La Prensa MedicaArgentina

Research Article

Acute Traumatic Coagulopathy in Iran; Incidence and Possible Risk Factors

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Abstract

Introduction: Acute traumatic coagulopathy (ATC) is a disruption of hemostasis at the moment of impact and is associated with increased mortality. Without quickly available diagnostic tests, risk factors play an important role in identifying those at risk. We aim to determine the incidence of ATC and find its risk factors in a previously unreported population.

Methods: A retrograde analysis of records was done on all severe trauma patients at two major trauma centers in Tehran for whom a coagulation panel had been ordered on admission. Rate of ATC was determined with different definitions and association with outcome measures was analyzed. Association between risk factors and ATC was analyzed first in a cross-sectional manner and then using logistic regression via SPSS21 software.

Results: Overall 246 patients were included (88.2% male). PTratio>1.2 was seen in 11.4% and best predicted outcomes. ISS score>23 (P=0.001), abdominal Abbreviated Injury Score (AIS)>3 (P=0.003), BE more negative than -4 (P=0.019), PR in the ED>90 (P=0.041), pH<7.30 (P=0.043), and PR at the scene>90 (P=0.046) were found to be associated with the development of ATC. Of these abdominal AIS more than 3 (P=0.001), and BE more negative than -4 (P=0.011) were found to be independent predictors of ATC in logistic regression.

Conclusion: We determined the rate of ATC for the first time in a Middle Eastern country and found it to be closer to the lower margin of previously reported frequencies. Our findings also cement previous reports that both severe injury and hypoperfusion put patients at risk for ATC.

Keywords

Traumatic coagulopathyl; Hypoperfusion; Trauma; Mortality

Introduction

Injuries are the number one cause of death in persons aged 5 to 44 [1] and this number is expected to increase at least 40% by 2030, with a higher impact seen in developing nations [2]. A third of deaths caused by injury have been attributed to hemorrhage many of which are preventable [3]. Acute Traumatic Coagulopathy (ATC) is used to describe patients with severe trauma which show evidence of coagulopathy upon admission to the emergency department (ED). Although the term ATC was first introduced in 2003 [4], only recently it was shown that the abnormality is an endogenous phenomenon which starts before any interventions [5]. It is estimated that up to 25% of severely injured patients manifest ATC. These have a four-fold increased risk of mortality and significantly greater transfusion requirements [6]. Even more importantly it has been shown that Management strategies targeting ATC may allow significant improvement in outcomes [3].

Many attempts have been made at diagnosing ATC in the early minutes of admission which matters the most [3,7,8]. Unfortunately currently available laboratory methods fail to achieve this goal. Therefore researchers have sought clinical factors which may predict the occurrence of ATC and therefore initiation of lifesaving treatments [9,10]. Risk stratification of patients based on clinical findings and laboratory studies which are quickly available can help recognized patients at risk of ATC. In this preliminary study we look at ATC for the first time in the Middle East region and aim to achieve basic understanding of its prevalence and possible risk factors within the Iranian population.

Methods

This is a preliminary study conducted as a retrospective cohort study of patients with severe trauma. The files of all patients admitted to the trauma ED of two major trauma centers in Tehran (Shohada-e Tajrish, Imam Hossein) during March 2013 to 2014 were assessed. The patients for whom a coagulation panel had been ordered were included. Patients with age less than 18 years, Injury Severity Score (ISS) less than 15, history of bleeding disorders or severe liver dysfunction, and using anticoagulation medications within the last two weeks, were excluded. In order to exclude patients at risk of dilution coagulopathy, those who had received more than 2 liters of fluids during transport and those who had been referred from other treatment centers were excluded from the study.

A specific data sheet was designed for collecting information. Data was collected from patients' files regarding demographics, injury causing event, vital signs in the field and ED, injured organs, ISS, laboratory results, and outcome measures. The laboratory results collected included coagulation profile, complete blood count (CBC), and Blood gas analysis. Outcome measures included were need of intensive care unit (ICU) admission, need for operative intervention, in-hospital mortality, need of blood products in the first 24 hours, and length of stay.

The study protocol was approved by the ethical committee of Shahid Beheshti University of Medical sciences. Authors adhered to the declaration of Helsinki in all parts of the study.

Definitions

Severe injury was defined as ISS score more than 15 [11]. All patients with injury scores below this number were excluded from the study.

