Coagulopathy in Penetrating Ballistic Cranial Trauma: A 7-Year Experience

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BACKGROUND AND OBJECTIVES: Penetrating ballistic cranial trauma (PBCT) carries significant mortality when compared with blunt trauma. The development of coagulopathy in PBCT is a strong predictor of mortality. The goal of the study was to describe the incidence and risk factors of coagulopathy in PBCT and to report the value of tranexamic acid administration in PBCT.

METHODS: We retrospectively analyzed 270 patients who presented with PBCT to a single, Level 1 trauma center between 2016 and 2023.

RESULTS: A total of 47% (127/270) of patients with PBCT developed coagulopathy at presentation. Fifty-seven patients received tranexamic acid at presentation, which did not affect the development of coagulopathy. Coagulopathic patients were more likely to have more serious injury patterns (bihemispheric [adjusted odds ratio, aOR: 2.6 CI: 1.4-4.9, $P = .004$] or transventricular trajectories [aOR: 4.9 CI: 1.9-19.6, $P = .03$]). In addition, they presented with a larger base deficit (aOR: 0.9 CI: 1.002-1.2 per mEq/L, $P = .006$) which negatively correlated with the international normalized ratio (ρ: −0.46, $P < .0001$, Spearman correlation). Using thromboelastography helped to identify an additional 20% of patients who presented with normal coagulation on conventional testing.

CONCLUSION: Coagulopathy is prevalent in approximately 50% of patients with PBCT and is persistent despite treatment in a substantial subset of patients. The addition of thromboelastography with its increased coagulopathy sensitivity can potentially guide treatment more efficiently than traditional coagulopathy laboratory tests and fibrinogen alone. Patients with a significant base deficit on arterial blood gas are at higher risk for coagulopathy.

KEY WORDS: Coagulopathy, Gunshot, Penetrating trauma, TBI

Penetrating ballistic cranial trauma (PBCT) related to gun violence is a developing health crisis with rising incidence over the last decade.[1] It carries significantly higher mortality and morbidity when compared with blunt-related traumatic brain injury (TBI).[2] PBCT carries a unique set of management challenges in surgical decision-making and critical care.[3] Unfortunately, owing to limited experience in the civilian setting, management guidelines for PBCT have yet to be established.

One of the management challenges in PBCT is the development of coagulopathy. Coagulopathy in patients with PBCT occurs more frequently than blunt-related injuries[4] and can be as frequently as 70%.[5,6] In addition, it can be refractory to standard resuscitation strategies.[7] In addition, the development of coagulopathy is a strong predictor for mortality.[8,9] Limited experience dealing with PBCT has hindered the development of effective management strategies for PBCT-related coagulopathy.

We report on the largest retrospective cohort of PBCT regarding the development of coagulopathy and related risk factors. We also compare the utility of using thromboelastography (TEG) during triage with conventional methods and administering tranexamic acid (TXA).

ABBREVIATIONS: PBCT, penetrating ballistic cranial trauma; **TBI,** traumatic brain injury; **TEG,** thromboelastography; **TXA,** tranexamic acid.

METHODS

We conducted a retrospective analysis of patients suffering PBCT related to gunshot wounds at a single, Level 1 trauma center between 2016 and 2023 who were identified from the local trauma registry. Data

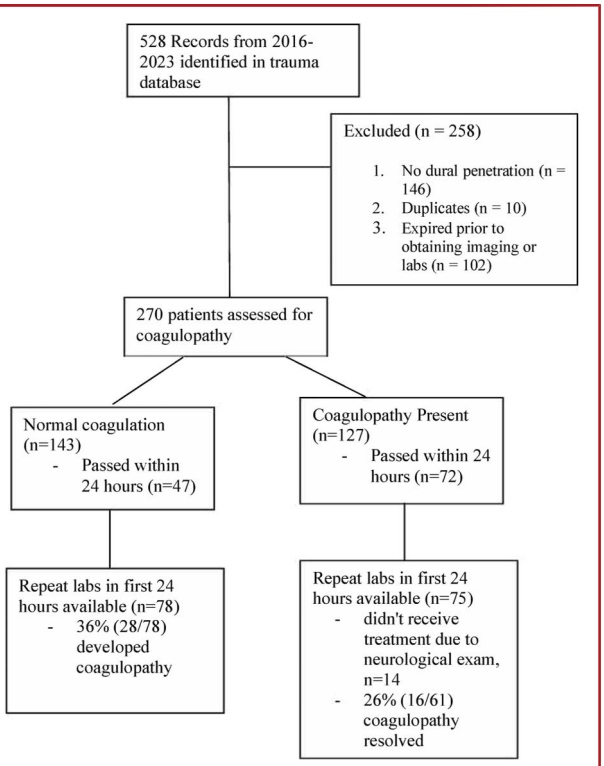

FIGURE. *Flow diagram detailing patient allocation for the study.*

were collected from electronic medical records. We included patients older than 16 years with evidence of dural penetration on computed tomography imaging. We excluded patients who died in the trauma bay before an initial work-up (n = 102). Figure details the cohort inclusion and exclusion. The study was approved by the local institutional review board; patient consent was waived.

