Original Study

Evaluation of acute traumatic coagulopathy in dogs and cats following blunt force trauma

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Abstract

Objective – To evaluate the presence of acute traumatic coagulopathy (ATC) in dogs and cats following blunt trauma and to relate coagulation variables with injury severity and admission variables.
Design – Prospective, single center, observational study from 2013 to 2014.
Setting – Urban private referral hospital.
Animals – Eighteen and 19 client-owned dogs and cats, respectively, sustaining blunt trauma within 8 hours of presentation without prior resuscitation; 17 healthy staff and client-owned control cats
Methods – Blood samples were collected upon presentation for measurement of blood gas, lactate, blood glucose, ionized calcium, PCV, total plasma protein, prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, platelet count, and thromboelastography.
Results – ATC was diagnosed in 1 dog and 1 cat on presentation. Hypercoagulability was documented in 4/18 (22%) of dogs and 1/19 (5.3%) of cats. In dogs, prolongation of PT ($P = 0.018$), aPTT ($P = 0.013$) and decrease in maximum amplitude (MA) ($P = 0.027$) were significantly associated with injury severity as measured by the animal trauma triage (ATT) score. In cats, PT, aPTT, MA, and clot strength (G) were not associated with injury severity. In cats, increasing blood glucose and lactate were significantly associated with decreasing MA ($P = 0.041$, $P = 0.031$) and G ($P = 0.014$, $P = 0.03$). In both dogs ($P = 0.002$) and cats ($P = 0.007$), fibrinogen concentration was significantly correlated with G.
Conclusions – ATC is rare in minimally injured dogs and cats following blunt trauma. In dogs, ATT score is significantly associated with PT, aPTT, and MA, suggesting an increased risk of ATC in more severely injured animals. ATT score does not appear to predict coagulopathies in cats. Future studies including more severely injured animals are warranted to better characterize coagulation changes associated with blunt trauma.

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Keywords: animals, hemostatic derangement, injury severity, TEG

Abbreviations

AFAST	abdominal-focused assessment with sonography for trauma
aPTT	activated partial thromboplastin time
ATC	acute traumatic coagulopathy
ATT	animal trauma triage
BE	base excess
BG	blood glucose
ER	emergency room
G	clot strength
HCC	healthy control cats
ISS	injury severity score
MA	maximum amplitude
PT	prothrombin time
ROTEM	rotational thromboelastometry
SBP	systolic blood pressure
TEG	thromboelastography
TFAST	thoracic-focused assessment with sonography for trauma

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Introduction

In human trauma patients, uncontrolled hemorrhage is responsible for more than 50% of all deaths within the first 48 hours of hospital admission.[1] Coagulation abnormalities are present in up to 25–34% of human major

trauma victims at the time of hospital presentation and the presence of coagulopathy on admission is associated with increased morbidity (eg, transfusion requirements and development of multiorgan failure) and a 3–4 times greater likelihood of mortality.[2–5] Twenty-nine percent of all human trauma patients with coagulopathy develop multiorgan dysfunction syndrome (MODS) during hospitalization, compared to only 12% of patients without significant derangements of coagulation.[2] Coagulopathy in this patient population was historically attributed to hemodilution, progressive acidosis and hypothermia, and systemic inflammation developing during and in part secondary to initial resuscitative efforts. While resuscitative injury has certainly been demonstrated to be a major factor in coagulopathy following trauma, documentation of coagulopathy in many trauma patients prior to resuscitative efforts has prompted further investigation into underlying causes. The term "acute traumatic coagulopathy" (ATC) has been used to describe the endogenous impairment of hemostasis occurring after traumatic injury prior to resuscitation. ATC is predominantly believed to be an anticoagulative and hyperfibrinolytic state resulting from tissue hypoperfusion and thrombin/thrombomodulin complex mediated activation of protein C.[6,7]

Illness severity scoring systems can be utilized in addition to coagulation testing in trauma patients to predict risk of developing ATC and outcome. Human studies have related increased trauma scores with a higher frequency of coagulopathy.[2,5,8,9] In Brohi's 2003 study that first described ATC as a unique condition following trauma, patients with an Injury Severity Score (ISS) > 15 (indicative of more severe injury) had a 33% incidence of coagulopathies when compared to an incidence of 10.8% in patients with a lower ISS.[8] This figure increased to 67% for those with an ISS over 45.[8] Mortality has been shown to be higher in people with coagulopathy across all grades of the ISS, highlighting the importance of early recognition and treatment of coagulopathies.