Previous studies have used different definitions for ATC. In our study we examined four definitions that had been used

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Received: December 09, 2016 **Accepted:** January 04, 2017 **Published:** April 10, 2017

in previous studies and analyzed which of these best predicts outcomes in our population. The definitions were: Prothrombin Time (PT) more than 18s, Partial Thromboplastin Time (PTT) more than 36s (7), PT ratio (patient PT/control PT) greater than 1.2 [3,12], or International Normalization Ration (INR) greater than 1.5 [9,10].

Frequency determination

The frequency of ATC in the study population was individually determined based on each of the above definitions. A combination of the definitions was also considered, i.e. any patient which met any of the criteria was considered to have coagulopathy. Then ability of each definition to better predict outcomes was analyzed.

Statistical analysis

The data was analyzed using SPSS 21 software. First the association between different ATC definitions and outcomes were measured to determine which definition best predicts outcomes. Then the association between risk factors and ATC was analyzed. Continuous variables were compared using the Mann-Whitney U test, categorical data were analyzed using Chi Squared. Finally logistic regression was used to determine the impact of risk factors on occurrence of ATC.

Results

Initially 503 patients were included in the study. Seventeen patients were excluded because of history of coagulation disorders, liver disease, or use of anticoagulant medication. A further 240 patients were excluded because they did not meet the injury severity, age criteria, or because of incomplete patient file. The final analysis was conducted on 246 patients.

Of the included patients 88.2% (n=216) were male. Mean age of patients was 36.57 ± 17.11. Motorcycle accidents were the most common mechanism of injury (33.7%), followed by motor vehicle collisions (19.5%), and falling (19.1%). Most patients included had been transported to the ED by the ambulance service (70.3%), for whom the mean transit time to ED was 37.07 ± 30.15 minutes. All those transported via ambulance received intravenous fluids (IVF). The mean amount of fluids received was 676.83±452.02 milliliters. The average ISS score was 21.83 ± 7.38 ranging from 16 to 54 with a median of 20.

Outcomes

The frequency of outcome measures is summarized in Table 1. Both the need for blood products and the amount of products used were considered. Need for surgical repair was the most frequency observed outcome measure (78%), while mortality was the least frequent (8.1%).

Frequency of ATC

Table 2 shows the frequency of ATC based on predefined criteria separately and in combination. The maximum and minimum frequencies of ATC were achieved with criteria of PTT greater than 36 seconds (31.3%) and PT greater than 18 seconds (2.4%), respectively. A combined definition included 94 patients (38.2%). As seen in Table 2 none of the definitions was able to predict in-hospital mortality. From the five definitions assessed, PT ratio of greater than 1.2 appeared to better predict outcomes and was used as the optimum definition in the rest of the study.

Risk factor determination

Table 3 summarizes the association between different factors and the occurrence of ATC in the population studied. The factors found to be significantly more prevalent in the ATC group were found to be abdominal trauma, oxygen saturation and Systolic Blood Pressure (SBP) in the ED, Pulse Rate (PR) in the field and in the ED, ISS, WBC counts, pH, base excess (BE), and serum bicarbonate levels. Statistically and clinically relevant cut points were applied to these variables. The variables still found to be significantly associated with occurrence of ATC were ISS score greater than 23 (P=0.001), abdominal Abbreviated Injury Score (AIS) greater than 3 (P=0.003), BE more negative than -4 (P=0.019), PR in the ED more than 90 (P=0.41), pH less than 7.30 (P=0.043), and PR at the scene more than 90 (P=0.046).

In a final step the ability of these variables to predict the occurrence of ATC was tested in a stepwise logistic regression analysis. The only two variable that were found to be able to independently predict the occurrence of ATC were abdominal AIS more than 3 (P=0.001), and BE more negative than -4 (P=0.011).

Discussion

This is the first study looking at ATC in Iran. Genetic factors are a well-known contributor to the occurrence of ATC [9,13] and therefore the study of this phenomenon in different settings may further expand our understanding of the contributing factors. In our study based on a definition of PT ratio greater than 1.2 we found 11.4% of our severely injured patients suffered from ATC on ED arrival. This is a relatively smaller number that that reported in other countries. The highest incidence has been reported in Uganda with 54% [7], while an Australian study found only 9.0% of their patients met the definition of coagulopathy (10). On the other hand, most studies from Europe have produced numbers between 24 and 34% [4,13]. The incidence we discovered in our study is closer to the lower margin of reported incidence.

