Int J Burn Trauma 2012;2(3):158-166
www.IJBT.org /ISSN:2160-2026/IJBT1210003

Original Article

Mechanistic determinates of the acute coagulopathy of trauma (ACoT) in patients requiring emergency surgery

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Received October 25, 2012; Accepted November 15, 2012; Epub December 5, 2012; Published December 15, 2012

Abstract: Introduction: The development of acute coagulopathy of trauma (ACoT) is associated with a significant increase in mortality. However, the contributory mechanisms behind ACoT have yet to be clearly defined. The purpose of this study was to evaluate the influence of multiple variables, including base deficit and injury severity, on development of ACoT within a subset of critically ill trauma patients. Methods: A retrospective review of all trauma laparotomies between 01/2004-12/2009 was performed. ACoT (+) was defined as an arrival INR ≥1.5, ACoT (-) defined as INR<1.5. Univariate and multivariate analyses were performed. Results: Of 1218 patients, 337 (27%) were ACoT (+) and 881 (73%) were ACoT (-) upon presentation. Groups were similar in demographics, ED fluid administration, GCS scores, and admission temperatures. Admission base deficit (8.5 vs. 4, p<0.001) and ISS (median 25 vs. 16, p<0.001) were higher in the ACoT (+) group, as were intra-operative RBC (median 4 vs. 0 U) and plasma (3 vs. 0 U) transfusions; both p<0.001. Multiple-linear regression revealed INR values were independently associated with arrival base deficit and pre-hospital fluid volumes (both p<0.001). On logistic regression, the development of ACoT (+) was associated with base deficit (OR 0.92, p=0.013) as well as ISS (OR 1.05, p<0.001). However, blunt mechanism alone was not an independent predictor of ACoT. Conclusion: The current study revealed that ACoT is independently associated with both shock (base deficit) and tissue injury. Additionally, tissue injury is a significant contributor to the development of early ACoT regardless of blunt or penetrating mechanism.

Keywords: Trauma, laparotomy, coagulopathy, base deficit, injury severity

Introduction

Hemorrhage is a major cause of mortality in civilian and military patients with traumatic injuries, accounting for up to 40% of trauma-related deaths [1]. The presence of the acute coagulopathy of trauma (ACoT) has recently been identified as a contributing factor to mortality secondary to hemorrhage. Brohi and colleagues showed a four-fold increase in mortality in patients presenting with ACoT [2]. ACoT presents as prolonged bleeding from mucosal lesions, serosal surfaces, wounds and vascular access sites, as well as hematoma formation at uninjured sites [3]. Although ACoT has a similar clinical presentation to disseminated intravascular coagulopathy (DIC), the processes appear to be physiologically distinct. Johansson et al recently differentiated the two demonstrating that although trauma patients arrive coagulopathic in regards to an elevated INR, the accompanying characteristics that define overt DIC, as per the International Society of Thrombosis and Hemostasis criteria, are not consistently demonstrated in this population [4].

ACoT has been defined as an increase in clotting time upon admission, usually 1.5 times the normal value [5]. Several authors have shown ACoT to be associated with increased transfusion requirements, increased incidence of multiple organ failure, and overall worsened outcomes [2, 6-8]. Additionally, retrospective studies have suggested that early correction of this coagulopathy via damage control resuscitation and increased plasma as well as platelet to RBC transfusion ratio is associated with reductions in mortality in the severely injured trauma patient [6, 9, 10].

The causes and mechanisms of ACoT appear to be multi-factorial and have yet to be clearly

defined. Frith and colleagues have stated that ACoT develops endogenously in response to a combination of tissue damage and shock. They employed ISS (injury severity score) to define tissue damage, and base deficit was used as the numerical representation of shock. They proposed that these are independent factors contributing to ACoT in a synergistic manner [11]. Niles et al suggested that the prevalence of coagulopathy increases as injury severity increases, but only in association with an increase in base deficit [12]. Other data has consistently demonstrated an association of worsening INR with increasing ISS. That is, for a given ISS, the rate of mortality is greater with increasing INR [13, 14]. In order to better define the relationship between these two determinants, we studied the most critically ill trauma patients that present to our level I trauma institution. We hypothesized that injury mechanism (blunt versus penetrating), shock (base deficit), and tissue trauma (injury severity score) would each contribute independently to the development of ACoT.