There are few studies evaluating the coagulation status of veterinary patients following trauma. The limited existing data focus solely on dogs and suggest that hemostatic abnormalities are present following trauma.[10–13] To the authors' knowledge, there are no studies evaluating for the presence of ATC in cats following trauma. Recently, 2 prospective studies evaluating dogs following blunt trauma were published.[12,13] A total of 70 dogs were included between these 2 studies. The first study, including 30 dogs, had more narrow inclusion criteria, enrolling only those dogs with animal trauma triage (ATT) scores ≥5 that had not received prior resuscitation.[12] One-third of these dogs (10/30) were hypercoagulable based on clot strength (G) value (ie, G as assessed by thromboelastography [TEG]) and

the remaining dogs were normocoagulable. No dog had coagulation parameters suggestive of hypocoagulability, potentially due to insufficient numbers of severely injured dogs. Injury severity was calculated for each patient but was not included in statistical analysis with coagulation parameters other than the G value.[12] The second study, a multicenter study including 40 dogs, allowed enrollment of those animals that had received fluid therapy prior to collection of study blood samples.[13] It is likely that some of the dogs in this study may have developed iatrogenic coagulopathy secondary to dilution from resuscitation in addition to ATC. A small percentage of injured dogs in this cohort study demonstrated hypocoagulable states as indicated by thrombocytopenia, prolonged activated partial thromboplastin time (aPTT), or TEG tracing abnormalities.[13] Illness severity as assessed by the Acute Patient Physiological and Laboratory Evaluation (APPLE) fast score positively correlated with aPTT and injury severity as assessed by ATT score was inversely correlated with fibrinogen concentration. No dog was hypercoagulable in this study.[13] The variable inclusion and exclusion criteria across these 2 studies raise the possibility that separate populations of injured dogs were evaluated.

The objectives of this study were to evaluate for the presence of ATC in cats following blunt trauma and to contribute to the limited data pertaining to ATC in dogs following blunt trauma. A secondary objective was to correlate coagulation variables with injury severity and other admission variables in both species. We hypothesized that ATC would be present in both dogs and cats following severe trauma and that patients of either species with higher injury severity or those in shock states would be more likely to develop ATC.

Materials and Methods

This study was a prospective observational study during a 15-month study period from April 2013 to August 2014 in the emergency room (ER) at the Animal Medical Center. Informed client consent was obtained prior to enrollment and the internal Institutional Animal Care and Use Committee approved all aspects of the study.

Study population
All dogs and cats presenting to the ER after sustaining blunt trauma were considered for study inclusion. Animals were eligible if they had not received intravenous fluids or blood products prior to presentation, the traumatic event was blunt force in nature and had occurred within 8 hours of presentation, and there was no known or suspected preexisting cause for coagulopathy. Animals were excluded if they were receiving any medications that might influence the results of coagulation

testing. Animals were also excluded if they presented to the hospital during the overnight hours when TEG analysis was not available.

Recorded variables

Clinical variables recorded on presentation included signalment, body weight, rectal temperature, systolic blood pressure (SBP) measured by Doppler, approximate time since trauma, type of blunt trauma, and ATT score. Laboratory variables recorded included venous PCV, total plasma protein, plasma lactate, blood glucose (BG), ionized calcium (iCa), base excess (BE), blood pH, PCO_2, platelet count, prothrombin time (PT), aPTT, fibrinogen, and TEG values. Additional diagnostic tests including radiographs, ultrasound and further bloodwork were performed at the discretion of the primary clinician.

For all included animals ATT score was determined on arrival. Dogs and cats were assigned scores ranging from 0 to 3 in each of 6 categories: perfusion, cardiac, respiratory, eye/muscle/integument, skeletal, and neurologic, with higher scores corresponding to more severe injuries as previously described.[14]

Blood collection

Blood samples were obtained immediately upon presentation to ER. The samples were obtained from the cephalic vein using a syringe upon intravenous (IV) catheter placement and prior to its use. If an IV catheter was not placed or if an adequate volume of blood could not be obtained from the IV catheter, direct venipuncture of a cephalic or saphenous vein was performed using a butterfly needle. The needle or catheter size was not recorded. Approximately 2–3 mL of blood was collected from each study participant and placed, in no particular order, into either two 3.2% sodium citrate tubes or 3.8% sodium citrate tubes for a final blood to citrate ratio of 9:1 for coagulation analyses (PT, aPTT, fibrinogen) and TEG, one EDTA tube (0.5 mL) for platelet count,[a] and 1 plastic lithium heparin syringe for venous blood gas, electrolytes, and lactate values using the Siemens Rapid Point 500.[b] One citrated tube was sent to the in-house laboratory for TEG analysis. The blood in the second citrated and the EDTA tubes was either used immediately to measure PT, aPTT, fibrinogen concentration, and platelet count, or, stored at 4°C overnight (between 4 and 8 hours) before being analyzed. Citrated blood samples were analyzed using the Stago Start 4 Hemostasis Analyzer[c] for PT, aPTT, and fibrinogen concentrations and were compared to preestablished institutional controls.

