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**Compliance with the European trauma guidelines: an observational single centre study**

**Application des recommandations européennes pour la prise en charge des patients**

**traumatisés : une étude observationnelle mono centrique**

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## **Abstract**

### Objectives

The European trauma guidelines were developed to assist clinicians in the early phase of trauma management to diagnose and treat coagulopathy and bleeding. This study aimed to determine compliance with these European trauma guidelines in a French referral trauma centre.

### Methods

Medical charts of trauma patients with an injury severity score  $\geq 16$  admitted between January 2013 and December 2014 were reviewed. Compliance with 21 recommendations in the first 24-hours of patient management was assessed.

### Results

There were 145 patients with median ISS of 34 (IQR 25-41). A good level of compliance (i.e. applied in  $\geq 80\%$  of patients) was identified for nine recommendations, inconsistent compliance (i.e. applied in 50 to 79% of patients) for six recommendations, including fibrinogen levels at hospital admission and achievement of a target mean arterial blood pressure (MAP)  $>80$  mmHg in patients with major bleeding and TBI (55.5%), and poor compliance (i.e. applied in  $<50\%$  of patients) for another six recommendations. Poorly applied recommendations included early measurement of lactate or base deficit (32%), early administration of tranexamic acid (18%), and achievement of normocapnia in patients with TBI undergoing invasive ventilation (3%).

### Conclusions

In a referral trauma centre, nine of the 21 evaluable recommendations in the European trauma guidelines were applied in  $\geq 80\%$  of patients. Early diagnosis and treatment of

trauma-related coagulopathy was identified as an area for significant practice improvement.

In patients with TBI, efforts should be made to achieve the targeted MAP and to maintain normocapnia.

**Key words:** trauma, injury, bleeding, guidelines, coagulopathy

## Résumé

### *Objectifs*

Les recommandations européennes pour la prise en charge des patients polytraumatisés ont été établies pour guider les cliniciens dans la prise en charge précoce transfusionnelle et hémostatique de ces malades. Notre étude a pour objectif de déterminer le respect de ces recommandations.

### *Méthodes*

Il s'agit d'une étude rétrospective effectuée dans un centre référent français pour la prise en charge des patients polytraumatisés. Les patients ayant un *injury severity score* supérieur ou égal à 16 étaient éligibles. L'application des recommandations européennes était analysée pour les 24 premières heures de la prise en charge.

### *Résultats*

Cent quarante-cinq patients ont été inclus sur une période de 2 ans, le score ISS médian était de 34 (IQR 25-41). L'application de 21 recommandations a pu être analysée : 9 étaient bien suivies (i.e. chez plus de 80% des patients), 6 étaient partiellement suivies (i.e. chez 50 à 79% des patients) et 6 étaient peu respectées (i.e. chez moins de 50% des patients). Les recommandations peu appliquées étaient la mesure précoce du lactate et de l'excès de base (32%), l'administration pré hospitalière d'acide tranéxamique (18%), l'obtention d'une pression artérielle moyenne (PAM) supérieure à 80 mmHg chez les patients ayant

conjointement un saignement majeur et un TC (55.5%), et l'obtention d'une PCO2 normale chez les patients avec TC et sous ventilation mécanique (3%).

### *Conclusions*

Les recommandations relatives au diagnostic et traitement précoce de la coagulopathie et chez les patients avec TC l'obtention des cibles de PAM et de capnie étaient peu respectées.

**Mots clés : traumatisé, polytraumatisé, saignement, coagulopathie, recommandations européennes**

## 1. Introduction

Worldwide, severe trauma is responsible for approximately 5 million deaths annually [1].

Haemorrhagic shock, secondary to uncontrolled bleeding, is the leading cause of preventable death in this population, making control of bleeding, transfusion and treatment of coagulopathy key elements of the early phase of severe trauma management [2]. A better knowledge of the acute coagulopathy related to severe injury led to changes in early management including prompt replacement of coagulation factors, transfusion of optimal ratios of frozen plasma (FP) and red blood cell (RBC) components, timely administration of anti-fibrinolytic agents and damage control resuscitation [3] [4] [5].

