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Original Article

Prediction of massive transfusion in trauma patients in the surgical intensive care units (THAI-SICU study)

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ABSTRACT

Purpose: After damage control surgery, trauma patients are transferred to intensive care units to restore the physiology. During this period, massive transfusion might be required for ongoing bleeding and coagulopathy. This research aimed to identify predictors of massive blood transfusion in the surgical intensive care units (SICUs).

Methods: This is an analysis of the THAI-SICU study which was a prospective cohort that was done in the 9-university-based SICUs in Thailand. The study included only patients admitted due to trauma mechanisms. Massive transfusion was defined as received ≥10 units of packed red blood cells on the first day of admission. Patient characteristics and physiologic data were analyzed to identify the potential factors. A multivariable regression was then performed to identify the significant model.

Results: Three hundred and seventy patients were enrolled. Sixteen patients (5%) received massive transfusion in the SICUs. The factors that significantly predicted massive transfusion were an initial sequential organ failure assessment (SOFA) ≥9 (risk difference (RD) 0.13, 95% confidence interval (*CI*): 0.03–0.22, $p = 0.01$); intra-operative blood loss ≥ 4900 mL (RD 0.33, 95% *CI*: 0.04–0.62, $p = 0.02$) and intra-operative blood transfusion ≥ 10 units (RD 0.45, 95% *CI*: 0.06 to 0.84, $p = 0.02$). The probability to have massive transfusion was 0.976 in patients who had these 3 factors.

Conclusion: Massive blood transfusion in the SICUs occurred in 5%. An initial SOFA ≥9, intra-operative blood loss ≥4900 mL, and intra-operative blood transfusion ≥10 units were the significant factors to predict massive transfusion in the SICUs.

Introduction

Trauma is the leading cause of death globally. The centers for disease control and prevention reported that trauma was the most common cause of death in the age range of 1–44 years in the United States.[1] Hemorrhage was the second most common cause of all deaths in trauma patients and was the most common cause of death in the first 24 h.[2]

Damage control resuscitation is a bundle that should be conducted in massive bleeding patients. It consists of permissive hypotension, hemostatic resuscitation, and damage control surgery.[3] Hemostatic resuscitation requires the blood bank to prepare blood and blood products in the proper ratio and timely fashion.

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Massive transfusion protocol (MTP) is a pre-set protocol for clinicians to communicate with the blood bank. Once patients meet the criteria the MTP is activated and the blood bank supplies blood and blood products. The MTP should last until deactivation when bleeding is controlled, the patient is hemodynamically stable, and the patient has adequate end organ perfusion whether it is achieved in the operative theater or in an intensive care unit (ICU). In Thailand, there is inconsistent use of the MTP. In 30% of the surgical intensive care units (SICUs) in the major university based hospitals, MTP only available in the emergency department. Furthermore, the blood bank cannot continuously implement the MTP because of insufficient resources. Therefore, this research aimed to report the incidence of massive transfusion in the SICUs and identify predictive factors of massive transfusion which may help to guide clinicians and blood banks to prepare blood and blood components when patients need further resuscitation in the SICUs.

Methods

Study design

This was an analysis of a prospective observational study of complications in nine university-based SICUs in Thailand (THAI-SICU study). The study collected data from 18 April 2011 to 30 November 2012. Only the study sites had submitted trauma patients' data. The final study sites consisted of 5 SICUs in the capital city–Bangkok, 1 SICU in Nakhon Nayok–a city near Bangkok and 3 SICUs in the main provinces of Chiang Mai, Khonkaen, and Songkhla in Thailand. The characteristics of the SICUs were published previously.[4] The study was approved by the ethics committee of the Faculty of Medicine, Prince of Songkla University.

Study population

The THAI-SICU study included all patients admitted to the SIUCs at the study sites that were able to obtain informed consent. The excluded patients were those who were <18 years old, expected to die, and expected to be admitted to the ICUs for <6 h. Trauma patients were more likely to be continuously resuscitated in the SICUs, especially after damage control surgery which occurred in severe trauma patients who had signs of coagulopathy, acidosis, or hypothermia. Those patients were brought to the SICUs after surgical bleeding and contamination were controlled. They were resuscitated in the SICUs to restoration of physiology before going back to the operating room again for definitive treatment. For this reason, only patients admitted due to a trauma mechanism were included in the analysis in this study.

