

Acute Trauma Coagulopathy: Prevalence and Impact on Outcomes of Trauma Patients Presenting to the Emergency Department

Dear Editor,

Trauma remains a leading cause of death and disability worldwide. Coagulopathy occurring within minutes of a major trauma is seen in 10-25%¹ of severely injured trauma patients. The pathophysiology behind this phenomenon is incompletely understood but is thought to involve tissue trauma as well as systemic hypoperfusion. This leads to activation of endothelial Protein C, followed by rapid anticoagulation and fibrinolysis.^{2,3} This phenomenon, termed Acute Trauma Coagulopathy (ATC), is associated with a four-fold increase in mortality, increased transfusion requirements and organ failure.^{4,5}

We aimed to determine the prevalence of ATC and its impact on outcomes in severely injured trauma patients presenting to our Emergency Department (ED). Our ED is one of the busiest in Singapore, seeing an average of about 450 patients a day.

Materials and Methods

A retrospective observational cohort study was performed, using our trauma database. The details of all patients who presented between 1 January 2013 and 31 December 2013 with a diagnosis corresponding to trauma and an Injury Severity Score (ISS) of 15 and above were extracted from this database. The following patients were then excluded: 1) Age at presentation below 16, 2) Patients who had missing or incomplete data, 3) Patients transferred in from another facility, 4) Patients whose initial blood tests were performed more than 24 hours from the time of injury, and 5) Patients who were known to be on anticoagulants such as warfarin.

Apart from epidemiological data, the following parameters were recorded: time of first blood test from time of injury, initial vital signs to calculate Revised Trauma Score (RTS), coagulation profiles such as activated Partial Thromboplastin Time (aPTT) and International Normalised Ratio (INR). ATC was defined as INR greater than 1.2 or aPTT greater than 54s (1.5 times the upper limit of our laboratory's normal range) on the initial laboratory test upon arrival in the ED, in line with the definitions used in the literature.¹⁻⁴ The two groups of patients were then compared.

Statistical analysis was performed using SPSS Statistics 19 (IBM), and results were expressed as mean standard deviation (SD) and median interquartile (IQR) range for

description of variable spread. Comparisons between groups were conducted using Fisher's Exact test or chi-squared test as appropriate, and we considered $P < 0.05$ to be statistically significant. This study was approved by the National Healthcare Group (NHG) Domain Specific Review Board (DSRB) for exemption according to its policies.

Results

The characteristics of the study population are as shown in Table 1. A total of 309 patients were included, with the majority being male (71.5%) and of Chinese ethnicity (79.9%). The ethnic distribution of the patients was similar to the general population of Singapore—a majority being Chinese, followed by Malays, Indians and then a small minority of other races (3%).

Almost all of our patients had blunt injuries; the most common mechanism of injury being fall from height (67.6%), and followed by motor vehicle accidents (25.9%). A breakdown of the different mechanisms of injury is shown in Figure 1.

The median ISS of the study cohort as a whole was 21 (IQR 17-26) and the mean probability of survival (PS) was 84.7% (SD 19). Time taken was calculated from the recorded time of injury to the time stamp on the laboratory investigation. The median time taken for the first blood test from time of injury was 115 min (IQR 66-223).

Table 1. Characteristics of Study Group

Variables	Values
Study population	309
Chinese	247 (79.9%)
Indian	31 (10.0%)
Malay	22 (7.1%)
Male gender	221 (71.5%)
Blunt injury	304 (98.4%)
Median ISS	21 (IQR 17 – 26)
Mean PS	84.7% (SD 19.0)
Median time to first blood	115 min (IQR 66 – 223)
Mortality	16.5%

IQR: Interquartile range; ISS: Injury severity score; PS: Probability of survival; SD: Standard deviation

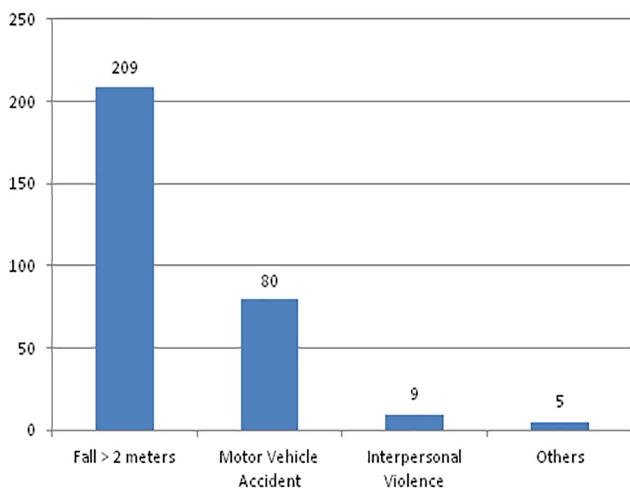


Fig. 1. Mechanisms of injury.

