

Accuracy of CHULA (Class-4 Hemorrhage Unresponsive to Lactated Ringer's) Criteria for Massive Transfusion Protocol Activation in Trauma Patients

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Background: In massive bleeding trauma patients, the use of massive transfusion protocol (MTP) has been shown to improve the outcome. However, the triggers for MTP activation vary among institutions. One of the most commonly used scoring systems to predict massive transfusion (MT) is the assessment of blood consumption (ABC) score. The authors' institution has used a simple clinical criterion, the Class-4 Hemorrhage Unresponsive to Lactated Ringer's (CHULA criteria), as a trigger for MTP activation.

Objective: To identify the accuracy of CHULA criteria for MTP activation in trauma patients.

Materials and Methods: Between April 2013 and April 2016, the authors retrospectively collected the data of trauma patients receiving blood transfusion in the first 24 hours at King Chulalongkorn Memorial Hospital, including demographic data, trauma scores, amount of blood transfusion, and mortality. The detail of CHULA criteria included 1) a patient with clinical signs of Class-4 hemorrhage, 2) not responding to one to two liters of Lactated Ringer's bolus, and 3) had suspected ongoing bleeding. MT was defined as 1) packed red blood cells (PRC) transfusion of equal to or greater than 10 units in 24 hours, or 2) PRC transfusion of more than four units in the first hour. The accuracy of CHULA criteria for MTP activation was analyzed. Comparison between CHULA criteria and ABC score (of equal to or greater than 2) was also performed.

Results: Three hundred fifty-eight patients were included in the present study, 292 males and 66 females. The mechanisms of injury were 68% blunt and 32% penetrating, with an average injury severity score of 21. MTP was activated by CHULA criteria in 100 patients and 73 received MT. Of the 258 patients who did not meet CHULA criteria, five received MT. As a trigger for MT activation, CHULA criteria had sensitivity, specificity, and accuracy of 93.6%, 90.4%, and 91%, respectively; while ABC score had sensitivity, specificity, and accuracy of 62.8%, 78.9%, and 75.4%, respectively.

Conclusion: CHULA criteria can predict MT in trauma patients with 91% accuracy. When compared with ABC score, CHULA criteria were not inferior to ABC score in predicting MT.

Keywords: Massive transfusion, CHULA criteria, ABC score

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Bleeding is the leading cause of deaths from trauma, accounting for 50% of mortality from trauma⁽¹⁾. Besides anemia and hypovolemia from blood loss, losing coagulation factors, platelets, and heat, altogether with lactic acidosis and activation of fibrinolysis play important role in trauma induced coagulopathy, which makes the bleeding worse⁽²⁾. In massive bleeding patients, the use of massive transfusion protocol (MTP) to prepare enough blood components for the patients has been shown to improve the outcome⁽³⁾. As demonstrated by Holcomb et al., a higher ratio of plasma to red blood cells in patients receiving massive transfusion (MT) resulted in a decreased mortality in the first 24 hours^(4,5).

Recently, damage control resuscitation (the concepts of delayed fluid administration, early bleeding control, and the use of MTP) has been adopted by many trauma centers to improve the outcomes of bleeding trauma patients⁽⁶⁾. However, the triggers for MTP activation vary among institutions⁽⁷⁻¹⁰⁾. The present study institution has used a simple clinical criterion, the Class-4 Hemorrhage Unresponsive to Lactated Ringer's (CHULA criteria), as a trigger for MTP activation since April 2013. Hence, the objective of the present study was to identify the accuracy of CHULA criteria for MTP activation in trauma patients.

Materials and Methods

A retrospective study was done on trauma patients receiving blood transfusion in the first 24 hours at King Chulalongkorn Memorial Hospital, a 1,400-bed university hospital and a level 1 trauma center in Bangkok, Thailand, between April 2013 and April 2016. The study was approved by the Institutional Review Board (IRB no.614/61). Data collection included demographic data, emergency department (ED) parameters, trauma scores, amount of blood transfusion in the first 24 hours, and outcome in terms of mortality. The decision to activate MTP was made by trauma surgeons using CHULA criteria. The details of CHULA criteria included 1) a patient with clinical signs of Class-4 hemorrhage (as per Advanced Trauma Life Support-ATLS® hemorrhage classification⁽¹¹⁾), 2) not responding to initial fluid resuscitation with one to two liters of Lactated Ringer's solution, and 3) had suspected ongoing bleeding. MT was defined as 1) packed red blood cells (PRC) transfusion of equal to or greater than 10 units in 24 hours⁽¹²⁾, or 2) PRC transfusion of more than four units in the first hour⁽¹³⁾.

