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Clinical assessment of trauma-induced coagulopathy and its contribution to postinjury mortality: A TACTIC proposal

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The concept of impaired coagulation following injury has been the subject of scientific investigation for a century,¹ but defining the responsible mechanisms to guide precision-evidence management for distinct phenotypes remains elusive. In 2010, the National Institutes of Health (NIH), recognizing the ongoing knowledge gaps in the diagnosis and management of coagulopathy associated with severe injury, organized a workshop and arrived at a consensus to name this phenomenon trauma-induced coagulopathy (TIC). The common denominator of TIC-related research has been a laboratory-based strategy for quantifying and stratifying TIC. While detailed analyses of laboratory data related to TIC have been correlated with outcomes, there is a spectrum of coagulopathic phenotypes, and investigative efforts have been limited by the lack of (1) a standardized clinical scoring system for coagulopathy and (2) criteria for determining whether coagulopathy impacted postinjury mortality, that is, are they dying because they are bleeding or bleeding because they are dying.²

Rather remarkably, resuscitation strategies have emerged to treat a condition that remains a vague clinical entity that is presently defined by subjective surgeon assessment and blood product/transfusion requirements. Although clinical scoring systems for disseminated intravascular coagulopathy in sepsis exist,³ to date, no consensus statement regarding the clinical presentation of TIC has emerged. Standardized scoring systems for key clinical definitions, which can be quantified, validated, and tested for interrater reliability, are critical to progress in challenging clinical entities. As an example, there was little progress in understanding the fundamental mechanisms of multiple-organ failure (MOF) until a standard definition was developed.^{4,5}

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DISCLOSURE

The authors declare no conflicts of interest.

In recognition of the significance of TIC as a clinical problem, the NIH has funded the Trans-Agency Consortium for Trauma-Induced Coagulopathy (TACTIC) through the National Heart, Lung, and Blood Institute.⁶ TACTIC represents a consortium of investigators who have partnered in a collaborative effort between the NIH and the Department of Defense to investigate the problem of coagulopathy after trauma, ranging from large-scale clinical research studies at multiple sites to basic mechanistic laboratory investigations. In designing a multicenter study, it immediately became apparent that the lack of a unifying clinical definition of coagulopathy severity presents a major barrier to communication between investigators at various sites. Furthermore, interpretation of ongoing laboratory testing of coagulation should be compared in real time with clinical assessment of hemostasis. Finally, evidence exists to suggest that coagulopathy is, in part, driven by the anatomic location as well as mechanism of injury results in distinguishable phenotypes of TIC.⁷⁻⁹ As such, a robust scoring system to quantify the severity of coagulation disturbance, taking into account important clinical variables, is needed.

Quantification of impaired hemostasis and bleeding due to coagulation disturbance as opposed to surgical bleeding (uncontrolled arterial or venous disruption) is, at times, challenging and at risk of misclassification. To address the potentially subjective nature of this assessment and to provide a balanced assessment, we propose to use a scoring system designed around a 5-point Likert scale (definitive positive, positive, possible positive, equivocal, and negative) to stratify the level of observer confidence in each assigned score.¹⁰ Such a stratified scheme prohibits calculation of sensitivity and specificity (no dichotomized results), and likelihood ratios will need to be used instead. Even though this is more complex, it better reflects the use of clinical scoring systems.

We therefore propose the following quantitative scoring system for TIC (Table 1). One goal of the system is to differentiate injuries requiring hemostasis, which are not complicated by a coagulopathy (mechanical bleeding alone) versus mechanical bleeding from injuries compounded by biologic coagulopathy. Through the use of this system, we are attempting to distinguish between bleeding severity resulting from injury alone, that is, controllable with pressure or suturing/stapling versus bleeding, which persists due to a coagulopathy. Thus, to score higher than I for coagulopathy, the trauma surgeon must conclude that the bleeding is not simply due to a severe injury requiring ordinary hemostatic intervention. In addition, to facilitate coagulation research, we propose to further subclassify bleeding according to the source of bleeding. A modifier is included to denote the mechanism of injury, namely (p) for penetrating or (b) for blunt. The location of the patient when the score is calculated is to be indicated in parenthesis as the emergency department (ED), operating room (OR), or intensive care unit (ICU). A series of example cases with the corresponding scores are included in Table 2. We suggest that the score be determined by the attending trauma surgeon immediately after achieving surgical hemostasis or at the earliest feasible time point so as to best achieve an early snapshot of the severity of coagulopathy before product-based resuscitation. A clear distinction must be made by the clinician between impaired hemostasis (due to uncontrolled surgical bleeding) versus coagulopathy to attempt to limit the scoring to assessment of impaired coagulation. However, an inherent limitation in this scoring is that often, both entities exist and are dependent on one another. It is anticipated that the reliability of the scoring will increase as the time from injury extends as the full composition

of injuries is identified and treated. The focus of the scoring system should be on bleeding diathesis after surgical hemorrhage is controlled.

We propose the use of this TIC scoring system for reliable and consistent quantification and reporting of the degree of coagulopathy. Generated by expert opinion, the score will be subjected to prospective validation as part of TACTIC's clinical investigations, and the clinical score will be linked to outcomes, morbidity, and mortality. In addition, comparison with laboratory testing is critical, and prospective analyses based on viscoelastic and other coagulation testing are needed to validate the clinical score. We believe that the TIC scoring system will provide a common language for the grading of clinical coagulopathy and allow for enhanced communication and research in this critical area.