A total of 58 patients were found to be coagulopathic on arrival in the ED, placing the prevalence of ATC at 18.8% (Table 2). The median time from injury to first blood test was 84 min (IQR 57-180) for the patients with ATC, and 121 min (IQR 72-235) in the patients without ATC. Patients in the ATC group had higher median ISS scores (26 vs 21) as well as worse PS (70.9% vs 87.9%). The association between probability of survival and presence of ATC was found to be statistically significant ($P < 0.001$).

RTS was calculated for each group of patients based on their systolic blood pressure and heart rate both on-scene as well as upon arrival at the ED, and the two values were compared. A greater proportion of patients with ATC had a worse RTS score in ED compared to on-scene ($P < 0.001$) than those in the non ATC group, likely reflecting clinical deterioration despite initial treatment by prehospital staff.

Discussion

ATC is a discrete phenomenon previously described,¹⁻⁵ and may be exacerbated by ongoing blood loss (if rapid haemostasis is not achieved), haemodilution due to intravenous fluid resuscitation, acidosis and hypothermia. One previous systematic review⁶ in 2011 found that ATC leads to increased mortality, longer ICU stay, hospital stay and increased risk of organ failure.

We set out to determine the prevalence and impact of ATC in our trauma population, and our findings are similar to those published in existing literature^{1,4,5,7} despite the differences in the trauma patient population in our local context. Leow et al⁸ demonstrated that in our setting, almost all trauma patients had blunt injuries (97.5%) as opposed to penetrating injuries; the most common cause was road traffic accidents, whereas Western studies^{9,10} reported

Table 2. Comparison between ATC and Non-ATC Groups

	Patients With ATC	Patients Without ATC	P Value
Median ISS	26 (IQR 19–30)	21 (IQR 17–26)	<0.01
Patients with worse RTS on arrival in ED compared to on-scene	18.9%	8.0%	<0.01
Mean PS	70.9%	87.9%	<0.01
Mortality rate	46.6%	9.6%	<0.01
Proportion of patients with base excess <-2	82.1%	61.5%	0.03
Proportion of patients with lactate >2 mmol/L	92.9%	50%	<0.01

ATC: Acute trauma coagulopathy; ED: Emergency department; ISS: Injury severity score; IQR: Interquartile range; PS: Probability of survival; RTS: Revised trauma score

varying rates of penetrating injuries (14-49%) and a lower proportion of road traffic accidents (22.4%).

The initial landmark studies done by Brohi and Macleod^{7,11} in identifying ATC used conventional laboratory-based PT, aPTT and INR tests in their studies. These are time consuming (with a turnaround time of 30-60 minutes) and do not assess other contributory pathways in the coagulation cascade such as the fibrinolytic and platelet aggregation systems. While these tests have good correlation in the outpatient population for monitoring of patients on warfarin, their utility in the trauma population is less certain. Some authors have found laboratory-based INR measurements to be valuable^{6,12} while others do not recommend their usage.^{13,14} In our ED, laboratory-based tests are widely used to make decisions on the management of coagulopathy.

Newer point-of-care (POC) tests have been developed to overcome these challenges and aid decision-making during the resuscitation process itself. Two examples of these are thromboelastography (TEG) and rotational thromboelastometry (ROTEM). These tests provide global information on dynamics of clot involvement, stabilisation and dissolution (reflecting in vivo haemostasis). They assess both thrombosis and thrombolysis, and in effect measure all the different pathways along the coagulation cascade. The availability of results within 10 minutes means that these tests can be used for rapid decision-making, both in an ED as well as a critical care setting.

The limitations to POC tests include the need for multiple daily calibrations, specially trained personnel and lack of familiarity among the general physician population. In addition, there remains technical variations on how these tests are performed and there is a lack of worldwide consensus on “normal” values. Recent studies^{13,15} have shown poor

correlation between POC tests and conventional laboratory-based tests, and only moderate quality observational studies are available with no randomised controlled trials as of yet. Resuscitation algorithms utilising POC tests have also not shown a convincing benefit in studies to date.

Even as more interest develops in identifying and treating ATC, there is no universally accepted definition. Different authors have used a variety of tests and cut-off values, and there is no consensus or evidence to prove one superior to another. Any conclusions drawn should thus be applied cautiously, taking into account local patient population and practice setting.