Once the MTP was activated, the patient's blood would be sent immediately to the blood bank for pretransfusion testing. In the meantime, four units of group O PRC (stored in the ED) would be initially transfused to the patient. The MTP in the present institution included a shipment of six units of group specific PRC, six units of fresh frozen plasma (FFP), and six units of platelet concentrate every 30 minutes until the MTP is terminated.

Statistical analysis was performed using the IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) with the statistical significance set at p-value of less than 0.05. Comparison of categorical variables was performed with the chi-squared test (with p-values reported by using twice one-tailed exact probability) and comparison of continuous

variables was performed with the Student's t-test. The non-parametric (Mann-Whitney U) test was used for comparison of variables that were not normally distributed (i.e., blood component transfusion). The accuracy of CHULA criteria for MT activation was analyzed. Comparison between CHULA criteria and the assessment of blood consumption (ABC) score (of equal to or greater than 2) was also performed. The four components of ABC score are 1) heart rate greater than or equal to 120 per minute, 2) systolic blood pressure less than or equal to 90 mmHg, 3) a positive focused assessment sonography for trauma (FAST) result, and 4) penetrating mechanism⁽⁷⁾. The ABC scores of all the patients were retrospectively calculated.

Results

During the present study period, 358 trauma patients received blood transfusion in the first 24 hours and included 292 males and 66 females, with mean age of 37 year. Blunt injury was the predominant mechanism, accounting for 69%. Seventy-eight patients received MT (21.8%, MT group), while 280 patients did not (78.2%, non-MT group). The MT group had lower arrival systolic blood pressure, Glasgow coma scale (GCS) score, revised trauma score, and trauma and injury severity score while they had a higher pulse rate, and injury severity score (Table 1). Moreover, the MT group also had more positive FAST results. During the first 24 hours, the MT group had median PRC, FFP, and platelet transfusion of 12, 12, and 12 units, respectively. The mortality rate was significantly higher in the MT group (34.6% versus 1.4%, $p < 0.001$).

The MTP was activated by CHULA criteria in 100 patients and 73 received MT. Of the 258 patients who did not meet CHULA criteria, five received MT (Table 2). Assessment of ABC score in the authors' patients revealed that if ABC score (of equal to or greater than 2) had been used as a trigger for MTP activation, the MTP would have been activated in 108 patients, with only 49 of these ended up receiving MT (Table 3). As a trigger for MTP activation, CHULA criteria have sensitivity, specificity, and accuracy of 93.6% (95% CI 85.7 to 97.9), 90.4% (95% CI 86.3 to 93.6), and 91% (95% CI 87.6 to 93.8), respectively, while ABC score has sensitivity, specificity, and accuracy of 62.8% (95% CI 51.1 to 73.5), 78.9% (95% CI 73.7 to 83.6), and 75.4% (95% CI 70.6 to 79.8), respectively (Table 4).

Of the five patients who did not meet CHULA criteria but eventually received MT, four had

Table 1. Demographic data, emergency department parameters, and mortality of patients by massive transfusion status

	Total (n=358) n (%)	No MT (n=280) n (%)	MT (n=78) n (%)	p-value
Sex				0.476
Male	292 (81.6)	231 (82.5)	61 (78.2)	
Female	66 (18.4)	49 (17.5)	17 (21.8)	
Age (year); mean±SD	37.1±14.6	37.1±14.3	36.4±15.4	0.725
Mechanism				0.922
Blunt	247 (69.0)	194 (69.3)	53 (67.9)	
Penetrating	111 (31.0)	86 (30.7)	25 (32.1)	
SBP; mean±SD	113.8±32.2	121.4±24.5	86.7±41.0	<0.001*
Respiratory rate; mean±SD	25.8±6.0	25.8±4.6	25.6±9.2	0.807
Pulse rate; mean±SD	102.6±25.7	99.5±21.4	113.6±35.2	<0.001*
GCS; mean±SD	13.3±3.4	14.0±2.5	10.8±4.8	<0.001*
Positive FAST	112 (31.3)	72 (25.7)	40 (51.3)	<0.001*
ISS; mean±SD	21.6±15.4	17.9±11.6	35.1±19.5	<0.001*
RTS; mean±SD	7.2±2.0	7.6±1.8	5.9±2.1	<0.001*
TRISS; mean±SD	88.3±22.9	94.6±10.9	65.6±36.3	<0.001*
PRC*; median (IQR)	3 (1 to 7)	2 (1 to 4)	12 (10 to 18)	<0.001*
FFP*; median (IQR)	2 (0 to 6)	0 (0 to 4)	12 (8 to 20)	<0.001*
Platelet*; median (IQR)	0 (0 to 6)	0 (0 to 0)	12 (6 to 18)	<0.001*
Mortality	31 (8.6)	4 (1.4)	27 (34.6)	<0.001*

