Management of Coagulopathy in the Patients With Multiple Injuries: Results From an International Survey of Clinical Practice

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Background: **Bleeding is one of the leading causes of preventable death after traumatic injury. Trauma-associated coagulopathy complicates the control of bleeding. The published approaches on the management of this coagulopathy differ significantly.**

Methods: **A qualitative international survey of clinical practice among senior physicians responsible for the treatment of patients with multiple injuries (Injury Severity Score ≥16) was conducted to document common practices, highlight the variabilities, and profile the rationale behind existing clinical practices around the world.**

Results: **Survey results are based on 80 (32%) completed returns, representing 25 countries with 93% of respondents employed by trauma centers and a mean of 20 years clinical experience. There are regional differences in the clinical specialty of physicians responsible for trauma management decisions. Blood loss, temperature, pH, platelets, prothrombin time/INR/activated partial thromboplastin time, and overall clinical assessment, were the most common criteria used to assess coagulopathy. Forty-five percent of respondents claimed to follow a massive transfusion protocol in their institution, 19% reported inconsistent protocol use and 34% do not use a protocol. The management of hypothermia, acidosis, blood products, and adjuvant therapy showed regional as well as institutional variability, and surprisingly few massive transfusion protocols specifically address these issues.**

Conclusions: **The results of this survey may serve to draw attention to the need for a common definition of coagulopathy and standardized clinical protocols to ensure optimal patient care.**

Key Words: **Trauma, Coagulopathy, Clinical practice, Survey.**

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Traumatic injury accounts for nearly 1 death in 10 worldwide, and 30% to 40% of trauma-related deaths are due to exsanguination.[1–3] Because traumatic injury is the leading cause of death in the 5-year to 44-year age group,[4] the impact on society is considerable. Posttraumatic bleeding is the leading cause of potentially preventable death and is usually attributable to a combination of vascular injury and coagulopathy. In the past, coagulopathy associated with

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trauma was viewed as a largely dilutional event.[5] Today posttraumatic coagulopathy appears to be the sum of the effects of injury severity, blood loss, factor depletion, fibrinolysis, hypothermia, hypocalcemia, acidosis, and the patient's individual biological response to both traumatic injury and treatment.[6–8] Although treatment modalities continue to improve, the early identification and management of coagulopathy may help to better control hemorrhage and may represent a key step in reducing mortality associated with traumatic injury.[9]

To gain insight into current clinical practices in the management of coagulopathy in the severely injured patient, a qualitative international physician survey of clinical practice was conducted. The survey was designed to document common practices, highlight the variabilities and profile the rationale behind existing clinical practices around the world. The results of the survey may serve as a basis for further discussion on the need for a common definition of posttraumatic coagulopathy and the implementation of standardized clinical protocols to ensure optimal patient care.

PATIENTS AND METHODS

A qualitative international survey of clinical practice was developed by the author group and distributed electronically to physicians worldwide (Fig. 1). Email addresses for professional contacts were provided by the authors and supplemented by additional contacts with a potential interest in patient management after traumatic injury. The physicians surveyed were primarily leaders of established trauma centers. A severely injured patient for the purpose of the survey was defined by an Injury Severity Score (ISS) ≥16. Surveys were distributed and collected between December 2006 and March 2007. All returned questionnaires were analyzed and results were grouped according to geographical areas.

Of 251 physician clinical practice surveys distributed and received electronically, 80 (32%) were completed and returned. Return rates were similar in the three geographical regions defined for the purpose of evaluating survey results: Europe and the Middle East (EM) (31%), the Americas (AM) (33%), and the Asia-Pacific region (AP) (31%). Nonrespondents were sent one additional request to complete the survey approximately 4 weeks after the initial request. Completed surveys were returned by physicians working in the United States of America (33), Germany (8), Japan (8), Canada (3), India (3), Australia (2), Israel(2), Italy(2), the Netherlands(2), and Spain (2). Single surveys were received from Austria, Belgium, the Czech Republic, Denmark, Finland, France, New Zealand, Norway, Poland, Portugal, Slovenia, Sweden, Switzerland, Turkey, and the United Kingdom. Four contacts responded but declined to complete the survey, citing emeritus status or employment by a nontrauma specialty center. Several surveys were completed anonymously by institutional colleagues or jointly by colleagues with complementary specialties (e.g., surgery and anesthesia) from the same

SURVEY OF CLINICAL PRACTICE

We estimate that this survey will require 10–15 minutes to complete.

Please note that multiple answers are possible in response to many of the questions posed in this survey. In addition, please feel free to add additional answers or comments if the choices offered do not apply to your institution.

Country of residence: _____

Your clinical title: _____

Years in practice: _____

Your area(s) of specialty (please tick all that apply):

- ☐ Surgery Specialty: _____
- ☐ Anaesthesiology
- ☐ Haematology
- ☐ Intensive Care
- ☐ Emergency Medicine
- ☐ Trauma
- ☐ Trainee
- ☐ Other: _____

Comment: _____

Type of medical institution:

- ☐ Trauma centre / equivalent tertiary emergency hospital
- ☐ Non-trauma centre / equivalent secondary emergency hospital

Comment: _____

Who in your institution is primarily responsible for making the initial management decisions when treating the critically bleeding polytrauma patient?