Treatment of ATC usually involves goal-directed therapy with balanced transfusion. In our practice, we use a 1:1:1 ratio of packed red blood cells, platelets and fresh frozen plasma to closely emulate the losses suffered by a severely injured patient. Tranexamic acid injections should also be considered for all trauma patients who have hypotension.

Additional limitations of this study were the small sample size and the lack of information about prehospital interventions such as intravenous fluid administration which could have a significant impact on our findings. Other limitations were incomplete data on other patient outcomes such as length of ICU stay and hospital stay that precluded their inclusion in the analysis.

Opportunities for future research in this field are significant, given the multiple areas of uncertainty. Although it would be difficult to conduct randomised controlled trials in this setting, it could potentially be informative to compare on-scene coagulation profiles using POC tests with those on arrival to ED. Evaluation of blood products required in patients with ATC could also be compared to patients without ATC to further delineate its impact on management.

Conclusion

ATC is a distinct phenomenon occurring in approximately 1 in 5 severely injured trauma patients, and has a recognisable impact on patients' clinical status and mortality rate. The prevalence and impact on morbidity in our population is similar to that published in the Western literature despite differences in the injury pattern. It is important to attempt to detect these patients early, and treat them aggressively with balanced transfusion to optimise patient outcomes.

REFERENCES

- Mitra B, Cameron PA, Mori A, Fitzgerald M. Acute coagulopathy and early deaths post major trauma. *Injury* 2012;43:22-5.
- Ganter MT, Pittet JF. New insights into acute coagulopathy in trauma patients. *Best Pract Res Clin Anaesthesiol* 2010;24:15-25.
- Davenport R. Pathogenesis of acute traumatic coagulopathy. *Transfusion* 2013;53:23S-27S.
- Frith D, Brohi K. The acute coagulopathy of trauma shock: clinical relevance. *Surgeon* 2010;8:159-63.
- Frith D, Goslings JC, Gaarder C, Maegele M, Cohen MJ, Allard S, et al. Definition and drivers of acute traumatic coagulopathy: Clinical and experimental investigations. *J Thromb Haemost* 2010;8:1919-25.
- Lier H, Böttiger BW, Hinkelbein J, Krep H, Bernhard M. Coagulation management in multiple trauma: A systematic review. *Intensive Care Med* 2011;37:572-82.
- Brohi K, Singh J, Heron M, Coats T. Acute Traumatic Coagulopathy. *J Trauma Inj Infect Crit Care* 2003;54:1127-30.
- Leow JJ, Lim VW, Lingam P, Go KT, Teo LT. Ethnic disparities in trauma mortality outcomes. *World J Surg* 2014;38:1694-8.
- Søreide K, Krüger AJ, Vårdal AL, Ellingsen CL, Søreide E, Lossius HM. Epidemiology and contemporary patterns of trauma deaths: Changing place, similar pace, older face. *World J Surg* 2007;31:2092-103.
- Plummer JM, Brown H, Jones K, Fearon-Boothe D, Meeks-Aitken N, McDonald AH. Trauma: the burden of a preventable problem. *West Indian Med J* 2010;59:26-8.
- MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M. Early Coagulopathy Predicts Mortality in Trauma. *J Trauma Inj Infect Crit Care* 2003;55:39-44.
- Peltan ID, Vande Vusse LK, Maier RV, Watkins TR. An International Normalized Ratio-Based Definition of Acute Traumatic Coagulopathy Is Associated With Mortality, Venous Thromboembolism, and Multiple Organ Failure After Injury. *Crit Care Med* 2015;43:1429-38.
- da Luz LT, Nascimento B, Rizoli S. Thrombelastography (TEG): Practical considerations on its clinical use in trauma resuscitation. *Scand J Trauma, Resusc Emerg Med* 2013;21:29.
- Da Luz LT, Nascimento B, Shankarakutty AK, Rizoli S, Adhikari NK. Effect of thromboelastography (TEG®) and rotational thromboelastometry (ROTEM®) on diagnosis of coagulopathy, transfusion guidance and mortality in trauma: descriptive systematic review. *Crit Care* 2014;18:518.
- Mistral T, Boué Y, Bosson J-L, Manhes P, Greze J, Brun J, et al. Performance of point-of-care international normalized ratio measurement to diagnose trauma-induced coagulopathy. *Scand J Trauma Resusc Emerg Med* 2017;25:59.

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