Thromboelastography

The Thromboelastograph (TEG) Hemostasis System 5000[d] was employed with 1:50,000 dilution of recombi-

nant tissue factor used for activation. TEG samples were maintained at room temperature for 30 minutes prior to analysis. TEG variables (reaction time [R], coagulation time [K], α angle [α], maximum amplitude [MA], and G) were determined using a computerized analyzer system. Manual pipetting for TEG analysis was performed by 2 clinical pathology operators using standardized protocols. Canine TEG reference intervals determined by the laboratory were used for comparisons. The G-value was calculated using the equation $G = 5,000 \times MA/(100 - MA)$, with an established reference interval of 3,300–9,300 Kdyn/cm^2. Animals were categorized as hypercoagulable based on MA and G values above the reference intervals and as hypocoagulable based on MA and G values below the reference intervals.

Acute traumatic coagulopathy

ATC was defined as a derangement in coagulation characterized by the presence of 2 or more of the following upon presentation: PT or PTT >1.5 times the upper limit of the reference interval or MA or G values less than the lower limit of the reference interval.

Healthy control cats

Seventeen healthy control cats (HCC) were used to develop a reference interval for TEG parameters.[15] These HCC were staff- and client-owned cats of varying ages with no known medical issues based on physical exam, complete blood count, and serum biochemistry profile results.[a,e]

Statistical methods

Descriptive statistics for the populations are presented as median values (range) for both normally and non-normally distributed variables. Kolmogorov–Smirnoff test was used to assess for normality in the patient populations. Mean differences between species for a given clinical response variables were analyzed with a one-way ANOVA. Simple linear regression was used to analyze the effect of continuous clinical variables on the 4 criteria used to define ATC (PT, aPTT, MA, and G) in separate models. Error residuals were analyzed for normality by visual inspection and Kolmogorov–Smirnoff and passed for models describing the effect of clinical variables on PT, aPTT, MA, and G for the ordinary least squares regression. All analyses were carried out for the dog and cat populations separately. All analyses were considered significant with a $P < 0.05$.

Results

Eighteen dogs and 19 cats were enrolled in the study between April 2013 and August 2014. No animal of either

species received any medications or treatment prior to presentation. Median time from the traumatic event to presentation was 90 minutes (range, 30–480 min).

Study populations

Of the 18 enrolled dogs, 4 were neutered males, 4 were intact males, 7 were spayed females, and 3 were intact females. Median age was 3.8 years (range, 0.58–12.5 years). Breeds included 4 Yorkshire Terriers, 3 Chihuahuas, 2 mixed breeds, and 1 of each of the following: Siberian Husky, Labrador Retriever, Pomeranian, Boston Terrier, Shiba Inu, Cocker Spaniel, Wheaten Terrier, pitbull, and Tibetan Terrier. Sixteen dogs presented following vehicular trauma, while 2 fell from a height.

Of the 19 enrolled cats, 5 were neutered males, 5 were intact males, and 9 spayed neutered females. The median age was 1.9 years (range, 0.5–14.75 years). Breeds included fourteen Domestic shorthairs, 2 Siamese, and 1 of each of Domestic longhair, Abyssinian, and American shorthair. Eighteen of 19 cats presented after falling from a height and 1 presented following vehicular trauma. The median height from which cats fell was 5 stories (range, 3–14 stories).

Injury severity

The median ATT score for all study subjects was 3.5, with median values for dogs and cats of 4 and 3, respectively (range, 0–15) (Table 1). Nine of 18 (50%) dogs had evidence of polytrauma, with injuries to multiple areas including the abdomen, thorax, extremities, or head. Seven (38.8%) dogs had pelvic or long bone fractures. Three of 18 dogs (16.6%) presented with traumatic brain injury. One dog (5.55%) presented with a proptosed eye as the sole injury. Twelve (66.7%) dogs had thoracic radiographs performed. Pulmonary contusions, pneumothorax, and diaphragmatic hernia (DH) were diagnosed in 3/12 (25%), 1/12 (8.3%), and 1/12 (8.3%), respectively. Five of 18 (27.7%) had extremity radiographs, with 3/5 (60%) demonstrating fractures of the hind limb and 2/5 (40%) demonstrating soft tissue swelling and subluxation of the carpi. Three (16.6%) dogs had pelvic radiographs that demonstrated multiple pelvic fractures in all 3 patients. One dog (1/18, 5.5%) had injuries limited to mild, superficial abrasions. Initial laboratory values indicated that no dog was anemic. No dogs in this study received blood products. Initial physical examination and selected hematologic variables are listed in Table 1.