Materials and methods

Study setting

Memorial Hermann Hospital is an American College of Surgeons verified level I trauma center that is the primary teaching hospital for the University of Texas Health Science Center at Houston. The hospital is an 800-bed facility within the Texas Medical Center and is home to the John S. Dunn Helistop, the busiest heliport in the United States for its size. The trauma center admits well over 5,000 trauma patients annually with the most severely injured cared for in the 23-bed Shock-Trauma ICU (STICU).

Selection of participants

Expedited approval was obtained from the University of Texas at Houston Institutional Review Board. This was a single-center, retrospective review of trauma patients admitted to Memorial Hermann Hospital using the institution's Trauma Registry of the American College of Surgeons (TRACS) database. We evaluated all adult trauma patients admitted between January 2004 and December 2009 who underwent immediate exploratory laparotomy (directly from the Emergency Department to the Operating Room). In accordance with the expedited approval process, vulnerable populations such as minors (age <18), prisoners, and pregnant women were excluded from this study. Patients were also excluded from analysis if they received ≥5 minutes CPR prior to operating room (OR) or died in the OR.

Definitions

ACoT was defined as an admission INR of ≥1.5. Patients who had admission INR ≥1.5 were therefore classified as ACoT (+) while those with INR <1.5 were classified as ACoT (-). INR has traditionally been indicated to be more reliable than aPTT for diagnosis of reduced coagulation factor levels in trauma patients, and coagulopathy has been traditionally defined as an INR≥1.5. This is based upon several international guidelines for initiating fresh frozen plasma transfusion in coagulopathic patients [5, 15-17]. However, the specific INR used in the trauma community to define ACoT has been controversial and varied. Hess et al recently reported a retrospective study of 15,728 patients for which admission INRs were available. The prevalence of abnormal coagulation results increased as a function of ISS in a stepwise fashion. For patients with an INR ≥1.3 and with an ISS >15, there was an increased risk of mortality [14]. Frith et al defined ACoT as a PT ≥1.2 with significantly higher mortality and transfusion requirements than patients with normal PT [11]. However, Niles et al correlated an INR≥1.5 with increased mortality in combat casualties, [12] and Schreiber et al also used the same numerical value of 1.5 to associate INR with need for massive transfusion and overall greater mortality in combat injuries [18]. Although the exact numerical definition of ACoT has been debated, given the traditional use of 1.5, and the supportive literature from the combat arena, 1.5 seems to be an appropriate numerical definition of traumatic coagulopathy.

We evaluated trauma registry data including age, gender, and mechanism of injury. Injury scores, including initial Glasgow Coma Scale (GCS), weighted Revised Trauma Score (w-RTS), and Injury Severity Score (ISS) were evaluated as well. The w-RTS incorporates the initial GCS, systolic blood pressure, and respiratory rate, using coded and weighted values that range from 4 (normal) to 0 (poor) for each of the physiological variables (yielding a high of 7.841 and

a low of 0). AIS is an anatomic injury scoring system that quantifies injuries in various body regions from a score of 1 (minor injury) to 6 (non-survivable). ISS is calculated by summing the squares of the three highest AIS scores in three different body regions (values range from 1-75).

Prehospital vital signs were recorded for all patients through a review of ground or air transport documentation. Prehospital fluids included all non-blood product related fluid administered to patients prior to arrival in the ED/trauma bay. ED vital signs were defined as the initial set of vital signs captured and documented in the trauma bay. All patients had a single comprehensive laboratory panel obtained in the ED. The results of these labs were used for populating the ED laboratory value data fields through an electronic medical records data query. OR vital signs were the initial set of vital signs documented in the electronic medical records "Anesthesia/OR" report. Similarly, the OR laboratory results were defined as the initial values obtained after arrival in the operating theater. OR fluid and blood products documentation were defined as the total amount of solutions and products delivered as recorded by the Anesthesia/OR report. The ICU vital signs and laboratory values were defined as the initial values obtained immediately after patient arrival in the ICU.