Outcomes

Massive blood transfusion was defined as received ≥10 units during the first day of admission in the SICUs. Acute kidney injury was identified by an increasing serum creatinine >0.3 from base line. Acute respiratory distress syndrome (ARDS) was defined by a PaO2/FiO2 ≤ 200. The outcomes were measured by nurses and recorded in the medical records. The data were verified by the main investigators at each site.

Exposure parameter

Characteristics, intra-operative details, laboratory results, and physiologic scores were obtained. The sequential organ failure assessment (SOFA) scores were calculated from the first laboratory results after the patients were admitted to the SICUs. The acute physiology and chronic health evaluation (APACHE) II scores were calculated from the worst parameters in the first day of admission.

Data collection process

A data dictionary was developed and the research assistants were trained in a workshop. After the data were collected, the principle investigator at each site verified and ensured the quality of the data collection before the data were submitted to the data center.

Statistical methods

Continuous variables are demonstrated by mean and standard deviation or median and interquartile range. Categorical variables are expressed by frequencies and percentages. Continuous variables associated with outcomes were dichotomized by modified receiver operating characteristic curve (ROC) analysis. Univariate analysis was performed. Multivariable logistic regression was performed by back-ward elimination in order to get the final predictors. All parameters in the final model that were used to calculate the probability of massive transfusion in the SICUs were calculated by logistic regression. A two-tailed $p<0.05$ was considered as statistically significant different.

Results

From 4652 patients who were included in the THAI-SICU study, 370 patients (8%) were admitted due to a trauma mechanism. The mean age was 41 year old and mean APACHE II score on admission was 10 (6–18). Sixteen trauma patients (5%) received massive blood transfusion in the SICUs. The most common injury site was abdominal injury (23%) followed by head injury (21%). The details of the characteristics are shown in Table 1.

A univariate analysis was performed to identify the potential factors to predict massive transfusion. The results are given in Table 2. In the multivariable analysis, the APACHE II score was not included in the analysis even though it was statistically significant in the univariate analysis because it consisted of the worst parameters during the first day. Therefore it was not practical to use this parameter to predict massive transfusion in the real situation. The multivariable analysis showed that an initial SOFA ≥9, intra-operative blood loss ≥4900 mL and intra-operative blood transfusion ≥10 units were significant predictors of massive transfusion in the SICUs. The amount of blood products that the patients received and he volume of blood loss were the strong predictive factors which had risk differences of 0.45 (95% *CI*: 0.06–0.84, $p = 0.02$) and risk differences 0.33 (95% *CI*: 0.04–0.62, $p = 0.02$), respectively. The results of the multivariable logistic regression are shown in Table 3.

The probability of receiving a massive blood transfusion was calculated from logistic regression. It was found that patients who received a massive blood transfusion of packed red blood cells ≥10 units in the operating room and had intra-operative blood loss ≥4900 mL had a probability of 0.753 (95% *CI*: 0.267–0.925) and if they also presented with SOFA ≥9, the probability was higher to 0.975 (95% *CI*: 0.260–0.952). The probability of requiring massive blood transfusion in the SIUCs is shown in Table 4. SOFA ≥9, Intra-op blood loss ≥4900 mL, and intra-op PRBC ≥10 units were good predictors of receiving a massive blood transfusion which was demonstrated by the area under ROC of 0.923 (Fig. 1).

The patients who received a massive blood transfusion had worse clinical outcomes. Specifically, the occurrences of organ failure and 28 day mortality were higher. The mortality rate in the group that received massive blood transfusion was 87.5% and in the

Table 1
Characteristics of patients.