Twelve of 18 (66.6%) and 4/18 (22.2%) dogs had abdominal-focused assessment with sonography for trauma (AFAST) and thoracic-focused assessment with sonograpy for trauma (TFAST), respectively. One dog (8.3%) had evidence of abdominal fluid on AFAST and was found to have a hemoabdomen via centesis.

One (25%) dog had an abnormal TFAST with evidence of abdominal organs in the thoracic cavity. Thoracic radiographs confirmed the presence of a diaphragmatic hernia.

Ten of 19 (52.6%) cats presented with polytrauma with injuries to multiple areas including the abdomen, thorax, extremities, and/or head. Eight (42.1%) cats had suspected (4/8, 21%) or confirmed (4/8, 21%) injuries referable to the pelvis or extremities. Of these 8 cats, 2 had pelvic radiographs taken and 2 had extremity radiographs. Pelvic radiographs confirmed multiple pelvic fractures in both cats and extremity radiographs demonstrated a left radius fracture and right tibial and fibular fractures in the 2 cats, respectively. Three of 19 (15.7%) had evidence of oral/facial trauma. All 3 of these cats had fractured teeth, with one each having a fractured mandible and a fractured hard palate. Five (26.3%) cats had thoracic radiographs. Rib fractures, pulmonary contusions, and pneumothorax were diagnosed in 1/5 (20%), 3/5 (60%), and 3/5 (60%) cats, respectively. Initial laboratory data indicated that no cat was anemic initially upon presentation to the ER. However, 2 (10%) cats received blood product transfusions during hospital stay. Initial physical examination and selected hematologic variables are listed in Table 1. Nine (47.3%) cats had AFAST performed and 2/9 (22.2%) were positive for abdominal fluid.

Control population healthy cats

Seventeen HCC were enrolled as controls to establish a reference interval for the institution's TEG assay: 8 neutered male, 8 spayed female, and 1 intact female. Median age was 6 years (range, 1.6–11 years). When compared to the age of the study population of cats, there was a significant difference in age between groups ($P = 0.007$), with HCC being significantly older. All coagulation testing, CBC, and serum biochemistry results for HCC were within reference intervals.

Coagulation testing

Complete coagulation parameter results are summarized in Table 1. One dog (5.5%) was diagnosed with ATC based on both prolonged PT and aPTT and decreased MA and G values. This dog also had a markedly decreased fibrinogen. Four of 18 (22.2%) dogs were hypercoagulable based on MA and G values and all 4 of them had fibrinogen concentrations greater than the reference interval. Thirteen (72.2%) dogs had normal TEG profiles.

One cat (5.2%) was diagnosed with ATC as evidenced by prolongations in both PT and aPTT. This patient had MA and G values at the low end of normal, bordering on hypocoagulable. This cat also demonstrated a markedly decreased fibrinogen concentration. One (5.26%) cat in our study population was hypercoagulable based on MA

Table 1: Physical exam, hematologic, and coagulation variables recorded in dogs and cats at presentation to the emergency room within 8 hours of trauma