The neurosurgical team collected data on patient demographics, medication status, and the Glasgow Coma Scale. We collected admission laboratory values collected in the trauma bay. Base deficit was based on arterial blood gas collected in the trauma bay. The injury severity score and abbreviated injury scores for each body part were obtained from the trauma quality database. We reviewed the initial noncontrast head computed tomography to assess for bullet trajectory and injury anatomy. We defined coagulopathy as any of the following: international normalized ratio >1.3, prothrombin time/partial thromboplastin time >1.5 times the upper limit, fibrinogen level <200 mg/dL, or platelet count <150 × 10^3/μL (based on our local laboratory definition of coagulopathy).

Repeat laboratory tests after resuscitation were available for a subset of patients (n = 153). Laboratory tests were collected 12 to 24 hours after presentation. Treatment was not initiated for 14 patients because of the withdrawal of care based on neurological examination, and those patients were excluded from the follow-up analysis.

We updated our PBCT protocol in 2019 to include the administration of TXA using the same dosing in the CRASH protocol.[10] While we included all patients with PBCT, adherence to the protocol was inconsistent in the first 2 years because of logistical issues during the pandemic. TEG was introduced at our facility in 2021 and was obtained on every patient with severe TBI. TEG measures the viscoelastic properties of blood during clot formation. We defined coagulopathy based on the following values and their interpretation: R-time >9.1 minutes (clotting factor activity), citrated functional fibrinogen amplitude <15 mm (fibrin clot strength), citrated rapid TEG amplitude <52 mm (platelet-fibrin clot strength), or clot lysis at 30 minutes > 2.6% (fibrinolysis). Reference values were based on TEG6 manufacturer values.

TABLE 1. Patient Characteristics for the Full Cohort (n = 270)

Variable	Mean (SD)/Count (%)
Age, y	34.6 (16)
Sex, male	233 (86.3%)
BMI	26.4 (6.2)
Bullet trajectory	
Unihemispheric or bifrontal	126 (47.4%)
Bihemispheric	99 (37.2%)
Posterior fossa	26 (9.8%)
Transventricular	15 (5.64%)
Race	
White	156 (57.8%)
Black	97 (35.9%)
Other	17 (6.3%)
Best motor examination	
M6	66 (24.4%)
M5	47 (17.4%)
M4	12 (4.4%)
M3	6 (2.2%)
M2	21 (7.8%)
M1	118 (43.7%)
Injury severity score	27.5 (9.6)
AIS other than head/face	1.8 (4.1)
Surgical decompression	73 (27%)
Received an ICP monitor	52 (19.3%)
Mortality, yes	163 (60.4%)
Mortality after 24 h	65 (24.1%)
Pupil examination	
Bilateral reactive	109 (40.5%)
Unilateral nonreactive	40 (14.9%)
Bilateral nonreactive	120 (44.6%)

AIS, abbreviated injury scale; BMI, body mass index; ICP, intracranial pressure.

TABLE 2. Patient Characteristics Comparison for the Development of Coagulopathy

Variable	No coagulopathy (n = 143)	Coagulopathy (n = 127)	*P* value
Age, y	36.3 (15.9)	32.6 (16)	.06
Sex, male	117 (81.8%)	116 (91.3%)	**.02**
Bullet trajectory			**<.001**
Unihemispheric or bifrontal	83 (58.9%)	43 (34.4%)	**<.001**
Bihemispheric	40 (28.4%)	59 (47.2%)	.0017
Posterior fossa	15 (10.6%)	11 (8.8%)	.60
Transventricular	3 (2.1%)	12 (9.6%)	.008
Sodium at presentation (mEq/L)	138 (4)	138 (5.6)	.96
Injury severity score	26.2 (9.8)	28.9 (9.3)	**.027**
AIS other than head/face	1.1 (2)	2.4 (5.5)	.26
Mortality, yes	61 (42.7%)	102 (80.3%)	**<.001**
Base excess (mEq/L)	−4.9 (6.2)	−7.9 (7.3)	**.0016**
Received TXA	31 (21.7%)	26 (20.5%)	.80

AIS, abbreviated injury scale; TXA, tranexamic acid.

We reported continuous data as mean and SD. We reported nominal values as count and percentage. We used *t*-tests to compare continuous data and χ^2 tests for nominal values. We correlated continuous variables using the Spearman correlation. We fit a multivariate logistic regression with coagulopathy at presentation as the response variable. We used significant variables from the univariate analysis as predictors. The analysis was performed using MATLAB (The Mathworks Inc.).