MT=massive transfusion; SBP=systolic blood pressure; GCS=Glasgow coma scale; FAST=focused assessment sonography for trauma; ISS=injury severity score; RTS=revised trauma score; TRISS=trauma and injury severity score; SD=standard deviation; IQR=interquartile range; PRC=packed red blood cells; FFP=fresh frozen plasma

* Transfusion in the first 24 hours, + Significant values (p<0.05)

Table 2. CHULA criteria vs. massive transfusion status

	No MT (n=280)	MT (n=78)
Criteria met (MTP activated)	27	73
Criteria not met	253	5

CHULA=Class-4 Hemorrhage Unresponsive to Lactated Ringer's; MT=massive transfusion; MTP=massive transfusion protocol

Table 3. ABC score ≥2 vs. massive transfusion status

	No MT (n=280)	MT (n=78)
ABC ≥2	59	49
ABC <2	221	29

MT=massive transfusion; ABC=assessment of blood consumption

normal initial systolic blood pressure and one was hypotensive but responded to two liters of Lactated Ringer's (Table 5). One patient had bleeding from the injured brain and received MT during a craniotomy (patient number 1), one patient received MT in the

Table 4. Comparison between CHULA criteria and ABC score ≥2 as a trigger for massive transfusion protocol activation

	CHULA criteria	ABC score ≥2
Sensitivity (95% CI)	93.6% (85.7 to 97.9)	62.8% (51.1 to 73.5)
Specificity (95% CI)	90.4% (86.3 to 93.6)	78.9% (73.7 to 83.6)
PPV (95% CI)	73.0% (69.3 to 79.5)	45.4% (38.5 to 52.5)
NPV (95% CI)	98.0% (95.6 to 99.2)	88.4% (85.0 to 91.1)
Accuracy (95% CI)	91.0% (87.6 to 93.8)	75.4% (70.6 to 79.8)

CHULA=Class-4 Hemorrhage Unresponsive to Lactated Ringer's; ABC=assessment of blood consumption; CI=confidence interval; PPV=positive predictive value; NPV=negative predictive value

intensive care unit during non-operative management for multiple injuries (patient number 2), two patients received MT during laparotomy for intraabdominal bleeding (patients number 3 and 4), and one patient received MT during extremity surgery (patient number 5). Since the MTP was not activated, FFPs were not given as early and as many as in the patients who met

Table 5. CHULA criteria false-negative patients who received a massive transfusion

No.	Sex	Age (year)	Mechanism	PR	SBP	FAST	Transfusion in the 1 st 24 hours	Death	Injury details
1	Male	49	Blunt	130	118	Negative	<ul style="list-style-type: none"> • PRC 11 units • FFP 8 units • Platelet 12 units 	No	<ul style="list-style-type: none"> • Motorcycle accident • Traumatic amputation left leg • Intracranial hemorrhage/craniotomy
2	Male	33	Blunt	130	70	Negative	<ul style="list-style-type: none"> • PRC 10 units • FFP 12 units • Platelet 0 unit 	No	<ul style="list-style-type: none"> • Fall • Rib fractures, hemothorax, femur fracture, subdural hematoma, thoracic spine fracture • Responded to 2 liters of Lactated Ringers
3	Male	22	Penetrating	130	120	Positive	<ul style="list-style-type: none"> • PRC 12 units • FFP 16 units • Platelet 0 unit 	No	<ul style="list-style-type: none"> • Abdominal stab wound • Splenic and pancreatic injury • Splenectomy, distal pancreatectomy
4	Male	41	Blunt	130	110	Positive	<ul style="list-style-type: none"> • PRC 10 units • FFP 4 units • Platelet 0 unit 	No	<ul style="list-style-type: none"> • Motorcycle accident • Splenic injury • Splenectomy
5	Male	46	Blunt	90	125	Negative	<ul style="list-style-type: none"> • PRC 10 units • FFP 6 units • Platelet 6 units 	No	<ul style="list-style-type: none"> • Motorcycle accident • Popliteal artery injury, left leg fracture • Arterial repair, external fixator of the left leg

PR=pulse rate; SBP=systolic blood pressure; FAST=focused assessment sonography for trauma; PRC=packed red blood cells; FFP=fresh frozen plasma

CHULA criteria. These five patients survived.

Discussion

Even though MTP helps improve outcomes in trauma patients with massive bleeding, there is still a controversy regarding when to activate it⁽⁷⁻¹⁰⁾. The modified traumatic bleeding severity score (mTBSS) is one of the most accurate scores in predicting MT (80% sensitivity and 91% specificity for the score greater than or equal to 15)⁽¹⁰⁾. Nevertheless, besides age, systolic blood pressure, and a FAST result, mTBSS needs pelvic X-ray and serum lactate level to complete the scoring and it may take several minutes to obtain these test results. On the other hand, ABC score proposed by Nunez et al⁽⁷⁾ is a simpler scoring system using four parameters immediately available in the ED and it has satisfactory accuracy (79% sensitivity and 78% specificity). Hence, several centers have adopted ABC score as a trigger for MTP activation^(5,14). More recently, a shock index of greater than or equal to 1 (calculated as initial heart rate divided by initial systolic blood pressure) has been proposed as a predictor for MT in trauma patients with sensitivity of 67% and specificity of 81%⁽¹⁵⁾.

