0.99	0.010
SOFA score at SICU admission	1.19	1.03-1.37	0.020
Hb level on admission (g/dL)	0.60	0.49-0.73	<0.001

CI = confidence interval; Hb = hemoglobin; OR = odds ratio; SOFA = Sequential Organ Failure Assessment

Table 3. Clinical outcomes after admission to surgical intensive care unit

	All (n = 288)	No transfusion group (n = 49)	Transfusion group (n = 239)	p-value
Adverse events				
All	128 (44.4%)	14 (28.6%)	114 (47.7%)	0.014
CNS	23 (8.0%)	6 (12.2%)	17 (7.1%)	0.247
CVS	7 (2.4%)	0 (0.0%)	7 (2.9%)	0.607
ALI/ARDS	25 (8.7%)	4 (8.2%)	21 (8.8%)	1.000
Pneumonia	68 (23.6%)	4 (8.2%)	64 (26.8%)	0.005
AKI required RRT	32 (11.1%)	0 (0.0%)	32 (13.4%)	0.007
LOS in SICU	8 (4, 17)	5 (3, 7)	9 (5, 19)	<0.001
LOS in hospital	27 (15, 54)	18 (11, 28)	31 (17, 56)	<0.001
Duration of MV	6 (3, 15)	3 (2, 6)	7 (3, 18)	<0.001
Mortality				
Hospital	78 (27.1%)	6 (12.2%)	72 (34.8%)	0.032
SICU	55 (19.1%)	3 (6.1%)	52 (21.8%)	0.011
28-day	53/246 (18.4%)	6/40 (15.0%)	47/206 (22.8%)	0.271

Data were presented as number (%) or median (interquartile range)

AKI = acute kidney injury; ALI = acute lung injury; ARDS = acute respiratory distress syndrome; CNS = central nervous system; CVS = cardiovascular system; LOS = length of stay; MV = mechanical ventilation; RRT = renal replacement therapy

who did not receive transfusion (47.7% versus 28.6%; $p = 0.014$, 26.8% versus 8.2%; $p = 0.005$, and 13.4% versus 0.0%; $p = 0.007$, respectively) (Table 3). No significant difference in rate of acute lung injury (ALI)/ARDS between two groups (8.8% in transfusion group versus 8.2% in no transfusion group; $p = 1.000$). Although there was no significant difference, seven patients in transfusion group, but none in no transfusion group, had cardiovascular adverse events. Of these, three had congestive heart failure and four had myocardial ischemia/infarction. Duration of mechanical ventilator as well as LOS in SICU and in hospital were also significantly longer in transfusion group (median 7 versus 3 days, 9 versus 5 days, and 31 versus 18 days respectively; all $p < 0.001$). Hospital and SICU mortality were significantly higher in patients received transfusion (34.8% versus 12.2%; $p = 0.032$ and 21.8% versus 6.1%; $p = 0.011$, respectively). No significant difference in 28-day mortality between groups (22.8% in transfusion group versus 15.0% in no transfusion group; $p = 0.271$).

Discussion

The incidence of RBC transfusion in our study was 83.0%. This was much higher than those reported in the previous cohorts which were approximately 30% to 40%^(3,5,10-12). This might be, in part, resulted from the disparity in patient population. The majority of population in the previous studies were composed of mixed medical and surgical critically ill patients

whereas our study included only surgical critically ill patients. In the recent retrospective cohort study in 5,925 surgical ICU patients⁽¹¹⁾, they reported the overall incidence of RBC transfusion of 30.9%. However, only 54.8% of patients in the that study required mechanical ventilatory support on admission and the mean SOFA score on admission was lower than that in the present study (5.9 ± 3.9 versus 7.0 ± 3.4). In the present study, if all admitted patients were included, the incidence of RBC transfusion would be probably lower than this reported. The present study recruited only patients who required mechanical ventilatory support for greater 24 hours. This patient population was likely to represent truly surgical critically ill patients rather than those who admitted to SICU for simple postoperative monitoring.

In the present study, the overall mean Hb level before RBC transfusion of 8.7 ± 1.2 g/dL was comparable to the worldwide reported pre-transfusion Hb levels that ranged from 8.2 to 8.6 g/dL^(3,5,11). Nevertheless, it was higher than that was suggested in current clinical practice guidelines⁽¹³⁻¹⁵⁾. In the TRICC trial⁽¹⁶⁾, the authors suggested that, in critically ill patients, RBC transfusion should be considered when their Hb level fell below 7.0 g/dL. It was also recommended that in high-risk surgical patients, RBC transfusion should be administered only when they had symptoms of anemia or when their Hb level fell below 8.0 g/dL⁽¹⁷⁾. In addition, other physiologic parameters such as venous oxygen saturation or serum

lactate level rather than only Hb level alone should be used in conjunction with clinical signs and symptoms of anemia in order to determine the administration of RBC transfusion^(2,18). During this study period, there was no implemented protocol of blood transfusion in SICU. The decision of administration of RBC was based on patient's conditions and physician's discretion. The results from this study emphasized the importance of the development of blood transfusion guideline in SICU.