Parameter	N	Median	Range	Reference range
Dogs				
Age (years)	17	4.16	0.58–12.5	n/a
Rectal temperature (°C[°F])	17	38.5 [101.4]	34.5–40 [94.2–104]	37.5–39.2 [99.5–102.5]
SBP (mm Hg)	11	120	78–196	>90
PCV (%)	17	52	40–60	35–55
TPP (g/L[g/dL])	17	70 [7]	51–90 [5.1–9.0]	60–75 [6–7.5]
Lactate (mmol/L)	18	5.07	1.31–9.89	0.5–2
BG (mmol/L[mg/dL])	18	6.5 [118.5]	5.2–19.8 [95–358]	3.6–6.2 [65–112]
pH	18	7.28	7.17–7.431	7.35–7.46
BE (mmol/L)	18	−5.35	(−17.2) to (+1.2)	(−1.2) to (+1.1)
iCa (mmol/L)	18	1.09	0.81–1.38	0.9–1.3
Platelets (×10³/μL)	9	225	151–411	143–448
Fibrinogen (g/L [mg/dL])	16	1.68 [168]	0.42–3.83 [42–383]	0.9–2.55 [90–255]
PT(s)	16	7.45	5.6–29.9	6.3–13.3
aPTT (s)	16	10.4	8.5–120	10.6–16.8
R (min)	18	3.2	1.3–6.2	1.6–6.2
K (min)	18	1.9	1.1–15.1	1.4–6.1
α angle (°)	18	65.4	22.2–74.5	42–69.
MA (mm)	18	59.9	21.2–76.8	40–65.8
G (Kdyn/cm²)	18	7,600	1,300–16,600	3,300–9,600
ATT score	18	4	0–10	0–18
Cats				
Age (years)	19	1.9	0.5–14.75	n/a
Rectal temperature (°C[°F])	19	38 (100.5)	35.5–40 [95.9–104.1]	37.5–39.2 [99.5–102.5]
HR (per minute)	12	205	140–270	140–240
SBP (mm Hg)	7	70	60–120	>90
PCV (%)	16	43	35–53	30–45
TPP (g/L [g/dL])	16	67 [6.7]	58–84 [5.8–8.4]	60–75 [6–7.5]
Lactate (mmol/L)	13	2.05	1.3–4.42	0.5–2
BG (mmol/L [mg/dL])	13	9.05 [163]	3.4–15.9 [62–287]	3.7–9.3 [67–168]
pH	13	7.29	7.213–7.414	7.31–7.46
BE (mmol/L)	13	−5.6	(−10.1) to (−2)	(−1.5)- (+1.5)
iCa (mmol/L)	13	1.08	0.79–1.26	0.9–1.3
Platelets (×10³/μL)	8	260	71–358	155–641
Fibrinogen (g/L [mg/dL])	16	1.27 [127.5]	0.48–3.54 [48–354]	0.87–3.4 [87–340]
PT (s)	16	10.65	8.8–20.2	7–12.7
aPTT (s)	16	14.65	11.2–37.1	10.1–28
R (min)	19	6.9	4.0–14.0	1.2–8.3
K (min)	19	2.1	1.1–5.6	0.8–3.4
α angle (°)	19	60.7	32.9–72.3	50.4–80.1
MA (mm)	19	61.6	39.9–75	39.7–72.4
G (Kdyn/cm²)	19	8,000	3,300–15,000	3300–13,100
ATT score	19	3	0–15	0–18

HR, heart rate; SBP, systolic blood pressure; ATT, animal trauma triage score; PT, prothrombin time; aPTT, activated partial thromboplastin time; R, reaction time; K, coagulation time; α, α angle; MA, maximum amplitude; G, clot strength; BE, base excess; TPP, total plasma protein; BG, blood glucose.

and G values. This patient had a fibrinogen concentration greater than the reference interval. Seventeen (89.47%) cats had TEG profiles within the reference interval.

Associations
Dogs

ATT was correlated with each of the following: PT ($r^2 = 0.58, P = 0.018$), and aPTT ($r^2 = 0.601, P = 0.013$). ATT was inversely correlated with the following: MA ($r^2 = 0.519, P = 0.027$) and fibrinogen concentration ($r^2 = 0.475, P = 0.06$).

ATT score was significantly associated with higher PT ($P = 0.018$), where for every one unit increase in ATT, the PT was expected to increase by 1.218 seconds. Similar observations were made for aPTT ($P = 0.013$), where for every 1 point increase in ATT, the aPTT was expected to increase by 6.018 seconds (Table 2). ATT score

Table 2: Simple linear regression of coagulation variables with significantly correlated admission variables at the time of emergency room presentation within 8 hours of trauma in dogs and cats

ATC definition	Variable	Estimate	*P* value
Dog			
PT	ATT	1.218	0.018
aPTT	ATT	6.018	0.0137
MA	ATT	−2.309	0.027
G	Fibrinogen	0.024	0.002
	Age	0.064	0.0008
Cat			
MA	Lactate	−5.768	0.031
	BG	−0.072	0.041
	Fibrinogen	0.071	0.018
G	Lactate	−1.9	0.03
	BG	−0.023	0.014
	Fibrinogen	0.024	0.007

ATC, acute traumatic coagulopathy; ATT, animal trauma triage score; PT, prothrombin time; aPTT, activated partial thromboplastin time; R, reaction time; K, coagulation time; α, α angle; MA, maximum amplitude; G, clot strength; BG, blood glucose.

was significantly associated with lower MA (*P* = 0.027) (Table 2). There was also statistically significant association between G value and fibrinogen concentration (*P* = 0.002) and G value and age (*P* = 0.0008) (Table 2). No other admission variable was demonstrated to relate with any of the coagulation variables.