Subjective assessment of MT requirement by trauma surgeons has been studied by Pommerening et al as a part of the prospective, observational, multicenter, major trauma transfusion (PROMMTT) study⁽¹⁶⁾. Ten minutes after the patient's arrival, the

investigators asked a gestalt question to trauma surgeons whether the patient was likely to be massively transfused. This subjective assessment was performed in 966 patients and yielded 65.6% sensitivity and 63.8% specificity. The author concluded that this subjective assessment has limited accuracy in identifying the need for MT and more reliable algorithm is needed.

In the present study, the authors established CHULA criteria using signs and symptoms of hemorrhage and the response to an initial crystalloid resuscitation, which could be quickly assessed after the patient's arrival at the ED. As a predictor for MT, CHULA criteria seem to be not inferior to other scoring systems in terms of accuracy. However, direct comparison of CHULA criteria and other scoring systems cannot be done since the populations are different among studies^(7-10,15). For instance, patients who meet MT criteria by ABC score of 2 or greater may have less bleeding (class 3 hemorrhage or less) as compared to patients who meet CHULA criteria. Furthermore, the definition of MT in the present study is broader than in previous studies. Specifically, the authors used both PRC transfusion of equal to or greater than 10 units in 24 hours and PRC transfusion of more than four units in the first hour as the definition for MT while other studies used just PRC transfusion of equal to or greater than 10 units in 24 hours^(7-10,15). The broader definition

of MT in the present study may have contributed to greater accuracy of CHULA criteria compared to other scoring systems.

In addition, CHULA criteria are a subjective assessment since the presence of “suspected ongoing bleeding” was judged intuitively by trauma surgeons and the patients were classified according to the 2013 ATLS® hemorrhage classification (ninth edition), which is also a subjective classification⁽¹¹⁾. For instance, there are no cut off values for “decreased blood pressure” or “decreased pulse pressure” in the ATLS® hemorrhage classification. Furthermore, a retrospective study on 3,411 trauma patients done by Mutschler et al demonstrated that in each class of hemorrhage, other measurable parameters like heart rate and GCS did not correlate well with systolic blood pressure⁽¹⁷⁾. Hence, the latest version of ATLS® uses trend of these parameters instead of fixed numbers to classify degree of hemorrhage⁽¹⁸⁾. Interestingly, the present study results support the 2018 ATLS® recommendation to activate MTP in a Class-4 hemorrhage patient⁽¹⁸⁾.

There are some limitations in the present study that deserve to be mentioned. Besides being a subjective assessment, CHULA criteria did not consider any laboratory tests (e.g., base deficit, hematocrit, serum lactate) and imaging studies, which may help increase accuracy of the criteria. Furthermore, the authors’ institution did not use the delayed fluid resuscitation strategy and routinely administered one to two liters of Lactated Ringer’s to hypotensive trauma patients. Hence, the use of CHULA criteria cannot be generalized to the centers using the delayed fluid resuscitation strategy. Finally, the present study is retrospective in nature and did not have some important data, such as the amount of fluid given, coagulation profiles, hospital length of stay, and complications of transfusion. Thus, a further prospective study is needed to evaluate CHULA criteria in terms of other outcomes (effects on hemostasis or coagulation, transfusion complications).

Conclusion

CHULA criteria can predict MT in trauma patients using data immediately available at the ED with good accuracy. When compared with ABC score, CHULA criteria were not inferior to ABC score in predicting MT. Since the response to an initial fluid resuscitation is imperative, CHULA criteria cannot be used in centers using the delayed fluid resuscitation strategy.

What is already known in this topic?

In massive bleeding trauma patients, the use of MTP has been shown to improve the outcome. However, the triggers for MTP activation vary among institutions. One of the most commonly used scoring systems to predict MT is the ABC score. ABC score is a simple scoring system using four parameters immediately available in the ED and it has satisfactory accuracy (79% sensitivity and 78% specificity). Hence, several centers have adopted the ABC score as a trigger for MTP activation.

What this study adds?

The present study demonstrated that CHULA criteria can predict the need for MT with good accuracy, not inferior to the ABC score. The results of the present study also support the 2018 ATLS® recommendation to activate MTP in a Class-4 hemorrhage patient. Since the response to an initial fluid resuscitation is imperative, CHULA criteria cannot be used in centers using the delayed fluid resuscitation strategy.

Conflicts of interest

The authors hereby certify that there is no conflict of interest in the present study.

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