- ☐ Anaesthesiologist
- ☐ Surgeon
- ☐ Haematologist
- ☐ Intensivist
- ☐ Multi-disciplinary team – please describe:

_____

_____

_____

_____

_____

If you work in a trauma centre, approximately how many polytrauma patients (ISS≥16) are admitted per year?

- ☐ <50
- ☐ 50 – 200
- ☐ 200 – 500
- ☐ >500

Comment: _____

Please estimate the proportion of polytrauma patients (ISS≥16) that are admitted to your institution with a PT and/or aPTT >1.6 times normal?

- ☐ <10%
- ☐ 10 – 30%
- ☐ 30 – 50%
- ☐ 50 – 80%
- ☐ >80%

Comment: _____

Which physiological or laboratory parameters are used in your institution to assess coagulopathy in polytrauma patients (ISS≥16), and when?

	ER	OR	ICU
Blood loss	☐	☐	☐
Temperature	☐	☐	☐
pH	☐	☐	☐
Ca++	☐	☐	☐
Respiratory rate	☐	☐	☐
Mental state	☐	☐	☐
PT/INR/aPTT	☐	☐	☐
ACT	☐	☐	☐
Fibrinogen	☐	☐	☐
Platelet number & function	☐	☐	☐
(Rotation) thromboelastography	☐	☐	☐
Clinical assessment / observation	☐	☐	☐
Other:	☐	☐	☐

_____

Comment: _____

Does your institution follow a written massive transfusion protocol?

- ☐ No
- ☐ Inconsistently
- ☐ Yes

If possible, please provide a reference or source from which a copy of this protocol could be obtained, or please submit an electronic copy of the protocol to XXX.

Comment: _____

Fig. 1. *Clinical practice survey.*

If you use a massive transfusion protocol, does the algorithm address the following issues?

- ☐ Hypothermia
- ☐ Acidosis
- ☐ RBCs
- ☐ Platelets
- ☐ FFP
- ☐ RBC:FFP ratio
- ☐ Cryoprecipiate
- ☐ Fibrinogen
- ☐ Adjuvant therapy

Comment: _____

Please outline the management of critical bleeding in the typical polytrauma patient admitted to your institution.

Hypothermia

		ER	OR	ICU
Pre-warmed environment	Temp (°C):			
Pre-warmed fluids		☐	☐	☐
"Bair huggers®" / warming devices		☐	☐	☐
Extracorporeal warming		☐	☐	☐
None		☐	☐	☐

Other: _____

Comment: _____

Acidosis

	ER	OR	ICU
Monitored	☐	☐	☐
Specifically treated	☐	☐	☐

- ☐ Empirical treatment
- ☐ Treatment threshold: _____
- ☐ Bicarbonate
- ☐ Other: _____
- ☐ Treatment protocol: _____

Comment: _____

RBCs

- ☐ Empirical treatment
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Platelets

- ☐ Empirical treatment
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

FFP

- ☐ Empirical treatment
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Proportion RBC : FFP

- ☐ Empirical treatment
- ☐ Ratio RBC : FFP
- ☐ Ratio changes during treatment
  How? _____
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment. _____

Fig. 1. *(Continued).*

Cryoprecipitate

- ☐ Not used / not available
- ☐ Empirical treatment
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Fibrinogen

- ☐ Not used / not available
- ☐ Measured
- ☐ Measured to guide cryoprecipitate treatment
- ☐ Administered separately from cryoprecipitate
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Whole blood

- ☐ Not available
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Fresh whole blood

- ☐ Not available
- ☐ Trigger: _____
- ☐ Treatment protocol: _____

Comment: _____

Adjuvant therapy

	Trigger:	Dose:
☐ Aprotinin		
☐ Tranexamic acid		
☐ Desmopressin		
☐ Ca++		
☐ Mg++		
☐ Albumin		
☐ PCC		
☐ Vitamin K		
☐ rFVIIa		
☐ Other:		

Comment: _____

Do you rely on point of care (near-patient) testing in making management decisions when treating the critically bleeding polytrauma patient?

- ☐ Not available
- ☐ No
- ☐ Yes

If yes, which point of care parameters do you use?

- ☐ PT / INR
- ☐ aPTT
- ☐ ACT
- ☐ Hb
- ☐ Base deficit
- ☐ Temperature
- ☐ Functional haemostasis monitoring (e.g. sonoclot, thromboelastography)
- ☐ Other: _____

Comment: _____

Fig. 1. *(Continued).*

institution. In addition to the information provided in response to survey questions, 16 respondents provided full written massive transfusion or other relevant institutional clinical practice protocols.

Survey respondents reported a mean of 20 years clinical experience (range, 5–40 years), reflecting a targeted sam-

Please estimate the mean turnaround time for laboratory parameters to assess coagulation at your institution.

Time (min)

_____ Clot formation times (ACT, PT, INR, aPTT)
_____ Clotting factor assays
_____ Platelet counts
_____ Platelet function analyses
_____ Other: _____

Comment: _____

In your opinion, do systemic or practical barriers to treating the polytrauma patient in your institution exist that may have a negative impact on clinical outcomes?

☐ No
☐ Yes

Please specify:
☐ Lack of protocols
☐ Inadequate implementation of existing protocols
☐ Lack of equipment
☐ Lack of team training
☐ Lack of communication
☐ Lack of blood product availability
☐ Lack of timely blood product release
☐ Lack of timely laboratory parameter results
☐ Other: _____

Comment: _____

In your opinion, would the integration and implementation of international clinical practice guidelines for the early management of coagulopathy in the polytrauma patient improve patient care at your institution?

