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ORIGINAL RESEARCH

Acute traumatic coagulopathy and the relationship to prehospital care and on-scene red blood cell transfusion

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Abstract

Objective: To identify the incidence of acute traumatic coagulopathy (ATC) in trauma patients presenting to the Royal Adelaide Hospital, analyse prehospital contributors, including red blood cell transfusion and assess the clinical significance of ATC.

Methods: A retrospective database review was undertaken using conventional coagulation assays and viscoelastic testing (ROTEM) for diagnosis of ATC.

Results: Baseline ATC incidence is 10% in trauma patients, increasing to over 80% among those where the prehospital team has attended and given a transfusion of red cells. ATC was significantly associated with higher severity of trauma (odds ratio [OR] 1.11, $P < 0.0001$), prehospital (OR 11.8, $P < 0.0001$) and in-hospital blood transfusions (OR 17.9, $P < 0.0001$), and massive transfusions ($P < 0.001$).

Conclusions: Prehospital blood transfusions are given to the most severely injured trauma patients and the incidence of ATC in this group is more than 80%. There is an association with prehospital blood transfusion and increased ATC in part related to patient selection and severity of trauma, with the contribution of red cell transfusions to ATC unclear. This association should allow earlier identification of patients at increased risk of ATC to ensure rapid correction of coagulopathy to decrease the morbidity and mortality of trauma.

Key words: *coagulopathy, transfusion, trauma.*

Key findings

- ATC is common and associated with increased severity of trauma, blood transfusions and massive transfusions.
- Prehospital blood transfusions are given to the most severely injured trauma patients and the incidence of ATC in this group is more than 80%.
- There is an association with prehospital blood transfusion and increased ATC in part related to patient selection and severity of trauma, with the contribution of red cell transfusions to ATC unclear.

Introduction

Acute traumatic coagulopathy (ATC) begins from the time of trauma[1] and is perpetuated by factors such as shock, fibrinolysis and resuscitation efforts.[2] The incidence of ATC is reported at between 25 and 40% of major trauma and increases mortality fourfold,[3] and uncontrolled haemorrhage remains the largest cause of potentially preventable trauma deaths.[2] The identification and treatment for ATC should begin as soon as possible in the prehospital phase of care and continue throughout the trauma resuscitation until coagulation has been restored. This will allow optimal treatment of injuries and minimise the morbidity and mortality of trauma.

Prehospital systems vary across state and international lines. The model of care in South Australia (SA) allows for the activation of a physician-led prehospital and retrieval team (MedSTAR) to complex and severe trauma. The MedSTAR response consists of a three-person combination of retrieval physician, retrieval nurse and special operations team intensive care paramedic. A team can be activated for a primary trauma response from the initial ambulance call depending on specific automated activation criteria via the Medical Priority Dispatch System,[4] on request from the first ambulance crews on scene or as

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an interfacility transfer from a country hospital.

MedSTAR teams will give blood transfusions to trauma patients if they consider the patient to be in haemorrhagic shock. The standard quantity carried is 2 units of red cells for a primary response, with the ability to take up to 8 units, if time and prehospital information permits. The use of prehospital blood has been the subject of multiple systematic reviews[5–8] without conclusive evidence of a decrease in mortality while observational studies have shown an improvement in haemodynamic markers such as blood pressure and heart rate.[7] The effects on coagulopathy and 24-h red cell transfusion requirements were unable to reliably be quantified in these studies.

The Royal Adelaide Hospital (RAH) is a Major Trauma Centre (MTC) receiving trauma patients from across South Australia and from parts of regional New South Wales, Victoria and Northern Territory. The RAH sees about 410 major trauma patients per annum (as defined by an Injury Severity Score >12).

Definition of ATC has evolved over time. ATC was first described by Brohi *et al.* in 2003[3] and used conventional coagulation assays (CCAs). Initial diagnostic standards of PTr/INR >1.5 for diagnosis were found to miss a significant percentage of patients suffering from ATC and the threshold was lowered to PTr/INR >1.2.[9,10] Viscoelastic testing (VET) criteria for ATC are based on correlation with CCAs and thresholds for identifying those who require massive transfusion.[11–13] Earlier studies involving VET in trauma suggested a reduction in mortality[14–16] and a decrease in use of blood products;[17–19] however, the landmark randomised controlled trial ITACTIC[20] found no difference in overall outcomes between standard treatment and VET, when standard treatment was balanced haemostatic therapy with intensive CCAs. While VET is the sole test able to demonstrate fibrinolysis, it is only validated for severe fibrinolysis.[20] Current literature and expert opinions state tranexamic acid should not be withheld based on viscoelastic values.[2,21]

The primary aim of the present study was to identify the incidence of ATC in trauma patients arriving at the RAH and to determine any factors which could help identify those patients at high risk for ATC. Secondary aims were to determine the clinical significance of ATC in this cohort by examining its association with in-hospital blood transfusion or massive transfusion requirements in the first 24 h, and in-hospital mortality.