Prehospital, ED, and OR crystalloid administration were defined as all normal saline, lactated Ringer's solution, and plasmalyte received or initiated while in these hospital locations. Prehospital, ED, and OR blood products (RBC, plasma, and platelets) were defined as those products received or initiated while in these hospital locations. 24-hour blood product calculations were defined as the total number of products received 24 hours from time of arrival to the hospital. This included blood in the trauma bay, operating room, and post-operatively up to the 24-hour post-admission mark. The incidences of 24-hour and 30-day mortality were recorded and evaluated.

Statistical analysis

Continuous data are presented as medians with 25th and 75th inter-quartile range (IQR) with comparisons between groups performed using the Wilcoxon rank sum (Mann-Whitney U test). Categorical data are reported as proportions and, where appropriate, tested for significance using χ^2 or Fisher exact tests. The primary data analysis evaluated the impact of demographic, pre-hospital variables, and ED variables on the prevalence of ACoT at admission. *P* values ≤ 0.05 were defined as significant.

A multivariate linear regression model was constructed evaluating those variables that (1) had biological plausibility to impact the occurrence of ACoT, (2) could be temporally correlated with the development of ACoT, and (3) were significant on univariate analyses ($p<0.05$). After identifying ACoT (INR ≥1.5) as our dependent variable and primary outcome of interest, the above independent variables were used in constructing the multiple logistic regression analysis. In an effort to minimize the risk of falsely identifying significant results with multiple comparisons, all regression models were pre-specified and judged *a priori* to be clinically sound. STATA Statistical software (version 10.0; College Station, TX) was used for analysis.

Results

Univariate analyses

A total of 1218 patients underwent an exploratory laparotomy immediately upon arrival throughout the time of data collection. 337 (28%) of patients had an INR≥1.5 (ACoT +) while 881 (72%) patients had an arrival INR <1.5 (ACoT -). (**Table 1**) The median PT in the ACoT (+) group was 17.7 vs. 13.5 seconds in the ACoT (-) group ($p<0.001$). Patients within these two groups had similar demographics, presenting GCS scores, and initial temperatures upon admission. The ACoT (+) group had a higher ratio of blunt trauma (62% vs. 44%). Similar to results previously reported by Brohi and colleagues, median ED base deficit was also greater in the ACoT (+) group (8.5 vs. 4; p=<0.001) and remained consistently greater intra-operatively (7 vs. 5; $p<0.001$). Initial venous blood gas pH values (7.23 vs. 7.30, $p<0.001$) as well as OR ABG pH values (7.27 vs 7.32, $p<0.001$) corresponded with greater acidosis upon presentation. Median ISS scores were also higher on the ACoT group (25 vs. 16; $p<0.001$). However, in addition to ISS scores, individual chest, head, abdomen, and pelvis/extremity median AIS scores were higher in the ACoT group ($p<0.001$). ACoT patients had lower

Table 1. Demographics, injury severity and prehospital variables compared by ACoT (INR≥1.5) status

	ACoT (+) (n=337)	ACoT (-) (n=881)	*p*-value
Median age (IQR)	33 (23, 46)	32 (24, 44)	0.549
Male gender, %	78%	82%	0.063
Blunt mechanism, %	62%	44%	<0.001
Median ISS (IQR)	25 (13, 38)	16 (9, 26)	<0.001
Median head AIS (IQR)	0 (0, 2)	0 (0, 0)	<0.001
Median chest AIS (IQR)	3 (0, 4)	0 (0, 3)	<0.001
Median abdominal AIS (IQR)	3 (2, 4)	3 (2, 3)	<0.001
Median pelvis/extremity AIS (IQR)	2 (0, 3)	0 (0, 2)	<0.001
Median pre-hospital SBP, mmHg (IQR)	101 (80, 130)	118 (100, 136)	<0.001
Median pre-hospital HR, bpm (IQR)	108 (88, 122)	100 (86, 115)	0.001
Median pre-hospital GCS (IQR)	14 (6, 15)	15 (14, 15)	<0.001
Median pre-hospital fluids, L (IQR)	0.9 (0.3, 1.8)	0.6 (0.25, 1.1)	0.002
Median pre-hospital RBC, U (IQR)	0 (0, 0)	0 (0, 0)	0.028