Variables	Massive blood transfusion ($n = 16$)	Non massive blood transfusion ($n = 310$)	p value
Male, n (%)	12 (75.0)	223 (71.7)	0.78
Age, year (range)	40.5 (32.5–52)	41 (27–65)	0.87
Injury regions, n (%)			0.34
Head	0 (0)	18 (6)	
Abdomen	5 (31)	59 (19)	
Chest	1 (6)	20 (6)	
Pelvis	2 (13)	29 (9)	
Extremities	0 (0)	33 (11)	
Spine	0 (0)	16 (5)	
Burn	0 (0)	13 (4)	
Chest and abdomen	4 (25)	27 (9)	
Multiple injuries	4 (25)	79 (25)	
Others	0 (0)	17 (6)	
APACHE II, score (range)	32 (23–37)	9 (6–16)	<0.001
SOFA, score (range)	10 (7.5–13)	3 (1–6)	<0.001
Intra-operative blood loss, mL (range)	7000 (1750–13500)	200 (0–1150)	<0.001
Intra-operative PRBC transfusion, mL (SD)	2983 (1726)	442 (809)	<0.001
Intra-operative FFP transfusion, mL (SD)	1896 (1278)	274 (581)	<0.001
Intra-operative fluid intake, mL (SD)	11,717 (6977)	2565 (3220)	<0.001

MT: mass transfusion, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment, PRBC: packed red blood cells, FFP: fresh frozen plasma, SD: standard deviation.

Table 2
Univariate analysis.

Variables	RD	95% *CI*	p value
Female	- 0.007	−0.06–0.04	0.77
Age ≥60 years	−0.02	−0.69–0.02	0.36
APACHE II ≥ 20	0.18	0.09–0.27	<0.001
Intra-operative blood loss ≥4900 mL	0.47	0.23–0.72	<0.001
Intra-operative PRBC ≥10 units	0.57	0.26–0.87	<0.001
Intra-operative intake ≥7000 mL	0.27	0.13–0.41	<0.001
Present of abdominal injury	0.06	0.001–0.12	0.04
SOFA ≥9	0.17	0.06–0.27	0.002

RD: risk difference, *CI*: confidence interval, APACHE: acute physiology and chronic health evaluation, PRBC: packed red blood cells, SOFA: sequential organ failure assessment.

Table 3
Multivariable analysis.

Variables	RD	p value	95% *CI*
SOFA ≥9	0.13	0.01	0.03–0.22
Intra-operative blood loss ≥4900 mL	0.33	0.02	0.04–0.62
Intra-operative PRBC ≥10 units	0.45	0.02	0.06–0.84

RD: risk difference, *CI*: confidence interval, SOFA: sequential organ failure assessment, PRBC: packed red blood cells.

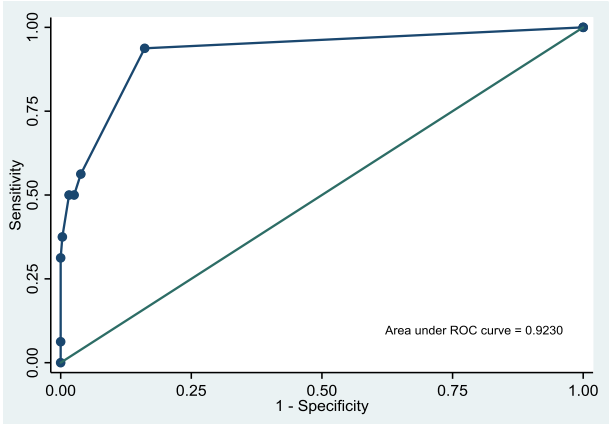

Fig. 1. The ROC curve for massive blood transfusion using SOFA ≥9, intra-op blood loss. ≥4900 mL, and intra-op PRBC ≥10 units.

group that did not receive massive blood transfusion was 17.4%. The clinical outcomes are shown in Table 5.

Discussion

We found the incidence of massive transfusion in the SICUs was 5% of trauma patients admitted to the SICUs. The incidence was the same as the reported incidence of 4.6%–12.4% in previous studies.[5,6] However, all of the previous studies reported the incidence for trauma patients overall and did not specifically report transfusion only when the patients were in the SICUs. Our incidence was slightly low because some of the patients who had massive transfusion did not survive the initial phase at the emergency departments or in the operating theaters to arrive at the SICUs.