Methods

Retrospective RAH Trauma Registry database review of all patients meeting Level 1 statewide trauma team activation (Appendix S1) at the RAH ED between 1 July 2018 and 30 June 2019. Data collected included arrival method, prehospital blood transfusion, first available coagulation tests including first available ROTEM results, blood transfusions in the first 24 h, Injury Severity Score (ISS) and mortality. Massive transfusion definition was greater than or equal to 10 units of red cells transfused in the first 24 h.[9] Records of prehospital blood transfusion were collected from MedSTAR blood audit data.

Trauma team response at the RAH is determined by the SA Adult Trauma Team Activation criteria and is a combination of patient physiological variables, injuries sustained and trauma mechanism (Appendix S1). It is a 2-tier system, and a Level 1 callout mandates a multi-disciplinary hospital-wide team response. This initial Level 1 trauma reception at the RAH includes the use of VET with thromboelastometry (ROTEM), using a point-of-care ROTEM Sigma® (Werfen, Barcelona, Spain) located in the resuscitation area of the ED. Trained medical officers complete the ROTEM testing in the ED, with the resulting Temogram immediately available on screens in the patient's trauma bay which can then be acted upon using treatment algorithms (Appendix S2).

First available coagulation tests and blood transfusions in the first 24 h were collected from electronic medical records (Sunrise EMR, Allscripts Healthcare v5963.9030) and initial ROTEM results were collected from the ROTEM machine located in the ED.

ATC was defined as either of INR >1.2 or ROTEM results FibTEM A5 <10 or ExTEM A5 ≤40.[10–13] No ATC was defined as those not meeting ATC definition and included those for whom coagulation testing was deemed not required by the trauma team leader. Patients with abnormal coagulation tests that were in keeping with pre-existing medication use, coagulation deficiencies or liver dysfunction, and had no evidence of ATC were classified as 'No ATC'. Three patients died in ED before coagulation testing could be collected and were excluded from analysis.

Patient and presentation characteristics were summarised using means and standard deviations, or medians and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables. Multivariable binary logistic regression was used to explore factors associated with ATC, including mode of arrival (SA Ambulance Service, MedSTAR, other) and prehospital transfusion (for MedSTAR patients), adjusting for patient age and ISS. Adjusted predicted probabilities for selected outcomes were estimated post-hoc. Due to the small number of patients receiving massive transfusion, assessment of this outcome is limited to univariable tests of association using Fisher's exact test. All analyses were conducted using Stata (Version 15; StataCorp, College Station, TX, USA). The level of statistical significance was set at 0.05.

Ethics permission was sought and obtained from the Central Adelaide Local Health Network Human Research Ethics Review Committee (reference number 12191).

Results

There were 294 patients with an ISS >12 in this cohort of trauma patients. This cohort of patients with major trauma had a median ISS of 22, with a range 13–75. The incidence of ATC in this group was

25% (73 patients) and the mortality was 16% (47 patients).

The observed incidence of ATC in the RAH ED was 9.6% of all Level 1 trauma team activations (85 patients with ATC from 885 total patients). Patient and presentation characteristics and selected clinical outcomes are summarised by ATC-status in Table 1. Median ISS for the ATC patient group was 25 compared with median ISS of 5 for the group without ATC. A multivariate analysis using transport mode, ISS and age, showed a statistically significant relationship between increasing ISS and increased likelihood of developing ATC. For each 1-point increase in ISS, the odds ratio (OR) of developing ATC was 1.11 (OR 1.11, 95% confidence interval [CI] 1.09–1.14, $P < 0.0001$).