Low body weight was found to be an independent risk factor for RBC transfusion in SICU in the present study. It might be explained by the fact that low body weight generally indicated malnutrition that was associated with anemia^(19,20). In addition, patients with low body weight had less reserved volume and might result in poor tolerance to blood loss leading to a high tendency to receive RBC transfusion. Other two factors associated with RBC transfusion in SICU were high SOFA score and low Hb level at SICU admission that were similar to the results in other studies^(3,5,11). In one large observational cohort study in ICU patients⁽⁵⁾, the authors pointed out that patients with lower baseline Hb level had significantly higher SOFA score. This might imply the fact that the more the patients were sick, the more tendency they would have anemia and subsequently receive resuscitation with blood transfusion.

The present study demonstrated that patients who received RBC transfusion had significantly higher rate of all adverse events, especially pneumonia and AKI required HD. Moreover, duration of mechanical ventilation and LOS in SICU and in hospital as well as SICU and hospital mortality were also significantly longer and higher in this patient group. It had been demonstrated in several studies that RBC transfusion in critically ill patients was associated with an increased morbidity, including higher nosocomial infection^(5,9) and AKI⁽²¹⁾, longer duration of mechanical ventilator support and LOS in ICU and in hospital⁽⁵⁾. The association between mortality and RBC transfusion was inconclusive. Mortality rate was seemed to increase in most critically ill patients who received blood transfusion^(3,5). On the other hand, RBC transfusion had been shown to associate with a decreased mortality in some patient population, namely acute ill patients⁽¹⁰⁾, surgical patients⁽¹¹⁾ or patients with severe sepsis and septic shock⁽¹²⁾.

One of the postulated hypotheses of such detrimental association between RBC transfusion and morbidity and mortality was "transfusion-related

immunomodulation" (TRIM). This term was referred to the association between transfusion of allogenic blood products and immunosuppression in recipients that was mediated by allogenic white blood cell^(22,23). Nevertheless, the beneficial effects of the leukoreduced RBC transfusion on morbidity and mortality were not proven in the recent meta-analysis⁽²⁴⁾. In our institute, administration of leukoreduced RBC had not been routinely implemented and types of each transfused RBC units were not recorded in the present study making it was unable to draw any conclusion.

The other proposed hypothesis of adverse outcomes associated with RBC transfusion was the "storage lesion". It occurred during RBC units stored after donation resulting in functional and structural alteration of RBC⁽²⁵⁻²⁷⁾. In the recent meta-analysis⁽²⁸⁾, transfusion of older stored RBC was found to be associated with an increased mortality. Nevertheless, there was no consensus on cut-off duration that defined fresher versus older RBC⁽²⁷⁾ and the beneficial clinical outcomes regarding to transfusion of fresh RBC in critically ill patients still required further confirmation from large randomized, controlled studies^(29,30).

There were some limitations in the present study. Firstly, based on the retrospective study design, some confounding factors that probably affected the decision of RBC transfusion might not be included in the analysis. For instance, Hb level before each transfusion was recorded and was used as a surrogate of transfusion trigger. However, clinical condition of patients, namely sepsis versus non-sepsis as well as other parameters such as venous oxygen saturation or serum lactate level before each transfusion which could potentially influence on the decision of administration of RBC transfusion, were not recorded. In addition, as stated before, types of transfused RBC units were not recorded as well. The second limitation was the sample size that was not originally calculated for determining either the significant difference in clinical outcomes or the independent risk factors for RBC transfusion. Thirdly, the information regarding RBC transfusion in patients who did not require ventilator support and who were on mechanical ventilator for less than 24 hours were not obtained. The incidence and threshold of RBC transfusion might be different if these patients were included in the analysis. Nevertheless, this is the first study that demonstrated the incidence and threshold of RBC transfusion in surgical critically ill patients in our country.

Conclusion

The present study demonstrated that the incidence of RBC transfusion in adult surgical critically ill patients was as high as 83.0%. The mean Hb level before transfusion that might indirectly indicate the transfusion trigger was higher than that was suggested in the literatures. In addition, RBC transfusion was shown to be significantly associated with an increase in adverse events as well as mortality in this population. However, whether there was a true association between RBC transfusion and an increased adverse events or it was only a marker of severity, large randomized controlled studies had been warranted to confirm the benefits and consequences of RBC transfusions in surgical critically ill patients.

What is already known on this topic?