TABLE 3. Multivariate Logistic Regression Model for Development of Coagulopathy

Variable	OR (95% CI)	*P* value
Intercept	0.25 (0.07-0.9)	**.03**
Sex, male	1.9 (0.8-4.9)	.15
Bullet trajectory		
Bihemispheric	2.6 (1.4-4.9)	**.004**
Posterior fossa	4.1 (1.3-13.1)	**.02**
Transventricular	4.9 (1.2-19.6)	**.03**
Base excess (mEq/L)	0.9 (0.89-0.98)	**.006**
Body AIS	1.1 (1.002-1.2)	**.045**
ISS	0.99 (0.96-1.02)	.60

AIS, abbreviated injury score; ISS, injury severity score; OR, odds ratio.
χ^2 vs constant model: 31.5, *P* value < .001.

RESULTS

We identified 528 records from the trauma database with PBCT. Based on our inclusion and exclusion criteria, we included 270 patients in the analysis as detailed in Figure. Based on conventional laboratory testing, coagulopathy was identified at presentation in 47% (127/270) of the patients. Patient characteristics are described in Table 1. Fifty-seven patients received TXA at presentation in the trauma bay: 103 (176) minutes on average after arrival. Only 3 patients were taking antiplatelet or anticoagulant medication (aspirin 81 mg [n = 2] and rivaroxaban [n = 1]).

The vast majority of the patients suffered isolated head injuries with 219 (81.1%) having an abbreviated injury scale ≤2 extracranially. Extracranial injury severity was not significantly different between patient groups (Table 2).

Coagulopathic patients were more likely to be male, sustain a worse injury pattern (bihemispheric or transventricular), and pass away (Table 2). In addition, they presented with a larger base deficit. The degree of base deficit was negatively correlated with the international normalized ratio (ρ: −0.46, $P < .0001$, Spearman correlation). Coagulopathic patients were more likely to have a base deficit lower than 6 (62.8% vs 37.5%, χ^2: 16.2, $P < .0001$). On multivariate analysis only bullet trajectory, base excess and body abbreviated injury scale scores were significantly associated with the development of coagulopathy (Table 3).

Coagulopathic patients were resuscitated based on our institution's massive transfusion protocol and received 8 (10) units of product on average. For the subset of patients with repeated laboratory tests, 45/61 (73.8%) had persistent coagulopathy despite

TABLE 4. Patient Characteristics for Patients With Follow-Up Laboratory Tests in the First 24 h

	Coagulopathic at presentation			Normal coagulation at presentation		
Variable	Resolved coagulopathy (n = 16)	Persistent coagulopathy (n = 45)	*P* value	No coagulopathy (n = 50)	Secondary coagulopathy (n = 28)	*P* value
Age, y	31.6 (14.9)	29.9 (14.5)	.7	35.8 (16.4)	32.9 (12.3)	.40
Sex, male	13 (81.2%)	41 (91.1%)	.29	38 (76%)	26 (92.9%)	.06
Bullet trajectory			.97			.69
Unihemispheric or bifrontal	7 (43.8%)	16 (37.2%)		30 (60%)	17 (62.9%)	
Bihemispheric	6 (37.5%)	18 (41.9%)		12 (24%)	8 (29.6%)	
Posterior fossa	2 (12.5%)	6 (13.9%)		7 (14%)	2 (7.4%)	
Transventricular	1 (0.6%)	3 (0.7%)		1 (2%)	0 (0%)	
Platelet count at presentation ($\times 10^3/\mu L$)	232.1 (67.9)	149.8 (68.8)	<.001	266.2 (75)	223.1 (67.7)	**.01**
INR at presentation	1.2 (0.14)	1.9 (1.2)	.03	1.1 (0.1)	1.1 (0.1)	.40
Fibrinogen at presentation (mg/dL)	148.8 (51.4)	115 (73.9)	.14	349.9 (178.7)	279.8 (78)	.30
ISS	27.6 (10.7)	26.7 (5.9)	.5	27.46 (12.5)	24.3 (5.8)	.21
AIS other than head/face	4.9 (8.6)	2.9 (6.1)	.3	0.7 (1.4)	1.3 (2.3)	.17
Base excess (mEq/L)	−5.7 (4.5)	−8.4 (8.4)	.24	−3.95 (5.3)	−7.6 (7.1)	**.02**
Received TXA	3 (18.8%)	6 (13.3%)	.6	10 (20%)	8 (28.6%)	.40

AIS, abbreviated injury score; INR, international normalized ratio; ISS, injury severity score; TXA, tranexamic acid.

resuscitation. A lower platelet level at presentation was the only significantly different factor when compared with patients who resolved their coagulopathy (Table 4). Separately, 28/78 (35.9%) patients with normal coagulation at presentation developed coagulopathy at repeat testing. Patients with lower platelet counts and larger base deficits at presentation were significantly more likely to become coagulopathic (Table 4). We did not observe an association between TXA administration and prevention of coagulopathy or its resolution.