The multidisciplinary Task Force for Advanced Bleeding Care in Trauma formed in 2004 issued recommendations based on the GRADE (Grading Recommendations Assessment Development and Evaluation) hierarchy of evidence [6]. These recommendations, known as “European Trauma Guidelines”, were first published in 2007 and are updated every 3 years. The guidelines aim to assist clinicians in the early management phase of severe trauma [7-9], and emphasise the need for timely diagnosis, treatment of coagulopathy and bleeding, as well as recommend implementation of measures to limit and prevent further haemorrhage. Evaluation of compliance with the European trauma guidelines has not been widely reported. The European Traumatic Shock Survey (ETRAUSS), conducted in 2015 on compliance with the European trauma guidelines, reported heterogeneity across 243 European trauma-related practitioners from 25 countries and highlighted a low compliance with recommended systolic blood pressure in bleeding patients and in patients with trauma brain injury (TBI) [10]. Therefore, we conducted a retrospective single centre observational study in a French academic referral trauma centre to determine the compliance with the European trauma guidelines.

## **2. Patients and Methods**

### *2.1. Study design and study population*

This was a retrospective single centre study conducted in the university-affiliated hospital of Brest, France. The hospital is the trauma referral centre for the western region of Brittany and services a population of around one million inhabitants. The academic trauma centre has a 21-bed surgical intensive care unit (ICU). All patients admitted to the hospital between January 2013 and December 2014 who were identified through the hospital diagnostic code system with a primary or secondary diagnosis of one of the following, “Trauma”, “Severe Trauma” or “Multiple Trauma” and had an Injury Severity Score (ISS)  $\geq 16$  [11], were eligible. Exclusion criteria were: patients  $< 18$ -years old, or who were admitted more than 24 hours after the injury. Patient outcomes were captured up to hospital discharge. The study was approved by the Research Ethics Committee of Brest University Hospital.

### *2.2. Data collected*

Data related to the trauma management, within the first 24-hour from injury, were collected from the medical history and clinical charts. Demographics, co-morbidities, ICU and hospital admission and discharge dates, severity based on the Simplified Acute Physiology Score (SAPS) II [12], the Sequential Organ Failure Assessment (SOFA) score [13] and the ISS [11] were collected. Trauma characteristics including mechanism, kinetics and presence or not of TBI, defined by either an Abbreviated Injury Scale (AIS)  $> 3$  or a Glasgow Coma Scale (GCS) of  $\leq 8$ , were recorded at the trauma scene before intubation and/or sedation.

The lowest systolic, diastolic and mean arterial blood pressure, the lowest body core temperature and GCS were recorded at the following settings: trauma scene/pre-hospital,

emergency department (ED), operating room (OR) and ICU within the first 24 hours following injury.

Data related to therapeutics included: 1) fluid replacement and type of product (crystalloids or colloids), 2) vasopressor administration, 3) blood components transfused (Red Blood Cell (RBC), Frozen Plasma (FP) and Platelet (PLT)) and 4) any other haemostatic agent including fibrinogen concentrate (FC), activated recombinant factor VII, prothrombin complex concentrate and tranexamic acid (TXA). When applicable, the volume and time of administration of these therapeutics were recorded. Time and results of laboratory tests included arterial blood gases, serum lactate, base deficit, haemoglobin, ionised calcium, platelet count, coagulation tests with prothrombin time (PT), ratio of activated partial thrombin time (aPTT) patient over referent aPTT, anti-Xa, and serum levels of fibrinogen, urea, creatinine and bilirubin. Viscoelastic methods were not standard practice during the study period at the study centre.

Imaging data included focused assessment with sonography for traumas (FAST) and total body computed tomography (CT) scan. Types and time of potential interventions including requirement for invasive mechanical ventilation, use of tourniquet, surgery and angiographic embolisation were also collected.

### *2.3. Management of trauma patients*

During the study period, severely injured trauma patients were managed in the pre-hospital setting by an emergency medical team with an emergency medicine physician. There was no dedicated trauma team for trauma patient management at ED admission. There was no massive transfusion protocol alert system in place. However, clinicians and blood bank scientists communicated closely when a severe trauma patient was admitted. Requests for blood components were routinely prioritised according to the three nationally applied levels

of emergency response: highly urgent (immediate delivery of blood component without cross match), moderately urgent delivery of blood component within 30 min and non-urgent. In practice, response times to the first two levels tended to be similar.