☐ Yes
☐ No
☐ Not sure

Comment: _____

Which factor(s) would be most effective in convincing your institution to implement international clinical practice guidelines for the early management of coagulopathy in the polytrauma patient?

☐ Peer-reviewed publications
☐ Consensus conferences / proceedings
☐ Certified continuing education courses
☐ Endorsement by international professional societies
☐ Endorsement by national professional societies
☐ Endorsement by government regulatory authorities
☐ Personal engagement by senior physicians at your institution
☐ Widespread implementation by leading institutions
☐ Other: _____

Comment: _____

Would you like to receive a copy of the results of this survey when available?

☐ No
☐ Yes

Please send to the following email address:

_____

Fig. 1. *(Continued).*

pling of fairly senior physicians. The most common clinical specialties represented among survey respondents were surgery (61%), intensive care medicine (63%), and trauma (64%), with some geographical variation that may reflect both regional and national differences in specialty training and clinical responsibility and variations in emergency medical systems in different countries (Table 1). The vast majority of respondents (74 of 80) were employed by trauma specialty centers. Mirroring this, respondents estimated that their institutions admit >50 (8%), 50 to 200 (36%), 200 to 500 (23%), >500 (21%) or an unspecified number (15%) of severely injured patients (ISS ≥16) annually.

The author group comprises an independent international medical Educational Initiative on Critical Bleeding in Trauma (EICBT), which aims to increase awareness among health care professionals that coagulopathy during the first hour after traumatic injury may play an important role in patient outcomes. The group includes seven trauma surgeons, two intensive care or emergency medicine specialists, a dedicated trauma anesthesiologist, and a hematologist or blood banker. The EICBT group operates as an independent faculty managed by Physicians World GmbH, Mannheim, Germany. The activities of the EICBT are supported by unrestricted educational grants from Novo Nordisk A/S, Bagsvaerd, Denmark.

RESULTS

Responsibility for the Management of Severely Injured Patients

Responsibility for the early management of severely injured patients in trauma centers differs between regions and hospitals. In this survey the trauma team leader was a surgeon (48 of 80), a multidisciplinary team (25 of 80), an anesthesiologist (16 of 80), or an intensive care specialist (11 of 80), although regional differences were apparent (Table 2). Some respondents indicated that the responsibility shifts as the patient moves from the emergency department to the operating theater or to the intensive care unit (ICU). When asked to describe the multidisciplinary team, responses included trauma surgeon plus anesthesiologist, emergency or critical care physicians, emergency physician plus hematologist or a combination of general, neuro- and orthopedic surgeon plus a radiologist as needed.

Variables Used in the Assessment of Coagulopathy

A coagulopathic patient for the purpose of the survey was defined as having a prothrombin time (PT)/activated partial thromboplastin time (aPTT) >1.6X normal, however several respondents specifically reported not using or not relying on these tests to assess patient condition at admission. Survey respondents estimated that <10% (35%), 10% to 30% (46%), 30% to 50% (14%), 50% to 80% (1%), or an unspecified number (6%) of patients with multiple injuries are admitted to their institution with a PT/aPTT>1.6X normal. The physiologic or laboratory parameters used to asses coagulopathy in patients with multiple injuries in the emergency room (ER), operating room (OR), and ICU are summarized in Table 3. Blood loss, temperature, pH, platelets, PT/INR/aPTT, and overall clinical assessment were reported to be the most commonly used assessment criteria. The use of thromboelastometry (rotational) showed considerable regional variation, with most common use in the EM group and least in the AP group, where use appeared to be restricted to the operating theater (Table 4). Other criteria that were specifically mentioned included a history of oral anticoagulant therapy, lactate, the amount of blood infused, D-dimers in the ICU, and the number of systemic inflammatory response syndrome factors.

Use of Massive Transfusion Protocols

Forty-five percent of respondents claimed to follow a massive transfusion protocol (MTP) in their institution, 19% reported inconsistent protocol use, and 34% do not use a protocol. Sixty-six percent of respondents who have an institutional MTP reported that the use of red blood cells (RBCs), platelets and fresh frozen plasma (FFP) are each specifically

Table 1 Reported Clinical Specialties Among Survey Respondents*

	Surgery (%)	Anesthesia (%)	Hematology (%)	Intensive Care (%)	Emergency Medicine (%)	Trauma (%)	Trainee (%)	Other (%)
Europe-Middle East	33	47	0	53	13	40	3	7
Americas	92	6	0	64	6	83	3	8
Asia-Pacific	43	29	7	79	71	64	7	7
Overall	61	25	1	63	20	64	4	8

*More than one answer possible, therefore responses do not add up to 100%.

Table 2 Responsibility for the Early Management of Severely Injured Patients

	Anesthesiologist (%)	Surgeon (%)	Hematologist (%)	Intensive Care Specialist (%)	Multidisciplinary Team (%)
Europe-Middle East	47	37	0	23	43
Americas	3	92	0	6	14
Asia-Pacific	7	29	0	14	50
Overall	20	60	0	14	31

Table 3 Variables Used to Assess Coagulopathy in the Severely Injured Patient in the ER, OR, and ICU

	Blood Loss (%)	Temperature (%)	pH (%)	Ca^{++} (%)	Respiratory Rate (%)	Mental State (%)	PT/INR/aPTT (%)	ACT (%)	Fibrinogen (%)	Platelets (%)	(RO) TEM (%)	Clinical Assessment (%)	Other (%)
ER	78	78	74	29	40	45	75	5	36	68	6	83	5
OR	88	84	76	44	21	16	84	19	59	80	21	86	5
ICU	81	79	78	51	24	28	84	24	78	88	23	85	6

ACT, activated clotting time; TEM (RO), thromboelastometry (rotational).