The ability of ATC to predict outcome measures appears to be both a matter of region in which the study is conducted and also the power of the study. Most studies have been able to find an independent and significant association between the presence of ATC and mortality [4,5,7,10,14]. This was not the case in our study. None of the four definitions used for ATC, nor their combination, were able to predict mortality in our study. We believe this to be in part due to the low rate of mortalities in our study which greatly limited the power of our study to find correlations between coagulation tests and this important outcome. In our study ATC successfully predicted the need for intensive care, need for blood products, and longer hospital stay as outcome measures. Higher transfusion and resuscitation requirements are another widely accepted predictable outcome of ATC [9,15,16], yet is not universal [7]. In our study ATC was able to strongly predict higher transfusion requirements.

Table 1: Frequency of outcome measures in the study population.

Outcome Measure	Number	Percent
Need for blood products	39	15.9
Need for ICU admission	103	42
Need for surgical intervention	192	78
Mortality	20	8.1
	Mean	**SD**
Duration of stay	11.93	11.37

Table 2: Frequency and Ability of different definitions of ATC to predict outcome measures.

			Ability to predict outcomes significantly					
Criteria for ATC	**Number of patients**	**percentage**	Mortality	ICU admission	Need for operative intervention	Duration of stay	Need for Blood Products	Amount of blood products
PT>18	6	2.4	-	-	-	-	+	+
PTT>36	77	31.3	-	-	+	-	-	-
PT ratio>1.2	28	11.4	-	+	-	+	+	+
INR>1.5	27	11	-	+	-	-	+	+
Combination	94	38.2	-	-	+	+	-	-

Table 3: Association between clinical and historical factors and ATC.

Variable	ATC (28)	No ATC (N=218)	Test	P	
Mechanism	-	-	Chi2	0.444	
Male Gender	192(88%)	24(86%)	Chi2	0.670	
Ambulance Transportation	151(73%)	21(72%)	Chi2	0.502	
Age	32.25 ± 13.74	37.12 ± 17.44	MWU	0.221	
Transport time	42.30 ± 39.49	36.34 ± 28.70	MWU	0.824	
Intravenous Fluids	767.86 ± 419.04	665.14 ± 455.66	MWU	0.237	
• Injury Severity					
ISS	25.75 ± 9.312	21.33 ± 6.95	MWU	0.017	*
Head and Neck AIS	1.71 ± 1.94	2.09 ± 1.90	MWU	0.365	
Face AIS	0.57 ± 1.20	0.66 ± 1.13	MWU	0.519	
Thorax AIS	1.07 ± 1.65	0.98 ± 1.44	MWU	0.996	
Abdomen AIS	2.07 ± 1.96	1.03 ± 1.48	MWU	0.004	*
Extremities AIS	1.61 ± 1.77	1.56 ± 1.80	MWU	0.884	
External AIS	0.39 ± 0.86	0.14 ± 0.52	MWU	0.083	
• Vital Signs					
GCS in the field	13.95 ± 1.96	13.79 ± 2.51	MWU	0.671	
SBP in the field	111.59 ± 20.08	114.20 ± 18.86	MWU	1	
PR in the field	91.41 ± 14.36	85.01 ± 13.68	MWU	0.014	*
Temperature in the field	37.07 ± 0.23	36.99 ± 0.21	MWU	0.133	
RR in the field	16.90 ± 1.92	16.66 ± 2.09	MWU	0.642	
GCS in the ED	12.75 ± 3.00	13.44 ± 3.01	MWU	0.139	
SBP in the ED	100.32 ± 17.48	117.25 ± 17.66	MWU	0.029	*
PR in the ED	95.07 ± 12.58	88.73 ± 15.23	MWU	0.004	*
Temperature in the ED	37.00 ± 0.32	37.04 ± 0.42	MWU	0.905	
RR in the ED	18.68 ± 4.25	17.49 ± 2.52	MWU	0.199	
O2 Saturation in the ED	92.70 ± 4.94	94.59 ± 5.36	MWU	0.014	*
• Lab Results					
BSG	143.32 ± 47.99	143.02 ± 47.34	MWU	0.794	
pH	7.31 ± 0.13	7.38 ± 0.12	MWU	0.044	*
PCO2	40.85 ± 14.62	39.92 ± 11.17	MWU	0.788	
HCO3	19.91 ± 5.62	23.88 ± 8.67	MWU	0.047	*
BE	-5.47 ± 5.61	-1.41 ± 6.99	MWU	0.026	*
WBC	14.03k ± 5.17k	12.15k ± 4.59k	MWU	0.034	*
Platelets	170.18k ± 88.32k	192.53k ± 84.87k	MWU	0.119	
Hb	11.51 ± 2.69	12.12 ± 2.79	MWU	0.230	