The incidence of ATC rises from 9.6% among all level 1 trauma patients, to 29.1% of patients brought in by a MedSTAR retrieval team (203 retrievals, 59 with ATC), and up to 81.8% among patients deemed by the MedSTAR team as requiring a prehospital blood transfusion (33 given blood, 27 with ATC) (Fig. 1). Controlling for age and ISS, the odds of ATC in a retrieval patient are 4.2 (95% CI 2.34–7.54; $P < 0.0001$) times higher than that for a patient brought in by the ambulance service.

Among MedSTAR retrieval patients, odds of ATC among those who received a prehospital blood transfusion were 11.8 (95% CI 4.06–34.0; $P < 0.0001$) times greater relative to those were not transfused, adjusting for ISS and age. With age and ISS variables fixed at their mean values, the predicted probability of ATC in the transfused group was 70% (95% CI 50.1–90.6).

After controlling for transport, ISS and age, the odds of death were on average 69% (adjusted OR 1.69, 95% CI 0.63–4.56; $P = 0.296$) higher in the ATC group (Table 2). When ISS, age and ATC were taken into account, there was no significant effect of arrival mode on mortality ($P = 0.905$). Among MedSTAR retrieval patients, no association was found between mortality and ATC (adjusted OR 2.63, 95% CI 0.80–8.70; $P = 0.113$) or mortality and prehospital blood transfusion (adjusted OR 0.41, 95% CI 0.11–1.55; $P = 0.189$).

Odds of in-hospital blood transfusion requirement in confirmed ATC was 17.9 times higher than those without ATC (adjusted OR 17.9, 95% CI 9.08–35.3; $P < 0.0001$). Massive transfusion was strongly associated with ATC (Fisher's exact $P < 0.0001$), those receiving blood prehospital (Fisher's exact $P < 0.0001$) and increased mortality (Fisher's exact $P < 0.001$).

TABLE 1. *Acute traumatic coagulopathy (ATC): demographics, mode of arrival and blood transfusions*

	All		No ATC		ATC		
	Freq	(%)	Freq	(%)	Freq	(%)	OR (95% CI), *P*
All level 1 traumas	885		800	(90.4)	85	(9.6)	
Age in years (mean ± SD)	43.0 ± 19.4		43.3 ± 19.6		39.8 ± 17.3		0.98† (0.97, 0.996), 0.012
Injury Severity Score, median (IQR)	6 (2, 16)		5 (1, 13)		25 (17, 34)		
Mortality	48	(5.4)	31	(3.9)	17	(20.0)	1.69‡ (0.63, 4.56), 0.296
Mode of arrival							
SAAS	627	(70.8)	604	(96.3)	23	(3.7)	
MedSTAR retrieval team	203	(22.9)	144	(70.9)	59	(29.1)	4.20† (2.34, 7.54), <0.0001
Other§	55	(6.2)	52	(94.5)	3	(5.5)	
Retrieval team	203		144	(70.9)	59	(29.1)	
Prehospital blood	33	(16.3)	6	(18.2)	27	(81.8)	11.8† (4.06, 34), <0.0001
No prehospital blood	170	(83.7)	138	(81.2)	32	(18.8)	
Blood Transfusion in first 24 h							
Blood transfusion	88	(9.9)	31	(35.2)	57	(64.8)	17.9¶ (9.08, 35.3), <0.0001
No blood transfusion	797	(90.1)	769	(96.5)	28	(3.5)	
Massive transfusion in first 24 h							
Massive transfusion	15	(1.7)	1	(6.7)	14	(93.3)	<0.0001††
No massive transfusion	870	(98.3)	799	(91.8)	71	(8.2)	

†Adjusted OR for ATC. ‡Adjusted OR for mortality for confirmed ATC. §Other modes of arrival – self-presentation, country Interhospital Transfer with non-doctor lead retrieval team, SA police. ¶Adjusted OR for in-hospital blood transfusion for confirmed ATC. ††Massive transfusion was significantly associated with ATC (Fisher's exact test). CI, confidence interval; IQR, interquartile range; OR, odds ratio; SAAS, South Australian Ambulance Service; SD, standard deviation.