Table 4 Use of (Rotational) Thromboelastometry to Assess Coagulopathy in Different Regions

	ER (%)	OR (%)	ICU (%)	Anywhere (%)
Europe-Middle East	13	30	37	47
Americas	3	19	19	28
Asia-Pacific	0	7	0	7
Overall	6	21	23	31

included in their protocol. Hypothermia and acidosis are each addressed in 41% of MTPs, and the use of cryoprecipitate (34%), fibrinogen (33%), a specific RBC:FFP ratio (33%), and adjuvant therapy (31%) less frequently. Specific adjuvant therapy measures that were mentioned included prothrombin complex concentrate (PCC), activated recombinant factor VII (rFVIIa), aprotinin, and tranexamic acid (Fig. 2).

Institutional Management of Critical Bleeding in the Severely Injured Patient

Hypothermia and Acidosis

Attention to the control and prevention of hypothermia is widespread, though the measures undertaken to control patient temperature vary widely. The reported use of a prewarmed environment was low compared with the application of extracorporeal warming or warming devices (Table 5). The range of reported environmental temperatures used to warm the patient or prevent cooling differed significantly (Fig. 3).

Survey respondents reported that acidosis is monitored in the ER (81%), OR (94%), and ICU (94%) with no large regional differences. Acidosis was reported to be specifically treated in the ER (34%), OR (51%), and ICU (54%). Treatment rates in the EM and AM regions was similar; specific treatment for acidosis in the AP region was somewhat less common (Table 6). Among those who specifically treat acidosis, bicarbonate use was reported by 49%. Other treatment modalities that were specifically mentioned included fluids, aggressive resuscitation, continuous veno-venous hemofiltration, tris(hydroxymethyl)-acrylamidomethane or variants thereof, acetate and hyperventilation, and warming and hypovolemia management. Twenty-nine percent of respondents reported using empirical treatment for acidosis, and 41% report using a treatment threshold or a treatment protocol or both (14%). Among those who reported using a treatment threshold, the most common was pH $<$7.2 (18 of 30) with a range of pH 7.08 to 7.3.

Blood Products

Survey respondents reported treating empirically with RBCs (55%), platelets (44%), and FFP (60%) whereas 61%, 65%, and 48% reported using a specific treatment trigger. Twenty-nine percent reported following an institutional protocol for RBC treatment, whereas 20% and 25% use a pro-

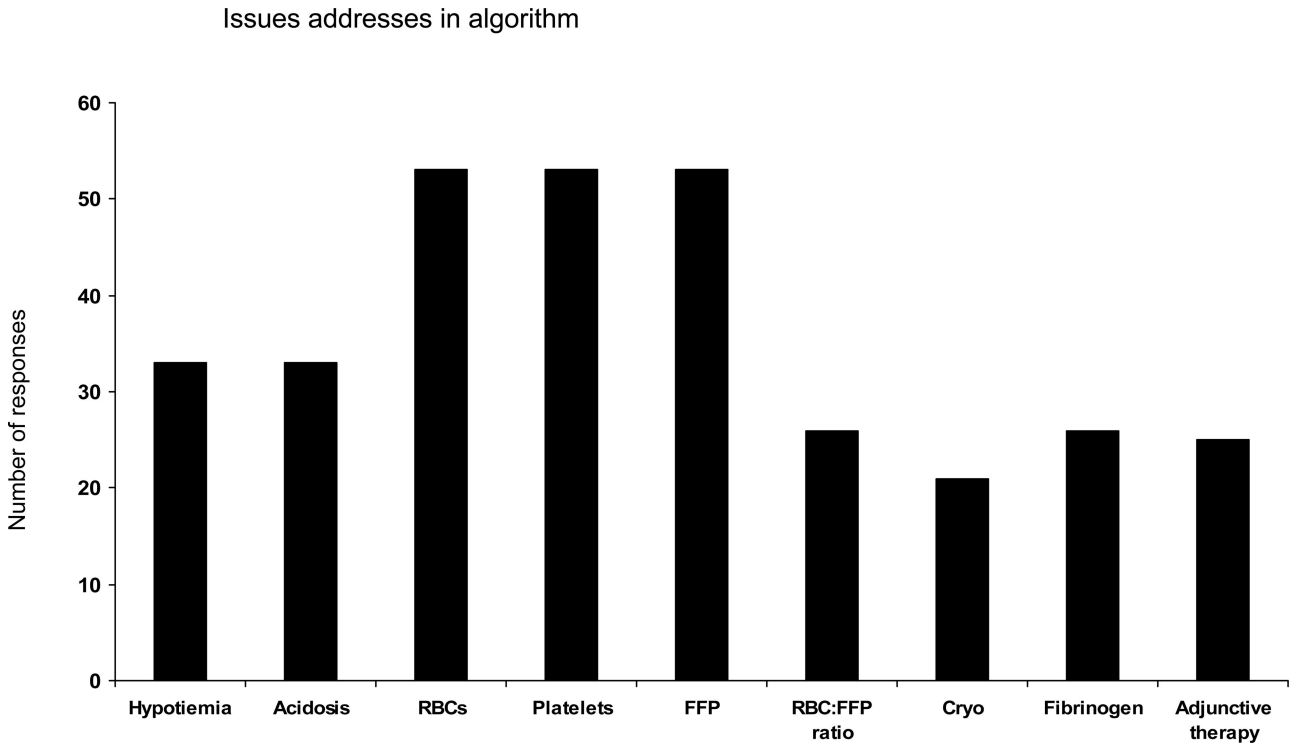

Fig. 2. *Issues addressed in massive transfusion protocol.*

Table 5 **Measures Employed to Control Patient Temperature and Prevent or Treat Hypothermia in the ER, OR, or ICU**