The incidence of red blood cell transfusion in critically ill patients reported in the previous studies was approximately 30% to 40%. This incidence might be higher in patients with longer stay in the intensive care unit or in some patient population such as surgical critically ill patients. The reported mean hemoglobin levels prior to red blood cell transfusion were between 8.2 and 8.6 g/dL, which were higher than that suggested in the literatures. In regards to culture, demographic, and socioeconomic differences, there has been very limited data of the incidence of RBC transfusion and transfusion trigger in Thai surgical critically ill patients.

What this study adds?

The present study firstly reported the incidence of red blood cell transfusion in adult Thai surgical critically ill patients. The transfusion trigger that might reflect our transfusion practice was also reported. The incidence of red blood cell transfusion and the transfusion trigger in this patient population remained within high threshold. In addition, the clinical outcomes of such patients who received red blood cell transfusion, in term of adverse events as well as mortality, were significantly worse than those who did not. This emphasizes physicians to consider the risks and benefits of red blood cell transfusion in this high-risk population.

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Potential conflicts of interest

None.

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อุบัติการณ์การให้เลือดในผู้ป่วยวิกฤตศัลยกรรมที่ต้องใช้เครื่องช่วยหายใจที่โรงพยาบาลศิริราช

อรรถนพ พิริยะแพทย์สม, อรุมา ชัยวัฒน์, เจษฎายุทธ สักดิ์อรุณชัย, วรพรรณ สุวันณะศรี, สวิตา คณาวิฑูรย์

ภูมิหลัง: ภาวะโลหิตจางเป็นปัญหาหนึ่งที่พบได้บ่อยในผู้ป่วยวิกฤต สำหรับโรงพยาบาลศิริราชเองข้อมูลเกี่ยวกับอุบัติการณ์และจุดกระตุ้นการให้เลือดในผู้ป่วยวิกฤตศัลยกรรมยังไม่เคยมีการรายงานมาก่อน

วัตถุประสงค์: เพื่อศึกษาอุบัติการณ์และจุดกระตุ้นการให้เลือดในผู้ป่วยวิกฤตศัลยกรรมที่ต้องใช้เครื่องช่วยหายใจนานกว่า 24 ชั่วโมง และเพื่อหาปัจจัยและผลลัพธ์ที่สัมพันธ์กับการให้เลือดในผู้ป่วยกลุ่มนี้

วัสดุและวิธีการ: การศึกษาแบบย้อนหลัง ข้อมูลผู้ป่วยจำนวน 288 ราย จากการศึกษาแบบไปข้างหน้าในผู้ป่วยที่เข้ารับการรักษาในหอผู้ป่วยวิกฤตศัลยกรรมและจำเป็นต้องใช้เครื่องช่วยหายใจนานกว่า 24 ชั่วโมง ลักษณะของผู้ป่วยข้อมูลการให้เลือด และข้อมูลทางคลินิกถูกเก็บรวบรวมในผู้ป่วยแต่ละราย

ผลการศึกษา: อุบัติการณ์การให้เลือดเท่ากับร้อยละ 83.0 (95% CI 78.0-87.0) โดยมีระดับความเข้มข้นของฮีโมโกลบินโดยเฉลี่ยก่อนได้รับเลือดเท่ากับ 8.7 ± 1.2 กรัมต่อเดซิลิตร กลุ่มผู้ป่วยที่ได้รับเลือดมีอัตราการเกิดภาวะแทรกซ้อนรวมถึงอัตราการเสียชีวิตที่สูงกว่ากลุ่มผู้ป่วยที่ไม่ได้รับการให้เลือดอย่างมีนัยสำคัญ ในการวิเคราะห์การถดถอยโลจิสติก ผู้ป่วยที่มีน้ำหนักตัวน้อย มีคะแนน SOFA ที่สูง และระดับความเข้มข้นของฮีโมโกลบินที่ต่ำเมื่อแรกรับในหอผู้ป่วยวิกฤตมีความสัมพันธ์อย่างมีนัยสำคัญกับการเพิ่มอุบัติการณ์การให้เลือด

สรุป: ผู้ป่วยวิกฤตศัลยกรรมมีอุบัติการณ์การให้เลือดและจุดกระตุ้นการให้เลือดที่สูง การได้รับเลือดนั้นเป็นผลให้เหตุการณ์ไม่พึงประสงค์เพิ่มขึ้นจริง หรือ เป็นเพียงตัวบ่งชี้ถึงความรุนแรงของการเจ็บป่วยนั้น ควรต้องมีการศึกษาควบคุมแบบสุ่มขนาดใหญ่เพื่อยืนยันการได้รับประโยชน์ที่อาจเกิดขึ้นจากการให้เลือดในผู้ป่วยดังกล่าว