ACoT: acute coagulopathy of trauma; IQR: 25th to 75th inter-quartile range; ISS: injury severity score; AIS: abbreviated injury scale; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; GCS: Glasgow coma scale; L: liters; ED: emergency department; RBC: red blood cells; U: units.

Table 2. Emergency department vitals, laboratory values and intervention compared by ACoT (INR≥1.5) status

	ACoT (+) (n=337)	ACoT (-) (n=881)	*p*-value
Median ED SBP, mmHg (IQR)	110 (81, 130)	122 (101, 142)	<0.001
Median ED HR, bpm (IQR)	106 (86, 126)	98 (83, 114)	<0.001
Median ED GCS (IQR)	14 (3, 15)	15 (14, 15)	<0.001
Median ED Temp, F (IQR)	97.2 (96.4, 97.9)	97.8 (97.0, 98.3)	<0.001
Median ED crystalloids, L (IQR)	1.0 (0.5, 2.0)	1.0 (0.5, 2.0)	0.015
Median ED RBC, U (IQR)	1 (0, 3)	0 (0, 0)	<0.001
Median ED plasma, U (IQR)	0 (0, 0)	0 (0, 0)	<0.001
Median ED platelets, U (IQR)	0 (0, 0)	0 (0, 0)	0.131
Median ED hemoglobin, g/dL (IQR)	12.1 (10.0, 13.6)	13.6 (12.5, 14.8)	<0.001
Median ED platelet count, x10^3 (IQR)	230 (182, 279)	262 (211, 317)	<0.001
Median ED PT, seconds (IQR)	17.7 (16.3, 19.6)	13.5 (12.6, 14.4)	<0.001
Median venous blood gas pH (IQR)	7.23 (7.10, 7.31)	7.30 (7.25, 7.36)	<0.001
Median ED base status (IQR)	-8.5 (-14, -4)	-4 (-8, -1)	<0.001

ACoT: acute coagulopathy of trauma; IQR: 25th to 75th inter-quartile range; ED: emergency department; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; GCS: Glasgow coma scale; L: liters; RBC: red blood cells; U: units; PT: prothrombin time.

Table 3. Comparison of intra-operative variables compared by ACoT (INR≥1.5) status

	ACoT (+) (n=337)	ACoT (-) (n=881)	*p*-value
Median time from ED to OR, min (IQR)	40 (19, 95)	51 (26, 111)	<0.001
Median OR time, min (IQR)	104 (71, 152)	98 (68, 141)	0.080
Median OR SBP. mmHg (IQR)	115 (93, 140)	128 (110, 143)	<0.001
Median OR HR, bpm (IQR)	102 (90, 120)	99 (85, 110)	<0.001
Median OR temperature, F (IQR)	95.5 (93.7, 97.0)	96.1 (95.0, 97.2)	<0.001
Median OR fluids, L (IQR)	3.0 (2.0, 4.7)	3.0 (2.0, 4.0)	0.037
Median OR RBC, U (IQR)	4 (0, 11)	0 (0, 3.5)	<0.001
Median OR plasma, U (IQR)	3 (0, 8.5)	0 (0, 2)	<0.001
Median OR platelets, U (IQR)	0 (0, 6)	0 (0, 0)	<0.001
Median OR arterial blood gas pH (IQR)	7.27 (7.16, 7.34)	7.32 (7.25, 7.37)	<0.001
Median OR base status (IQR)	-7 (-12, -4)	-5 (-8, -3)	<0.001
Closed at initial laparotomy, %	50.1%	75.5%	<0.001

ACoT: acute coagulopathy of trauma; ED: emergency department; OR: operating room; IQR: 25th to 75th inter-quartile range; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; L: liters; RBC: red blood cells; U: units.