	Prewarmed Environment (%)	Prewarmed Fluids (%)	"Bair Huggers" or Warming Devices (%)	Extracorporeal Warming (%)	None	Other
ER	9	81	65	20	1	0
OR	15	91	94	34	1	0
ICU	11	80	90	36	1	0

tocol for platelet and FFP treatment. Reported RBC treatment triggers included hematocrit ranging between 20% and 28% or hemoglobin between 6 g/dL to 10 g/dL with a tendency to treat more aggressively in patients with cerebral trauma, cardiac disease or otherwise compromised oxygen transport to tissues, active bleeding or fluid infusion >2,000 mL. Platelet count triggers were varied widely and ranged between 10,000 and 100,000 $\times$ 10^9/L. Other platelet triggers included blood loss, clinical bleeding or coagulopathy, and previous RBC transfusions. FFP triggers included clinical bleeding or coagulopathy, volume loss, prolonged or abnormal PT/aPTT/INR or thromboelastometry (rotational), previous oral anticoagulant therapy, and previous RBC transfusions. Forty-six percent reported treating empirically with respect to a RBC:FFP ratio, whereas only 9% reported using a specific trigger and 13% claimed to use an institutional protocol. Forty-three percent reported using a specific ratio of RBC:FFP and 20% indicated that the ratio changes during treatment.

Cryoprecipitate use appeared to be localized to the AM, whereas treatment with fibrinogen may be more common in the EM region. Sixty percent of respondents in the EM region and 71% in the AP region reporting no use or no availability of cryoprecipitate, compared with only 6% in the AM region. Fibrinogen was reported to be not used or not available by 23% of EM, 33% of AM, and 71% of AP respondents. Thirty-three percent of EM respondents reported use of a trigger for fibrinogen treatment, and 20% reported a treatment protocol, whereas reports of fibrinogen triggers and treatment protocols in the AM and AP regions were minimal (Table 7). Cryoprecipitate treatment triggers included measured fibrinogen levels <100 mg/dL or <200 mg/dL, uncontrolled coagulopathy or severe hemorrhage, abnormal clotting times and previous RBC, FFP or coumarin treatment. Fibrinogen treatment triggers were reported to be similar and in the range of <100 mg/dL to 150 mg/dL or 200 mg/dL or based on thromboelastometry (rotational) results.

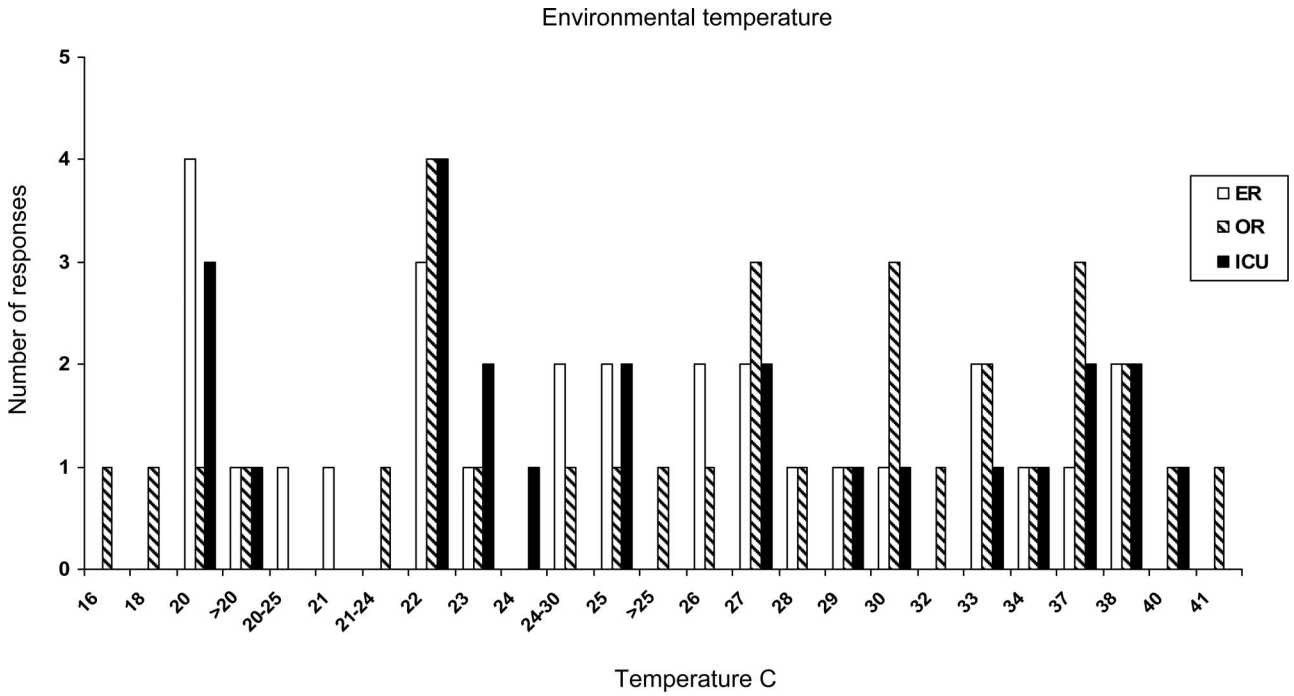

Fig. 3. *Environmental temperatures used to prevent or control hypothermia.*

Table 6 **Monitoring and Specific Treatment of Acidosis in the ER, OR, and ICU in Each Region**