To effectively conduct multicenter investigations, the TACTIC team also addressed another major limitation in clinical investigation of TIC, that is, defining the role of coagulopathy in postinjury mortality. Uncontrolled hemorrhage and shock eventually produce refractory coagulopathy; in TIC, patients continue to bleed despite hemostatic maneuvers and hemostatic resuscitation. Perhaps, the most common scenario of TIC as a *coincidental* phenomenon is massive traumatic brain injury (TBI) with uncal herniation. Although coagulopathy may be profound, the clear cause of death is TBI (the patient dies *with* coagulopathy, not *due to* coagulopathy). Because postinjury mortality is the ultimate research outcome, the cause of mortality must be clearly defined and subject to a system similar to the coagulopathy definition. Therefore, we propose the following definitions for death with TIC, further refined by clinician assessment of whether coagulopathy was a primary cause of death (Table 3).

In conclusion, we have proposed a quantitative scoring system for TIC and a clinical outcomes definition for postinjury mortality due to coagulopathy to overcome a critical and necessary barrier to progress in TIC. Application of standardized clinical scoring and death criteria should be highly useful for research in TIC and ultimately improve patient outcome.

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TABLE 1

Clinical Coagulopathy Score (I–V)

Score	Description
I	Normal hemostasis (negative)
II	Mild coagulopathy, no intervention required except direct pressure or temporary gauze tamponade (equivocal)
III	Coagulopathy refractory to direct pressure, requiring advanced hemostasis techniques (e.g., electrocautery, topical hemostatic agents, staples, or suturing). (possible positive)
IV	Coagulopathy requiring adjunctive blood component therapy or systemic therapeutics in response to continued bleeding despite above surgical hemostatic maneuvers (positive)
V	Diffuse persistent bleeding from multiple sites remote from injury; e.g., endotracheal tube, intravenous catheter, chest tubes, etc. (definitive positive)
Subclassifications	
A	Isolated TBI
B	Neck/thoracic/abdominal/pelvic injury
C	Extremity injury
D	Polytrauma *
E	Polytrauma + TBI

* The current consensus definition of *polytrauma* is significant injuries with Abbreviated Injury Scale (AIS) score of 3 or more points in two or more different anatomic AIS regions in conjunction with one or more additional variables of systolic blood pressure of 90 mm Hg or less, Glasgow Coma Scale (GCS) score of 8 or less, base excess of 6 or less, or age of 70 years or older.¹¹

To be determined by the attending trauma surgeon after mechanical hemorrhage control is obtained. Modifiers are included to denote blunt (b) or penetrating (p) mechanism.

TABLE 2

Clinical Case Examples for TIC Scoring System

Clinical Case	Intervention/Resuscitation	Location	Clinical Score
Unhelmeted motorcyclist with severe TBI; GCS score, 3; and evidence of intracranial herniation returns from computed tomographic scanner with blood actively exuding from scalp lacerations, endotracheal tube, intravenous lines, and mucous membranes.	Manual compression, blood product administration	ED	V-A(b) (ED) [Definite positive coagulopathy]
Isolated extremity slash wound with large-volume venous bleeding in ED taken to OR for ligation. After vascular control noted to have residual ongoing bleeding with no identifiable source. Direct pressure applied to area of suspected bleeding, which stops after several minutes of pressure.	Manual compression alone	OR	II-C(p) (OR) [Equivocal coagulopathy]
Polysystem blunt trauma patient with Grade III hepatic injury and moderate TBI (GCS score, 10) after fall. Taken to the ICU for nonoperative management. Tertiary survey identifies large scalp laceration with nonpulsatile continuous bleeding. After direct pressure and staples, the laceration continues to bleed. Patient received several units of fresh frozen plasma and platelets due to transient drop in blood pressure and concerns for ongoing blood loss from scalp and possible intra-abdominal injuries. After blood product transfusion, scalp bleeding resolves, and repeat hemoglobin remains stable.	Blood products, suture/staples to wound	ICU	IV-E(b) (ICU) [Positive coagulopathy]

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TABLE 3

Causes of Postinjury Death

Early (<24 h)	Late (>24 h)
Uncontrolled mechanical bleeding*	MOF ¹²
With coagulopathy**	Adult respiratory distress syndrome ¹³
Without coagulopathy	Sepsis ¹⁴
TBI	Myocardial infarction ¹⁵
With coagulopathy**	Pulmonary embolism
Without coagulopathy	Frailty ^{16,17}
Refractory coagulopathy [†]	Management error
Airway compromise	Other
With coagulopathy**	
Without coagulopathy	
Anoxia due to high cervical spine injury	
With coagulopathy**	
Without coagulopathy	
Refractory shock [‡]	
With coagulopathy**	
Without coagulopathy	
Management error	
With coagulopathy**	
Without coagulopathy	
Other	

* Uncontrolled mechanical bleeding, defined as ongoing bleeding (>250 mL/15 min) from inaccessible site precluding direct tamponade.

** "With coagulopathy" defined as Grade II or higher.

[†] Refractory coagulopathy, defined as continued bleeding from multiple sites despite ongoing blood component administration, Grade III or higher (Table 1).

[‡] Refractory shock, defined as progressive lactate greater than 10 mmol/L or base deficit greater than -20 mEq/L.

MOF, by Denver MOF score; adult respiratory distress syndrome, by the Berlin criteria; sepsis and myocardial infarction by consensus guidelines; frailty, defined as evidence of preinjury aging-associated decline in reserve and function across multiple physiologic systems.