Table 4. Comparison of ICU arrival and 24-hour transfusion variables compared by ACoT (INR≥1.5) status

	ACoT (+) (n=337)	ACoT (-) (n=881)	*p*-value
Median ICU SBP. mmHg (IQR)	130 (110, 149)	135 (118, 151)	0.006
Median ICU HR, bpm (IQR)	97 (83, 115)	95 (83, 110)	0.292
Median ICU Temp, F (IQR)	97.0 (94.5, 98.6)	97.7 (96.0, 98.6)	<0.001
Median ICU hemoglobin, g/dL (IQR)	11.1 (9.5, 12.4)	11.8 (10.4, 13.1)	<0.001
Median ICU platelet count, $x10^3$ (IQR)	144 (90, 226)	189 (130, 252)	<0.001
Median ICU arterial blood gas pH (IQR)	7.34 (7.26, 7.40)	7.34 (7.28, 7.39)	0.689
Median ICU base status (IQR)	-3 (-6, 0)	-3 (-6, 0)	0.911
Median ICU lactate (IQR)	4.7 (2.5, 7.2)	4.4 (2.6, 6.1)	0.117
Median ICU PT, seconds (IQR)	15.8 (14.4, 17.6)	14.9 (13.8, 16.3)	<0.001
Median 24-hour fluids, L (IQR)	7.5 (4.9, 12.0)	6.5 (4.7, 9.7)	0.003
Median 24-hour PRBC, U (IQR)	7 (0, 14)	1 (0, 5)	<0.001
Median 24-hour plasma, U (IQR)	4.5 (0, 15)	0 (0, 4)	<0.001
Median 24-hour platelets, U (IQR)	0 (0, 6)	0 (0, 0)	<0.001
Median 24-hour cryoprecipitate, U (IQR)	0 (0, 0)	0 (0, 0)	<0.001

ACoT: acute coagulopathy of trauma; IQR: 25th to 75th inter-quartile range; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; L: liters; OR: operating room; PRBC: packed red blood cells; U: units; PT: prothrombin time.

Table 5. Multiple linear regression model predicting arrival (ED) INR values

	Coef.	95% C.I.	*p*-value
Age in years	-0.001	-0.005, 0.003	0.675
Male gender	0.086	-0.061, 0.232	0.248
Blunt mechanism of injury	0.159	-0.019, 0.337	0.080
Injury severity score	0.003	-0.003, 0.008	0.334
Pre-hospital SBP, mmHg	-0.002	-0.004, 0.001	0.224
Pre-hospital HR, bpm	0.0003	-0.004, 0.004	0.884
Pre-hospital fluid in liters	0.0001	0.00006, 0.0002	<0.001
ED/arrival SBP, mmHg	0.0002	-0.002, 0.002	0.839
ED/arrival HR, bpm	0.00006	-0.003, 0.003	0.965
ED/arrival temperature, F	-0.022	-0.071, 0.028	0.385
ED/arrival base status	-0.028	-0.042, -0.015	<0.001

INR: international normalized ratio; coef: coefficient of correlation; 95% C.I.: 95% confidence interval; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; ED: emergency department; F: Fahrenheit.

systolic blood pressures in the pre-hospital setting, the ED, and the OR (p<0.001), and more tachycardia in the pre-hospital setting (p=0.001), the ED, and the OR (p<0.001). (**Table 1** and **3**) Hemoglobin levels (12.1 vs. 13.6 g/dL) and platelet levels (230 vs. 262 $x10^9$/L) were lower upon presentation as well (p<0.001). (**Table 2**) Correspondingly, there were more RBC and plasma transfusions in the ED and in the OR (p<0.001) in the ACoT (+) group. (**Table 2** and **3**) Pre-hospital fluid administration was also slightly greater in the ACoT (+) group (0.9 L vs. 0.6 L; p=0.002). However, crystalloid administration in the ED was the same in both groups (1.0 L; p=0.015).