	ER		OR		ICU	
	Monitored (%)	Specifically Treated (%)	Monitored (%)	Specifically Treated (%)	Monitored (%)	Specifically Treated (%)
Europe-Middle East	93	40	100	53	100	60
Americas	69	31	92	56	92	58
Asia-Pacific	86	29	86	36	86	29
Overall	81	34	94	51	94	54

Table 7 **Reported Availability and Use of Fibrinogen in Different Regions**

	Not Used or not Available (%)	Level Routinely Measured (%)	Measured to Guide Cryo Treatment (%)	Administered Separately From Cryo (%)	Trigger (%)	Treatment Protocol (%)
Europe-Middle East	23	53	23	27	33	20
Americas	33	28	44	8	3	6
Asia-Pacific	71	21	7	7	0	0
Overall	36	36	30	15	14	10

No survey respondent reported the use of whole blood or fresh whole blood.

Adjuvant Therapy

According to survey responses, rFVIIa was the most commonly used form of adjuvant therapy, reported by 75% of respondents, followed by Ca^{++} (53%) and vitamin K (38%), and to a lesser extent tranexamic acid (28%), aprotinin (26%), desmopressin (24%), and Mg^{++} (25%). Adjuvant therapy with albumin and PCC was reported by 16% and 18% of respondents. Some regional differences in the reported use of specific adjuvant therapies were apparent. The use of tranexamic acid appears to be restricted to the EM and AP regions, with little use in the AM region, the use of aprotinin, desmopressin, and PCC much more common in the EM region than the AM or AP regions, and the use of rFVIIa approximately three times higher in the EM and AM regions than in the AP region (Table 8). Both the use of aprotinin and thromboelastometry (rotational) are most common in the EM region, therefore, perhaps not surprisingly, the use of both throm-

Table 8 Reported Use of Adjuvant Therapy by Region

	Aprotinin (%)	Tranexamic Acid (%)	Desmopressin (%)	Ca^{++} (%)	Mg^{++} (%)	Albumin (%)	PCC (%)	Vitamin K (%)	rFVIIa (%)	Other (%)
Europe-Middle East	47	53	43	53	27	17	33	43	83	3
Americas	14	3	11	50	25	14	6	31	86	0
Asia-Pacific	14	36	14	57	21	21	14	43	29	7
Overall	26	28	24	53	25	16	18	38	75	3

Ca^{++}, calcium; Mg^{++}, magnesium.

boelastometry (rotational) and aprotinin by the same institution, though not necessarily together, is also most common in the EM region.

Specific triggers for aprotinin and tranexamic acid use were very similar, with the largest number of respondents reporting (hyper) fibrinolysis with or without thromboelastometry (rotational). Other responses included the use of D-dimer >15% within 60 minutes or ISS >25, massive bleeding, and massive blood transfusion as triggers. Reported aprotinin doses were variable and ranged between 500,000 and 2 million, with one respondent reporting 6 million units. Tranexamic acid doses were reported in the range of 0.5 g to 2 g with one respondent reporting 4 g to 6 g.

Desmopressin triggers included pretreatment with oral anticoagulants, known or suspected clotting dysfunction and renal failure, with doses of 0.2 mcg/kg to 0.4 mcg/kg. Reported triggers for Ca^{++} treatment were commonly <0.8 mmol/L to 1.2 mmol/L or massive transfusion or both. Mg^{++} administration was reported to be triggered by levels <0.6 mmol/L to 1.3 mmol/L. Vitamin K use appeared to be restricted to the reversal of anticoagulant treatment or elevated clotting times; doses ranged from 1 mg to 20 mg. Reported triggers for the use of rFVIIa as adjuvant therapy were largely empirical and based on clinical judgment in the presence of uncontrolled or refractory nonsurgical bleeding or massive transfusion or both. Some respondents reported clinical protocols with transfusion triggers in the range of 6 to 10 RBC units. Reported rFVIIa doses ranged between 50 mcg/kg and 200 mcg/kg often with repeat dosing.

Laboratory Assessment

Survey respondents were asked whether they rely on point-of-care or near-patient or bedside testing when making clinical decisions about the treatment of the critically bleeding trauma patient. Sixty-six percent reported that they rely on such tests, whereas 10% do not and 20% reported that such tests are not available. Among respondents who do rely on bedside testing, base-deficit (87%), hemoglobin (81%), and temperature (79%) are the most common, followed by PT/INR (53%), aPTT (32%), functional hemostasis monitoring (25%), and activated clotting time (23%). Other bedside tests (15%) mentioned included thromboelastometry (rotational), lactate, and bedside blood analysis systems. The mean turnaround time reported for platelet counts was 23 minutes, clot formation assays 33 minutes, platelet function analyses 56 minutes, and clotting factor assays 57 minutes.