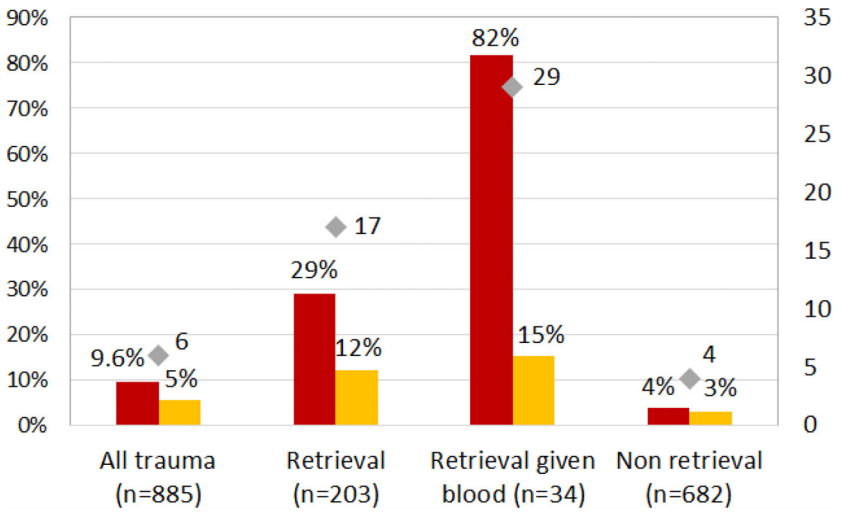

Figure 1. *Trauma at Royal Adelaide Hospital: acute traumatic coagulopathy (ATC), Injury Severity Score (ISS) and mortality. (■), ATC; (■), mortality; (■), median ISS.*

Age showed no effect on blood products or massive transfusion requirements. Increasing age did have a weak statistically significant association with increased mortality (adjusted OR 1.06, 95% CI 1.04–1.08; $P < 0.001$) but increasing age had a weak protective effect against ATC, with each 5 year increase in age having an adjusted OR 0.91 of developing ATC (95% CI 0.84–0.98; $P = 0.012$).

The majority of patients diagnosed with ATC were done so with ROTEM testing (71 patients, 83.5%) (Table 3). The diagnostic criteria met most often was FibTEM A5 <10 (66 patients, 77.6%). Fourteen patients (16.5%) were diagnosed with ATC on the basis of INR >1.2. Of the patients diagnosed on INR alone, five had no evidence of ATC on ROTEM, and the remaining nine patients did not undergo ROTEM testing. No ROTEM testing in some patients is likely an inability to get sufficient blood for testing or at the trauma team leaders' discretion.

Discussion

This review indicates that ATC is common among trauma patients seen in an Australian MTC.

TABLE 2. *Mortality*

	Survived to hospital discharge		Died		
	Freq	(%)	Freq	(%)	Adjusted OR (95% CI), *P*
Mode of arrival					0.905†
SAAS	605	(96.5)	22	(3.5)	
MedSTAR retrieval team	178	(87.7)	25	(12.3)	
Other‡	54	(97.1)	1	(2.9)	
Coagulation					
ATC	68	(80.0)	17	(20.0)	1.69 (0.63, 4.56), 0.296
No ATC	769	(96.1)	31	(3.9)	
Retrieval team					
ATC	44	(74.6)	15	(25.4)	2.63 (0.80, 8.70), 0.113
No ATC	134	(93.1)	10	(6.9)	
Given blood prehospital	28	(84.8)	5	(15.2)	0.41 (0.11, 1.55), 0.189
No blood	150	(88.2)	20	(11.8)	
Massive transfusion in first 24 h					
Massive transfusion received	10	(66.7)	5	(33.3)	0.001§
Massive transfusion not received	827	(95.1)	43	(4.9)	

†Global *P*-value from Wald test assessing overall significance of categorical predictor. ‡Other modes of arrival – self-presentation, country Interhospital Transfer with non-doctor lead retrieval team, SA police. §*P*-value from Fisher's exact test. ATC, acute traumatic coagulopathy; CI, confidence interval; IQR, interquartile range; OR, odds ratio; SAAS, South Australian Ambulance Service.

TABLE 3. *Acute traumatic coagulopathy (ATC) diagnostic criteria*

	ATC diagnostic criteria met	
	Freq	(%)
All ATC	85	(100)
FibTEM A5 <10†	66	(77.6)
ExTEM A5 ≤40	5	(5.9)
INR >1.2‡	14	(16.5)

†Of those meeting criteria for FibTEM A5 <10, 40 patients also met criteria for ExTEM A5 ≤40. ‡For those with INR >1.2, nine had no ROTEM testing and five had ROTEM testing.