The predicting factors of massive transfusion in the SICUs that we found were intra-operative blood transfusion ≥10 units, intra-operative blood loss ≥4900 mL, SOFA score ≥9, and intra-

Table 4
Probability of requiring massive blood transfusion in the SICUs.

Variables	Results							
SOFA ≥9	−	+	−	−	+	+	−	+
Intra-operative blood loss ≥4900 mL	−	−	+	−	+	−	+	+
Intra-operative PRBC ≥10 units	−	−	−	+	−	+	+	+
Probability	0.008	0.091	0.097	0.177	0.588	0.740	0.753	0.976
95% *CI*	0.223–0.779	0.303–0.734	0.179–0.847	0.172–0.872	0.312–0.877	0.221–0.939	0.267–0.925	0.260–0.952

Note: + means positive result, – means negative result.
SICUs: surgical intensive care units, SOFA: sequential organ failure assessment, PRBC: packed red blood cells, CI: confidence interval.

Table 5
Clinical outcomes.

Variables	Massive blood transfusion, *n* (%)	Non massive blood transfusion, *n* (%)	*p* value
Sepsis	1 (6.3)	53 (17.0)	<0.001
Acute kidney injury	8 (50)	48 (15.4)	<0.001
ARDS	3 (18.8)	18 (5.8)	=0.036
28-day mortality	14 (87.5)	54 (17.4)	<0.001

ARDS: acute respiratory distress syndrome.

operative intake ≥5000 mL. A blood transfusion volume greater than 10 units and intra-operative blood loss more than 4900 mL were equivalent to the total blood volume of adults who weigh 70 kg and were the definitions of massive transfusion.[7,8] It could be implied that patients who needed massive transfusion before admission to the SICUs potentially needed blood transfusions in the SICU. This fact could change the policy of a limited MTP of only 1 pack or a limited protocol only in the operating theaters.

The SOFA score represents functions of the respiratory system, nervous system, cardiovascular system, liver, coagulation and kidney. A high SOFA score indicates organ dysfunction and in this study it was also a predictor of massive transfusion. It correlated with what was mentioned in a review by Cantle et al[9] and also a study from Canada that found SOFA at ICU admission was a significant predictor of massive blood transfusion in trauma patients who survived at least 48 h.[10] The reason the SOFA score could be a good predictor may be because higher SOFA scores are more likely to indicate coagulopathy, liver failure or cardiovascular failure. Those organ failures have a high tendency to bleed which leads to a blood transfusion.

The strength of this study was the study design which was a prospective cohort study that provided very precise data with good quality. It was conducted in almost all of the university-based hospitals that were also level-1 trauma centers in the country. The centers were well equipped and had established protocol for taking trauma patients.

This study has a limitation of trauma-related parameters since this study focused on the adverse events in the SIUCs. We did not have injury severity score (ISS) which represent the severity of trauma patients. According to a study from Rau et al[11] patients who had massive blood transfusions had a higher ISS.

This study used the THAI-SICU database which collected parameters mostly from the SICUs and operations that the patients were received before admission to the SICUs. Therefore, the parameters in the emergency departments were not available and were not included in this study. If the parameters from the emergency departments were included, the model might be more precise. Besides the lacking of emergency departments data, this database did not included some laboratory results which would have represented the clot forming ability of the patients and would possibly have affected the results such as the international normalized ratio, platelet count, or serum urea nitrogen.

The incidence of massive blood transfusion in the SIUCs was not low compared with trauma patients over all. The results of this study are very useful for centers that have limited resources for MTP especially for centers where the MTP is not accessible in the SICUs. The results can also help physicians to communicate with the blood bank to supply blood and blood products continuously in high risk patients in order to improve outcomes.

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Ethical statement

The study was approved by the ethics committee of the Faculty of Medicine, Prince of Songkla University.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cjtee.2019.04.004.

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