A subset of 39 patients had simultaneous TEG results at presentation, and 16 (41%) met our conventional criteria for coagulopathy. However, 21 (53.9%) had abnormal TEG results. Table 5 reports the concordance of the results across modalities.

TABLE 5. Test Concordance Between TEG and Conventional Coagulopathy Testing

Variable	TEG+	TEG−
Coag+	12	4
Coag−	9	14

Coag, coagulopathic; TEG, thromboelastography.

DISCUSSION

Our cohort represents the largest series investigating coagulopathy after gunshot-related PBCT. Our results showed that coagulopathy was closely tied to the admission base deficit. We also showed that PBCT-related coagulopathy can be refractory and can develop in a delayed fashion in a subset of patients. In addition, we compared the efficacy of novel and conventional testing strategies for coagulopathy in PBCT. Finally, we did not observe an association between the administration of TXA and resolving or preventing the development of coagulopathy.

Coagulopathy in PBCT has been well documented, with an incidence ranging between 35% and 70% across 320 subjects in 5 studies.[5,6,11-13] Our rate fell close to the population mean at 47% with our cohort size. Most prior studies relied on conventional testing for diagnosis. We showed that coagulopathy is persistent and difficult to correct, similar to previous reports.[8] In addition, we showed that a significant segment develops coagulopathy in a delayed fashion. This suggests the need for continued monitoring for coagulopathy, especially in patients with significant base deficits at admission.

We investigated the utility of TEG in the setting of PBCT. We found TEG diagnosed an additional 20% of patients who presented with normal coagulation on conventional testing. We observed another discrepancy in testing in patients with isolated

hypofibrinogenemia who had normal TEG results. Previous laboratory studies have shown high concordance between fibrinogen levels and their functional assay on TEG in normal circumstances.[14] This discrepancy can be explained by the fact that TEG measures the functional contribution of fibrin in creating clots which can be normal despite the quantitatively low levels measured using conventional testing. These findings suggest that TEG is more sensitive in the detection of coagulopathy and better at guiding resuscitation strategies, although it remains to be proven empirically. Folkerson et al[5] used TEG solely for diagnosing coagulopathy in PBCT and found a rate of 64%, supporting our findings of underestimating coagulopathy based on conventional testing.

PBCT is associated with substantial brain tissue damage and subsequent tissue factor release. Tissue factor has been implicated in the development of coagulopathy seen after TBI.[15] However, Cohen et al[16] show that the development of coagulopathy occurred more frequently in patients with significant hypotension as evidenced by their base deficit. Hypoperfusion causes derangements in the protein C pathway leading to coagulopathy in isolated TBI.[17] As PBCT has a significantly higher incidence of coagulopathy, base deficit can be used as a fast-screening method for more aggressive resuscitation for coagulopathy.

Finally, we reported on the use of TXA in PBCT. Despite the theoretical benefit of TXA in preventing coagulopathy and furthering bleeding, it has not been studied specifically in PBCT.[10] In fact, PBCT was an exclusion criterion in some of the trials for TXA in TBI.[18] Two case series reported its limited use in PBCT: Chen et al[11] with 12 patients and Mukerji et al[8] with 7 patients. Despite our significantly larger cohort of 57 patients receiving TXA, we did not observe any benefit for TXA administration for the prevention of coagulopathy. However, our allocation was not uniform because of provider preferences and changes to our protocol. The allocation bias and group imbalance make drawing conclusions regarding TXA effects difficult to support. Therefore, the use of TXA in gunshot-related PBCT remains an open question for future prospective studies.

Limitations

Our cohort is only retrospective, and TXA administration was not randomized. Selection bias in our data makes drawing conclusions regarding TXA unsupported. Repeat laboratory tests were not uniformly performed because our protocols changed over the years introducing selection bias regarding the rates of persistent and delayed coagulopathy. We did not investigate different resuscitation strategies to help with the treatment of coagulopathy.

CONCLUSION

Coagulopathy is prevalent in almost 50% of patients with PBCT and can be persistent despite treatment with blood products or TXA in a subset of patients. TEG is more sensitive in detecting coagulopathy and can potentially guide treatment more efficiently when used in conjunction with traditional coagulopathy laboratory tests and a fibrinogen assay. Patients with a significant base deficit are at higher risk for coagulopathy. TXA administration on arrival to the hospital does not seem to prevent the development of coagulopathy in PBCT.

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