Cats

ATT score was not correlated with any of the aforementioned coagulation variables. None of the covariates showed significant correlation with PT or aPTT. Lactate concentration was significantly associated with lower MA (*P* = 0.031) and G (*P* = 0.03) values such that for every 1 unit increase in lactate, MA, and G are expected to decrease by 5.768 mm and 1.9 units, respectively. BG was significantly associated with lower MA (*P* = 0.041) and G (*P* = 0.014) values such that for every 1 unit increase in BG (in mg/dL), MA and G are expected to decrease by 0.072 mm and 0.023 units, respectively. Fibrinogen concentration was significantly associated with MA (*P* = 0.018) and G (*P* = 0.007) values, such that for every 1 unit decrease in fibrinogen concentration, MA and G values are expected to decrease by 0.071 mm and 0.024 units, respectively (Table 2). No other admission variables was demonstrate to relate with any of the coagulation variables

Discussion

In the current investigation, ATC, as defined by prolonged PT, aPTT, or decreased MA and G values prior to resuscitative efforts, was documented in 1 dog and 1 cat following blunt trauma. Of the dogs in our study, 13/18 (72%) had normal coagulation parameters, 4/18 (22%) were hypercoagulable, and 1/18 (5.5%) was hypocoagulable on presentation, based on TEG tracings. Of the study cats, 17/19 (89.47%) had normal coagulation parameters, 1/19 (5.26%) was hypercoagulable and 1/19 (5.26%) was hypocoagulable based on TEG tracings. Although the sample size is small, this spectrum of coagulopathies is similar to what has been identified in human studies.[16-19] ATC appears to be a dynamic process, progressing through hypercoagulable, hypocoagulable, and hyperfibrinolytic phases.[16] The type of coagulation derangements in human patients also appears to vary with illness severity, in that higher ISS correlated with hypocoagulation, while mild to moderately injured patients are more likely to show normo- or hypercoagulation.[16-18] A prospective observational study of 80 human trauma patients compared TEG and biomarker profiles upon hospital admission. In this study, trauma patients had normal (86%), hypercoagulable (11%), and hypocoagulable (1%) TEG clot strength. Hypercoagulable patients had higher age, fibrinogen, and platelet count.[16] Kaufmann et al recorded TEG results, PT, aPTT, platelet count, ISS, blood product transfusions, and outcome in 69 adult human patients following blunt force trauma.[17] Of the 52 patients with abnormalities identified on TEG, 86% were hypercoagulable and only 11.5% were hypocoagulable. In both of these studies, ISS correlated with TEG tracings with the hypercoagulable patients having moderate ISS scores and the hypocoagulable patients having higher ISS scores.[2-16]

In veterinary medicine, Abelson et al identified 33% of dogs as hypercoagulable based on the G value following moderate-to-severe trauma.[12] That study did not identify any dogs as being hypocoagulable and found no correlation between G value and ATT score.[12] Sixty percent of enrolled patients had ATT scores of 5 or 6 and the highest ATT score was 12.[12] The most recent prospective multicenter study of severely traumatized canine patients identified ATC (as defined by 2 or more of the following: activated clotting time >105 seconds, platelet count < lower limit, PT or aPTT >1.5 times the upper limit of the reference interval, and MA or α < the lower limit of the reference interval) in 15% of dogs at admission to the ER.[13] ATC was present more commonly in dogs with increased disease severity (as measured by APPLE-fast score), decreased SBP, and increased lactate concentration.[13] Fibrinogen concentration was negatively correlated with ATT score. This study did not identify any dogs as being hypercoagulable. This study, however, included patients that had received fluid therapy prior to sample collection.[13] Therefore, effects of resuscitative efforts on patient

coagulation status could not be discounted in this patient cohort.

One of the hypotheses of the present study was that increased ATT score would correlate with the presence of ATC. Positive associations between injury severity and coagulopathy have been documented in multiple human studies.[2,3,7,8] Similarly, Holowaychuk et al demonstrated moderate correlation between disease severity, as measured by APPLE-fast score, and increased aPTT.[13] The underlying explanation for these correlations between illness severity and ATC in both people and animals is believed to result from more severe tissue injury and hypoperfusion evident in more severely injured populations. For the dogs in the current study, ATT showed correlation with PT, aPTT, and MA in univariate analysis. This result differs from the Abelson et al study of traumatized dogs, which showed no correlation with ATT score and G.[12] However, the Abelson et al study did not assess for correlation with ATT score and other coagulation parameters (PT, aPTT, and MA). In contrast to dogs, in the present study, illness severity demonstrated no relationship with the presence of ATC in cats. A likely explanation for this lack of correlation is due to small sample size leading to increased risk of a type II error. The number of severely injured animals of both species was minimal in the current study, offering a likely explanation for the low incidence of ATC.