ACoT (+) patients arrived to the ICU more hypothermic and acidotic when compared to the ACoT (-) group. (**Table 4**) This group also had significantly higher transfusion volumes than the non-coagulopathic patients. As others have shown, overall mortality was significantly higher in the ACoT group at 6-hours (11.8% vs. 0.8%), 24-hours (14.5% vs. 1.1%), and 30-days (22.5% vs. 4.2%) as compared to the non-coagulopathic group (all p<0.001). An increased ICU length of stay (median 2 days vs.1 day, p<0.001) was also noted in the ACoT population.

Multivariate analysis

A multiple linear regression model was developed to evaluate predictors of arrival INR (continuous dependent variable) using demographics, injury severity, and pre-hospital and arrival vitals. Our linear model revealed that arrival

Table 6. Multiple logistic regression model predicting ACoT (INR≥1.5) present on admission

	Odds ratio	95% C.I.	*p*-value
Age in years	1.01	0.989, 1.027	0.403
Male gender	0.65	0.340, 1.261	0.206
Blunt mechanism of injury	0.74	0.329, 1.677	0.476
Injury severity score	1.05	1.024, 1.083	<0.001
Pre-hospital fluid in liters	1.00	0.999, 1.000	0.060
ED/arrival SBP, mmHg	0.99	0.983, 1.006	0.387
ED/arrival HR, bpm	1.00	0.987, 1.022	0.604
ED/arrival base status	0.92	0.874, 0.984	0.013

ACoT: acute coagulopathy of trauma; 95% C.I.: 95% confidence interval; SBP: systolic blood pressure; HR: heart rate; bpm: beats per minute; ED: emergency department.

INR values were independently predicted by both arrival base deficit and pre-hospital fluid administration (both p<0.001). (**Table 5**) A similar model, dichotomizing the outcome into ACoT (+) or ACoT (-) was developed using similar independent variables. On multiple logistic regression, ED base deficit and ISS were found to be independent predictors of ACoT on arrival. (**Table 6**).

To evaluate the individual contributions of specific body regions (individual AIS scores), we removed ISS from each of the models and replaced it with head AIS, chest AIS, and abdominal AIS scores. In the linear model, head AIS predicted increasing INR values (coef. 0.047, 95% C.I. 0.008 to 0.085, p=0.016), while chest (coef. -0.011, 95% C.I. -0.045 to 0.023, p=0.496) and abdomen (coef. -0.020, 95% C.I. -0.075 to 0.035, p=0.475) AIS scores did not. In the logistic model, abdominal AIS was an independent predictor of developing ACoT (OR 1.63, 95% C.I. 1.190 to 2.254, p=0.002). However, head (OR 1.16, 95% C.I. 0.966 to 1.407, p=0.109) and chest (OR 1.02, 95% C.I. 0.854 to 1.224, p=0.806) AIS scores did not predict the presence of ACoT on arrival.

Discussion

Over the past decade, there has been increasing interest and an extensive amount of information revealed regarding the etiology, diagnosis, prevention, and treatment of ACoT. Although there is evidence to support the association of multiple variables in regards to the progression of ACoT, the exact mechanisms by which tissue trauma, shock, and inflammation initiate coagulopathy are complex and not entirely understood. Hess et al proposed six key factors to be involved in the progression of ACoT: shock, tissue trauma, hemodilution, acidemia, hypothermia, and inflammation. While shock is thought to be a primary influence behind early ACoT, tissue injury is felt to be the catalyst [19]. Wafaisade et al also identified tissue damage, shock, hypothermia and hemodilution as risk factors for ACoT [20]. Brohi and colleagues revealed a correlation between ACoT and increasing ISS. However, their data did not reveal a correlation between the volume of intravenous fluids administered and the development of traumatic coagulopathy [2]. In the current study, we demonstrate a strong and linear correlation between pre-hospital fluid resuscitation volumes with not only traumatic coagulopathy on arrival (ACoT), but also in regards to the degree of shock upon presentation as measured by arrival base deficit.