Improving Patient Care

When asked, 65% of survey respondents felt that systemic or practical barriers within their institution exist that may have a negative impact on patient outcomes; 34% of respondents felt that no such barriers exist. Among those who felt that hindrances to optimal patient care are present, 36% cited lack of protocols or lack of protocol implementation (28%), and 33% reported a lack of timely laboratory parameter results, lack of team training (26%), lack of communication (23%), lack of equipment (18%), and lack of timely blood product release (13%) or availability (10%).

Sixty-one percent of respondents felt that the integration and implementation of international clinical practice guidelines for the early management of coagulopathy in the patients with multiple injuries would improve patient care at their institution; 14% of respondents did not feel that clinical practice guidelines would lead to improvement and 25% were not sure. The factors that were estimated to be the most effective in convincing each respondent's institution to implement international clinical practice guidelines for the early management of coagulopathy in the patients with multiple injuries were peer-reviewed publications (80%), consensus conferences or proceedings (71%), endorsement by national (51%) or international (46%) professional societies or government regulatory authorities (26%), personal engagement by senior physicians (46%), continuing medical education courses (33%), and widespread implementation by leading institutions (31%).

DISCUSSION

The appreciation of posttraumatic coagulopathy as a relevant factor for the outcome of severely injured patients is evolving.[5,10–13] In the past, many thought that coagulopathy was not a problem of the first hour after traumatic injury.[14] Today we know that coagulopathy is already present at arrival in the ER in up to 30% of severely injured patients and that it is associated with higher mortality rates.[10–13] Coagulopathy seems to be one of the major sources of secondary injury. Today many experts advocate early diagnosis and aggressive treatment of posttraumatic coagulopathy to improve patient outcomes.[9,15–18]

We therefore conducted an international survey of clinical practice to determine the extent to which this new knowledge has disseminated into daily practice. This qualitative survey was not designed to produce statistically rigorous results, but to give an impression of clinical practices in this field around the world. The survey deliberately targeted high-level trauma centers because these institutions were most likely to have mature massive transfusion protocols. Some bias in the survey may have been introduced by the large proportion of professional contacts identified by the author group to be targeted for the survey. These features may also have contributed to the relatively high response rate and willingness to share full institutional protocols. Response rates among individual countries were quite variable, perhaps reflecting structural differences in the amount of time that physicians can or are willing to devote to clinical versus research activities. Quantitative assessments were therefore performed on a regional basis to partially compensate for these potential imbalances.

The main conclusion that can be drawn from this survey is that recognition and management of early posttraumatic coagulopathy varies widely. The scattered opinions and practices reflected by the survey highlight the diversity in clinical practice that exists around the world and within each region. Many aspects of clinical practice seem to be based on tradition and dogma rather than scientific evidence. Respondents felt a need for protocols, guidelines, and further research where little or no evidence exists. Although no effort was made to document outcome differences between responding institutions, based on ongoing studies of massive transfusion patients, it is likely that significant outcome variability exists in this severely injured group of patients.

Responsibility

The survey results suggest that responsibility for coagulation management in severely injured patients differs throughout the world. Whereas surgeons are mostly responsible in the AM region, anesthesiologists are predominantly responsible in the EM region and a multidisciplinary team in the AP region. Hematologists seem not to participate in the immediate decision-making process during early trauma management. These differences in responsibility may also explain differences in clinical practice. Specialists may have different backgrounds and therefore favor different approaches to the management of posttraumatic coagulopathy.

These data are important with respect to education and evolving treatment practices. It is clearly insufficient to restrict educational efforts to one specific group of physicians. On a global scale this discussion must involve surgeons, anesthesiologists, emergency physicians, intensive care specialists, and hematologists.

Diagnosis

With respect to the early detection of posttraumatic coagulopathy, blood loss, temperature, pH, platelets, PT/INR/aPTT, and overall clinical assessment were reported to be most commonly used. Thromboelastometry (rotational) is not used extensively in the ER. Not all institutions appear to screen for posttraumatic coagulopathy in the ER, some assessing coagulation disorders only when the patient arrives in the OR or ICU due to better availability of the necessary technology. The results presented here support the impression that some routine laboratory assessments are performed in any severely injured patient. The important question is how conscientiously returned laboratory values are reviewed. Several studies have demonstrated that elevated PT/PTT values are one of the most important predictors of outcome,[10–12] however, this survey shows that this evidence is not yet being applied in all trauma teams.

The detection of patients at risk for posttraumatic coagulopathy at the earliest possible point in time necessitates new diagnostic approaches.[18] Measurement of PT and PTT in the ER is still associated with the problem that most hospitals experience a delay of 45 minutes to 60 minutes before the results are available to the treating physicians. Point of care diagnostics for PT and PTT are not widely accepted, and the same is true for thromboelastometry. In some European hospitals, thromboelastometry (rotational) has become more and more popular in a variety of indications; however, the availability of results in the ER within 30 minutes after patient arrival remains the exception. First attempts have been made to develop predictive scores that rely on clinical parameters available in the ER within 10 minutes that can predict massive transfusion.[19] Prospective evaluation of these scores in a clinical setting are ongoing.