Scoring systems such as ATT rely on utilization of vital signs and physical examination parameters in order to generate a score. However, traditional vital signs alone may not be reliable markers of decreased perfusion due to rapid activation of compensatory mechanisms.[20-21] Therefore, excessive reliance on illness severity scoring systems in trauma patients can lead to underrecognition of those with occult shock and may underestimate the degree of injury. The current study included all trauma patients, regardless of ATT score in an attempt to collect as much data as possible and to decrease the possibility excluding those cases of occult shock, even though these animals were unlikely to have ATC. Occult hypoperfusion is characterized by an imbalance between tissue oxygen demand and oxygen delivery.[21] When oxygen delivery is inadequate to meet normal tissue demands, anaerobic metabolism and subsequent metabolic acidosis occurs, leading to a decrease in BE and pH and an increase in lactate.[21] Ongoing shock, as evidenced by temperature ≤35°C, SBP ≤ 90 mm Hg, or BE < −10 mmol/L in human trauma patients has been recently reported to be associated with a threefold increased risk of developing coagulopathy following trauma.[5] In contrast, humans patients without shock have been shown to have normal coagulation parameters on presentation even with severe ISS.[7] The purported mechanism underlying shock-induced coagulopathy is

activation of protein C (aPC) after increased thrombomodulin activity as well as hyperfibrinolysis due to aPC consumption of plasminogen activator inhibitor-1 and reduced activation of thrombin-activatable fibrinolysis inhibitor.[6] The relationship between perfusion and coagulation following trauma demonstrated in people has recently been investigated in dogs. Holowaychuk et al found increased plasma lactate concentration, negative BE, and decreased pH to be moderately correlated with increases in aPTT and activated clotting time, decreased MA and α.[13] In the present study, although ATT score was not associated with coagulation variables in cats, increased plasma lactate concentration was associated with lower MA and G values, suggesting hypoperfusion may be associated with decreased G. Other indicators of poor perfusion such as rectal temperature, BE, SBP, and pH did not show correlation with coagulation variables in either species. Future studies with higher numbers and more severely injured dogs and cats are needed to further investigate the association between traumatic shock and severe tissue hypoperfusion and development of ATC as the present study had only a limited number of patients with severe shock.

In the cat study population, BG was significantly correlated with MA and G values. With every 1 point increase in the BG (in mg/dL), the MA decreased by 0.072 mm and the G decreased by 0.02 units, implying that patients with higher BGs have decreased G as indicated by these TEG parameters. Hyperglycemia following trauma is thought to result mainly from stress-induced increases in counterregulatory hormones such as glucagon, cortisol, and epinephrine, which serve to increase gluconeogenesis and has been shown to be associated with severity of head trauma in dogs and cats.[22] It is possible that the degree of hyperglycemia could have correlated with injury severity, explaining why the more hyperglycemic cats had lower G. As previously discussed, ATT score alone may not adequately reflect injury severity.

In the present study in dogs and cats, lower fibrinogen concentration was significantly associated with decreased MA and G values. These results are in agreement with the human studies, which have documented a critical threshold for fibrinogen of 1.5 g/L (150 mg/dL), below which patients exhibit increased bleeding tendencies due to decreased G.[23] Traumatized people have decreased fibrinogen concentrations in the early post-injury phase, and recent findings suggest that fibrinogen availability may play an important role in the survival of trauma patients.[23-25] Fibrin is essential to stabilize the initial fragile platelet plug to prevent secondary bleeding. Profound activation of fibrinolytic pathways and fibrinogen depletion appear to be fundamental processes in the development of ATC and offer potential

therapeutic targets.[23] However, therapeutically targeting fibrinogen concentration via administration of transfusion products concentrated with this factor has not yet been demonstrated to improve outcome in human patients with ATC.

Diagnostic criteria for ATC are variable and study-dependent and sensitive coagulation tests are not always readily available at the patient bedside. These factors contribute to the difficulty in achieving a diagnosis of ATC in trauma patients. The more common definitions of ATC include prolonged PT and aPTT by 50%, platelet count < 100,000, international normalized ratio (INR) >1.5, PT ratio (patient PT/mean laboratory PT) >1.5, fibrinogen concentration < 1 g/L, and reduced G as measured by TEG or rotational thromboelastometry (ROTEM).[25-28] Thromboelastometry and TEG are considered more global tests of coagulation when compared to tests such as PT and aPTT. Viscoelastic tests are able to evaluate all components of the coagulation process from fibrin formation to fibrinolysis, while PT, aPTT, and INR are only sensitive at identifying hypocoagulation. In one prospective study of human trauma patients, PT and PT ratio were only slightly prolonged in approximately 30% of the most severely injured patients identified as having ATC based on ROTEM.[28]