Specialised retrieval teams sent to the most severely injured patients, with the resources to give prehospital blood transfusions to those in haemorrhagic shock, in this review, identified a group of patients at high risk of developing ATC, and possibly contributed to the ATC with red cell transfusions. The most severely injured patients arriving at the MTC had the highest incidence of ATC and those patients given red cells by the prehospital team had an ATC incidence of 82%.

Our finding of ATC in 25% of those with an ISS >12 is consistent with the literature.[3] The adjusted OR for ATC with respect to mortality suggested odds of death were increased with confirmed ATC. The effect was not statistically significant, which may be attributed to the relatively small sample size and low event rate. In keeping with previous reports, ATC is associated with increased blood product and massive transfusion requirements, and higher ISS.

The finding of higher odds of ATC among retrieval patients given prehospital blood was predictable (OR 11.8). Blood transfusions are given to those in haemorrhagic shock, which in turn are often the most severely injured patients. The contribution of red cell transfusion itself to the development of ATC cannot be ascertained from the available data, because of the interdependence of severity of trauma, haemorrhagic shock and ATC, and the observational nature of the review. There is however likely to be an element of resuscitation induced coagulopathy as a result of the red cell transfusions from effects such as dilution and worsening acidaemia. A concern with dilution coagulopathy following resuscitation fluids has led to minimal crystalloid use in trauma but dilution also occurs with red cell transfusions. Red cell transfusions contribute oxygen carrying capacity but do not provide platelets or clotting factors; in particular red cells provide no fibrinogen. The trend towards a decrease in mortality in the group given prehospital blood suggests blood transfusion may confer a beneficial effect but given low numbers in the mortality cohort, no definitive conclusions can be made.

The finding of significantly higher odds of ATC in patients for whom increased prehospital resources had been allocated suggests further opportunities for early identification and treatment of ATC in specialist prehospital trauma care settings. Prehospital scoring systems for potential ATC[22] have been shown to be moderately sensitive to identification but have not been externally validated to correlate with patient outcomes.[23] The prehospital treatment of ATC currently involves avoiding hypothermia, omitting excessive crystalloid infusions to prevent dilution, and minimising prehospital scene times. Some centres have added judicious red cell transfusions and early tranexamic acid to the prehospital treatment package. The recent COMBAT[24] and PAMPer[25,26] randomised trials have shown mixed results with prehospital fresh frozen plasma. A meta-analysis[27] showed reduced 24-h mortality in the plasma arm but no difference in mortality at 1 month or multi-organ failure, while a post-hoc analysis[28] of combined data showed a significant reduction in mortality at 24-h and 28 days, more so in the group with transport times greater than 20 min.

In-hospital trauma studies have shown an early fibrinogen load to potentially have a positive effect on morbidity and mortality[14,15,17,18,25,26] and the results of ongoing trials such as CRYOSTAT-2[29] are expected to further inform this debate. An early fibrinogen load could be delivered in the prehospital phase with products such as fibrinogen concentrate[30] and may aid in treating ATC.

Damage control resuscitation principles[31] are fundamental in modern trauma centres. An awareness of the increased incidence of ATC among patients allocated the highest level of prehospital trauma care and the observation that as many as four out of five patients given prehospital blood have ATC allows the trauma centre to adequately prepare to receive these critically injured patients.

Limitations

The limitations of the present study include the retrospective nature of database reviews. This data can show the association, but not causation, between ATC and prehospital blood transfusions. Our study had incomplete data, most marked when looking at prehospital intra-venous non-transfusion fluid use and transport times to the MTC. The relatively small number of in-hospital deaths limited the statistical power of mortality calculations. Not all trauma patients seen in the ED underwent coagulation studies, with only those meeting the highest level of trauma team activation reviewed.

Conclusions

ATC is common and associated with increased severity of trauma, blood

transfusions and massive transfusions. Prehospital blood transfusions are given to the most severely injured trauma patients and the incidence of ATC in this group is more than 80%. There is an association with prehospital blood transfusion and increased ATC in part related to patient selection and severity of trauma, with the contribution of red cell transfusions to ATC unclear. This association should allow earlier identification of patients at increased risk of ATC to ensure rapid correction of coagulopathy to decrease the morbidity and mortality of trauma.

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Author contributions

DH and DM involved in data collection. JB and DH in statistical analysis. All authors contributed to manuscript writing and revisions.

Competing interests

None declared.

Data availability statement

Data available on request from the authors.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Appendix S1. Statewide trauma team call-out criteria.
Appendix S2. RAH ROTEM transfusion algorithm for adults trauma.