Treatment

Forty-five percent of respondents reported the use of massive transfusion protocols. The survey did not examine whether protocols are activated in any severely injured patient or only when patients reach the massive transfusion threshold, which is 10 units of RBCs in most institutions. Independent of the use of written protocols, the proportion of respondents who reported using specific triggers for treatment with RBCs, FFP, or platelets is surprisingly low. The diversity with respect to treatment becomes even larger when the triggers are examined in more detail. RBC triggers range between 6 g/dL and 10 g/dL and for platelets between 10,000 and 100,000 $\times$ 10^9/L. Only a minority of institutions use a targeted RBC:FFP ratio.

Issues such as hypothermia and acidosis appear to be addressed more frequently. Many institutions use prewarmed fluids and extracorporeal warming devices and monitor acidosis, therefore these potential contributors to coagulopathy appear to be widely recognized. Therapeutic measures to counteract hypothermia and acidosis vary widely, however.

Awareness

From recent studies, we know that 25% to 30% of severely injured patients are coagulopathic upon arrival in the

ER,[10,12] and we set out to determine how many senior physicians are aware of these data. Our data suggest that more than 50% of respondents are not aware that early posttraumatic coagulopathy is present in their patients. We think that if awareness of this problem is low, diagnosis and treatment is likely to begin too late. This might explain the clinical observation that many physicians involved in early trauma care react to posttraumatic coagulopathy when it is obvious in the OR, rather than early and proactively in the patient management process.

Awareness is important because it determines at what time point action is taken to solve the problem. Bleeding is still a major cause of death in trauma patients. Coagulopathy is the fuel that continuously supports bleeding. This is not only relevant for major bleeding leading to massive transfusion but also in minor bleeding at "dangerous" sites such as intracranial hematomas or subcapsular hematomas of the liver or spleen. Coagulopathy can make the difference between responders and nonresponders in trauma patients with a circulatory problem bleeding from different fracture sites. The identification of patients at risk for posttraumatic coagulopathy is, therefore, an important step in early trauma management. If a patient is at risk, a damage control resuscitation strategy must be implemented to prevent posttraumatic coagulopathy, and treatment must begin as early as possible, thereby preventing secondary injury.[9,17]

The apparent seniority and specialization in this area among survey respondents may represent a bias that the awareness of these issues is even less common among less experienced or less specialized treating physicians. The physicians surveyed here were primarily leaders of established trauma centers who were likely to have an interest in the management of coagulopathy, and may have themselves considered many of the issues addressed here. Many respondents suggested that, particularly in light of the lack of hard clinical evidence, clinical practice guidelines in this area would be helpful, supplemented by well-designed clinical trials addressing the fundamental clinical questions reviewed in this survey.[20–22]

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EDITORIAL COMMENT

This international survey evaluating the management of postinjury coagulopathy in severely injured patients throughout the world is timely, and serves to "highlight the variabilities and profile the rationale behind existing clinical practices."

The survey deliberately targeted professionals in high level trauma centers personally known to the author group, which could lead to some bias. Furthermore, although the survey return rates were similar in the three geographical

regions (Europe and Middle East, Americas, and Asia-Pacific), 33 (41%) of 80 of the surveys representing the 25 participating countries originated from the United States. Despite these potential shortcomings, a number of observations were noted which deservedly call attention to the need for a more scientific approach to coagulopathy.

Recognition of postinjury coagulopathy as a direct cause of preventable death is, of course, not new. For example, over 27 years ago, our group reported that many patients died of persistent coagulopathy with associated acidosis, and hypothermia despite surgical control of their vascular injuries, which we initially termed "the bloody vicious cycle."[1] Subsequently, progressive coagulopathy has become the fundamental rationale for damage control surgery.[2] Indeed, it is universally recognized that the decision to abort definitive operative intervention in this setting must occur early, before overt laboratory evidence of advanced coagulopathy. The challenge is to identify these patients at the time of hospital arrival, (optimally in the field), but the fundamental question is how to manage these patients pre-emptively. The major barriers to achieving this goal are: (1) poor understanding of the scientific basis for coagulation derangements after severe injury, and (2) the lack of real-time assessment of coagulation status to assess the impact of our interventions.

Recent evidence suggests that an "acute endogenous coagulopathy" (before clotting factor depletion) is present shortly after injury.[3] In fact, in our recent prehospital trial of a hemoglobin oxygen carrier, nearly 30% of seriously injured patients manifested a "coagulopathy" within 15 minutes of injury. The knowledge that these findings are a robust indicator of subsequent hospital mortality underscores the imperative of diagnosis and treatment. Despite more than 25 years of "research" in this arena, strategies are inconsistent and largely driven by expert opinion.

The current survey provides compelling evidence that early postinjury coagulopathy should be an international research priority. The authors appropriately point out that "The detection of patients at risk for posttraumatic coagulopathy at the earliest possible point in time necessitates new diagnostic approaches," and further state that "point of care diagnostics for prothrombin time and partial thromboplastin time are not widely accepted, and the same is true for thromboelastometry." Although partial thromboplastin time and international normalized ratio are the most commonly used tests to assess coagulation function, their principle use has been for anticoagulation therapy and their reliability in massive transfusion of trauma patients remain to been proven.[4] The survey did, however, indicate emerging progress with thromboelastography, although primarily in European centers. Evidence that the newer point of care rapid thromboelastography provides more timely and accurate determinations of qualitative and dynamic thrombostatic function may facilitate a scientific basis for therapy, with the potential for goal-directed resuscitation strategies,[5] rather than the current "damage control resuscitation."[6]

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