ATC: Acute Traumatic Coagulopathy, ISS: Injury Severity Score, AIS: Abbreviated Injury Score, GCS: Glasgow Coma Scale, SBP: Systolic Blood Pressure, PR: Pulse Rate, RR: Respiratory Rate, BSG: Bedside Glucometer, BE: Base Excess, WBC: White Blood Cell count, Hb: Hemoglobin concentration, MWU: Independent-Samples Mann-Whitney U Test

Another aspect to our study was to identify historical, clinical, and even quickly available laboratory data that may point towards presence of ATC. This has been a longtime interest of researchers since the coagulation profile is rarely made available in the early minutes of ED admission [3]. In the absence of a rapid diagnostic tool, management of ATC currently relies on suboptimal empirical transfusion strategies [16-19].

In an attempt to predict the occurrence of ATC before coagulation profile is available, Mitra et al. devised the coagulopathy of severe trauma (COAST) score to help with the early diagnosis of ATC. In

this system history of entrapment, Systolic blood pressure (SBP) of less than 100, Chest decompression, and Abdominal or pelvic content injury, and core body temperature of less than 35°C each received 1 score, while SBP of less than 90 and hypothermia of less than 32°C received 2. The researchers found that at scores equal or greater than 3 was predictive of ATC with acceptable sensitivity and specificity (10). In another study based in Germany, Yucel et al. devised a more complicated scoring system aiming to predict ATC and the need for massive transfusion. In the Trauma Associated Severe Hemorrhage (TASH) score, items like Hemoglobin, Base excess, Systolic blood pressure, Heart rate, confirmed free intra-abdominal fluid, instable pelvic fracture, femur fracture, and Male gender are scored [20]. A TASH score of greater than 16 has been suggested as the cutoff for prediction of ATC.

Other studies have also searched for risk factors for ATC. Abdominal and thoracic trauma, pelvic fractures, mechanism of injury, and evidence of anemia and shock have been listed among the risk factors for ATC [9,21]. The importance of male gender has also been emphasized [15,22]. In our study although we didn't find any association between ATC and gender, significant and independent associations were realized with degree of abdominal trauma, and a base deficit of greater than 4. This is in accordance with previous findings which state coagulopathy is more prevalent when severe injury and hypo perfusion co-exist [23-25]. In the current study we found that in our population of Iranian patients with severe trauma, the presence of serious abdominal trauma or laboratory evidence of hypoperfusion (i.e. BE<-4), there should be concern for ATC and proper measures to treat the phenomenon are justified.

Limitations and Conclusion

This was a preliminary attempt at estimating the prevalence and recognizing the factors associated with ATC in Iran. The retrograde design of the study predisposes it to several limitations, the most important being incomplete coverage of the target population and missing data. We selected patients for whom a coagulation panel had been ordered by the treating physician in the initial order. We believe since these tests are generally ordered for severely injured patients and those who require operative intervention we have most likely not missed a large portion of our target population. The low rate of mortality in our patients may again be due to selection bias; in that test results of patients with early mortality may not have been sought and included in their file, leading to their elimination from the study. Another more feasible explanation for the low reported mortality in our setting, may be a high incidence of prehospital mortality. It has been reported that, in developing countries, more than 70% of deaths due to injury occur in the field [21]. In such a setting much early mortality never reach hospital-based studies. Despite these limitations, this is the first study looking at the ATC phenomena in Iran. While determining the incidence of ATC at 11%, our study reinforces the role of hypoperfusion and abdominal injuries in creating ATC. A prospective multi-center cohort should be considered the next step for evaluating ATC in Iranian patients.

Acknowledgement

This work has been excerpted from the residency thesis number 216, by Ali Tabatabaey MD, supervised by Hojjat Derakhshanfar MD at the school of medicine, Shahid Beheshti University of Medical Sceinces, Tehran, Iran.

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