ISS has traditionally been used as the surrogate for the magnitude of tissue damage. Brohi and Cohen put forth the hypothesis that ACoT is predominately promulgated by tissue damage and the subsequent release of tissue factor and activation of the protein C pathway [21-23]. In their murine model of trauma and hemorrhagic shock, the authors found neither trauma nor shock alone induced coagulopathy, but that the combination of the two components was necessary. They theorized that ACoT developed in response to a combination of both tissue damage and shock as demonstrated by base deficit [7, 11]. We found that both tissue injury (ISS) and shock (base deficit) were critical and independent predictors of early development of ACoT. Shock demonstrated a strong linear relationship and the ISS correlated via logistic regression models.

It has also been argued that blunt trauma is necessary for ACoT to develop, whereas pene-

trating injuries are either rapidly lethal or are survivable but do not cause significant and massive tissue trauma or coagulopathy and ACoT. The ISS was originally contrived to predict survival rather than tissue damage and therefore may either over or under estimate the degree of tissue damage sustained [19, 20]. For example, a lethal penetrating injury to the heart results in an ISS of 75, yet it is associated with limited tissue damage. Yet a massive crush injury to the lower extremities has an ISS value of 25, but certainly has a greater quantitative amount of tissue injury. Alternatively, a gunshot wound to the abdomen with multiple injuries usually yields an ISS of 16 or less. As the ISS has been the standard for the measurement of tissue trauma, we also utilized the calculated values to analyze the correlation between ACoT and mechanism. In the present study, over one-third of the patients sustained a penetrating mechanism of injury (almost all gunshot wounds). The greater number of penetrating injuries may reveal a flaw in using the massive tissue trauma argument (and in using ISS to represent tissue injury). Alternatively, these data might suggest that in patients with penetrating trauma and less actual tissue injury, severe shock by itself is enough to lead to early ACoT development. Our regression models did not find blunt mechanism to be predictive of either INR values or the development of ACoT.

Coagulopathy has long been attributed to severe brain injury [24]. However, in the absence of shock, Cohen and colleagues have recently demonstrated that traumatic brain injury (TBI) alone does not cause early coagulopathy. The authors noted that TBI must be coupled with hypo-perfusion to lead to coagulation derangements, which are associated with the activation of the protein C pathway [23]. In contrast, investigators from LA County noted that early coagulopathy after TBI does not occur exclusively in patients experiencing tissue hypo-perfusion (as measured by base deficit) [25]. In the present study, worsening head AIS scores were associated with increasing INR values on arrival. However, TBI (head AIS) was not an independent predictor of ACoT when controlling for base deficit.

The present work has several limitations. First, this is a retrospective study with predictable inherent limitations. It was also performed at a single center over a six-year period. Certainly there are regionalized clinical applications and evolving practice patterns that are not accounted for which may influence outcomes. As mentioned previously, the ISS was not created to measure and reflect tissue damage. Therefore, ISS is certainly not the ideal modality for quantifying tissue injury. However, it has been set as the standard by the trauma community. Finally, we have focused on a single patient population, those patients needing emergent trauma laparotomy. This population, in our opinion, represents one of largest populations of trauma patients that could potentially benefit from the early treatment of ACoT. However, our data does discount a large population of polytrauma patients who unmistakably presented with clinical ACoT, but were not included and are therefore not reflected or represented by our data.

The current study found in patients requiring emergent laparotomy, ACoT is independently associated with shock (base deficit) and tissue injury as represented by the ISS in either blunt or penetrating trauma. Early therapies to address ACoT can be initiated based upon the known variables that correlate with ACoT upon presentation such as extensive tissue injury and profound shock. Attempts to address this highly lethal model should focus on treatment of each of these individual components.

Acknowledgements

The authors would like to thank Angela Beeler for her editorial support. This work was supported in part by a grant from the State of Texas Emerging Technology Fund (BAC). No other financial support was used for this study. The authors have no conflicts of interest to declare.

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