The major limitation of this study was that all blunt trauma patients were included, regardless of injury severity or perfusion status (19/37 [51.3%] enrolled patients were minimally injured, with ATT scores ≤3). As previously discussed, the primary initiators of ATC are considered to be severe tissue injury and profound hypoperfusion. Thus, it should follow that patients with minimal injuries and adequate perfusion would not have ATC. This likely explains the low incidence of ATC documented in the study participants. Another limitation of our study was reliance on a single admission ATT score to assess injury severity in traumatized dogs and cats. Initial injuries can be extensive and subsequent tissue trauma, inflammation, and hypoperfusion may be dynamic, progressive, and possibly occult. While ATT score was not associated with coagulation variables in cats, plasma lactate and BG concentrations, both potential indicators of increased injury severity, were associated with decreased MA and G. Serial illness severity scores, and incorporation of this score into a more global assessment of the patient that includes physical examination, bedside laboratory tests such as lactate BE and central venous oxygen saturation, A/TFAST and BP measurements to assess severity of illness, may be more sensitive at accurately assessing trauma patients. A further limitation was the absence of significant data from electronic medical records. Some coagulation values were missing due to sample handling errors (2 dogs

and 3 cats). The authors chose to include these animals in the study as they all had normal TEG tracings. It is thus possible that there could have been an underestimation of animals with prolonged PT and aPTT values, although this would appear less likely with normal TEG tracings. While every patient had all vital signs assessed during triage and complete physical examination, some of the information was inadvertently not recorded in the medical record. However, the accuracy of the ATT score calculations was not affected as these scores were assigned immediately on patient presentation.

A potential additional study limitation included the use of different concentrations of sodium citrate tubes for coagulation testing. There is conflicting data on whether citrate concentration affects coagulation parameters. Two human studies concluded that the use of 3.2% sodium citrate is preferable to 3.8% sodium citrate.[29-30] Conversely, veterinary data in dogs suggest little to no significant difference between concentrations of sodium citrate.[31-32] Recent veterinary guidelines on rotational viscoelastic assays conclude that there is insufficient evidence to recommend using one citrate concentration over another, and no identified study in people or animals specifically examined the impact of citrate concentration on TEG/ROTEM results.[33] However, it would seem prudent, especially for the purposes of research, to choose one concentration of citrate for coagulation testing. This could serve to ameliorate any inconsistencies secondary to concentration differences. In this study, both 3.2% and 3.8% sodium citrate were used and this could have led to minor discrepancies in coagulation test results. The current recommendation is to store citrated tubes for no more than 4 hours at 4°C prior to performing coagulation testing. Approximately 20% of citrated plasma samples in this study were refrigerated for 4–8 hours overnight prior to coagulation testing. This also may have led to minor inconsistencies in these results.

A final, and likely less relevant study limitation was the difference in age between the study cats and the HCC. Reference intervals are an integral part of laboratory diagnostic testing and clinical decision making and represent estimated distribution from healthy populations of comparable individuals. Differences between study and control populations can contribute to inherent errors in data analysis. In the current study, there was a statistically significant difference in age between the HCC population and the cat study population. However, this is likely of limited clinical significance as all cats in both groups were adult cats; none were geriatric or pediatric and it is unlikely that TEG results would have differed significantly. The current study adhered to consensus guidelines from the 2011 American

Society for Veterinary Clinical Pathology (ASVCP) for determination of de novo reference intervals for the HC population.[15]

Conclusions

In this group of dogs and cats with overall low injury severity following blunt trauma, derangements in coagulation prior to resuscitation were rare. Although uncommon in this study population, ATC was documented in animals with severe injuries. In the dog population, injury severity as measured by ATT score was related with ATC as evidence by prolongation of PT and aPTT and decreased MA and fibrinogen concentration. In the cat population, injury severity did not relate with coagulation variables. Our limited data suggest that ATC is rare in dogs and cats that are minimally injured and advanced coagulation testing is likely unnecessary. Future studies with larger sample sizes and more severely injured animals are warranted to further characterize ATC in these veterinary populations as well as to assess for associations between the presence of ATC and morbidity and mortality following trauma.

Footnotes

[a] Sysmex America, Mundelein, IL.
[b] Siemens Rapid Point 500, Malvern, PA.
[c] StagoStart 4, Asnieres-Sure-Seine, France.
[d] TEG 5000, Thromboelastograph Hemostasis Analyzer, Haemonetics Corporation, Braintree, MA.
[e] Beckman-Coulter, AU 680, La Brea, CA.

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