For this study, major bleeding was defined as the transfusion of at least two RBC units within 24 hours, based on the major bleeding definition of the International Society on Thrombosis and Haemostasis (ISTH) [14]. Although this definition is not specific to trauma patients, we reasoned that it would capture all profoundly injured trauma patients who met the study inclusion criteria but died of their injuries before transfusion of greater numbers of RBC units was possible. Massive transfusion was defined as  $\geq 8$  RBC units transfused within 6 hours [15].

#### *2.4. European trauma guidelines*

Two versions of the European trauma guidelines were used in this study; the 2<sup>nd</sup> edition (2010) and the 3<sup>rd</sup> edition (2013) published mid-way through the data collection period of this audit study [7] [8]. The total study population was analysed against the recommendations that were common to both versions of the European trauma guidelines, while patients hospitalised in 2013 were analysed against additional recommendations specific to the 2010 version and patients hospitalised in 2014 were analysed against additional recommendations specific to the 2013 version.

There were 31 and 37 recommendations in the 2010 and 2013 versions of the guidelines, respectively [7, 8]. Some recommendations were identified *a priori* as not assessable retrospectively and were excluded from the study (Table 1). For recommendations comprised of several parameters, only certain parameters may have been evaluable retrospectively for this study dependent on data availability. We defined the following level of compliance: good level of compliance when the recommendation was applied in  $\geq 80\%$  of

patients, inconsistent compliance (i.e. applied in 50 to 79% of patients) and poor compliance (i.e. applied in <50% of patients).

### *2.5. Statistical analysis*

Descriptive statistics are reported as mean  $\pm$  standard deviation (SD) or median [inter quartile range (IQR)] according to data distribution. Characteristics of patients admitted in 2013 were compared to those admitted in 2014. Hypothesis testing was performed using Chi-square and Fisher test for categorical variables, Student's t-test for normally distributed continuous data and Wilcoxon rank-sum for non-parametric continuous data. Differences were considered significant if the p value was < 0.05. Statistical analysis was performed using SAS 9.1 Statistical Software<sup>®</sup> (SAS Institute. Cary. NC. USA). No sample size was calculated for this observational study. Based on known hospital admission numbers, the review of all consecutive trauma patients admitted to hospital within the two-year study period was expected to capture a sufficient number of cases for the purpose of this compliance audit study. No imputation or any other form of replacement for missing data was done; assessment of compliance with the guidelines included only cases with all required data available.

## **3. Results**

### *3.1. Patients and trauma characteristics*

Enquiry of the hospital diagnosis code system identified 173 patients hospitalised for trauma during the study period. Of these, 28 patients were excluded; 14 cases were misclassified and were not trauma patients, six patients were admitted after the first 24 hours since injury and eight patients had an ISS <16. There were 145 patients who met the inclusion criteria. Patient and trauma characteristics are summarised in Table 2; there were

no statistically significant differences between the study cohort of patients admitted to hospital during 2013 compared to 2014.

### *3.2. Hemodynamic parameters and resuscitation*

Crystalloids were used for initial fluid/blood volume resuscitation in 95.2% of cases. Colloids were administered to seven patients (4.8%) at the trauma scene and a total of 39 patients (26.9%) within the first 24 hours (recommendation 8, Table 3). In non-TBI patients (n=79), the mean lowest systolic arterial blood pressure recorded at the four treatment settings (trauma scene/pre-hospital, ED, OR and ICU) was  $90 \pm 22$  mmHg, and in 35 of the 46 patients (76%) with major bleeding, the lowest systolic arterial blood pressure was  $>80$  mmHg (recommendation 6, Table 3). In the 65 patients with TBI, the lowest mean arterial blood pressure (MAP) was  $64 \pm 15$  mmHg. The MAP was maintained above 80 mmHg in 55.5% (10/18) of patients with TBI and major bleeding admitted in 2013 (recommendation 7, Table 3).

### *3.3. Coagulopathy diagnosis and treatment*

PLT count and coagulation tests, including PT and aPTT, were performed at ED admission for most of the patients ( $>98\%$ ) (Table 4). A subgroup of 100 patients (68.9%) had all the coagulation measures including fibrinogen level performed early at the ED admission (recommendation 4, Table 3). Although lactate or base deficit were measured in most patients (92%) within the first 24 hours, the tests were performed during the ED admission in only 46 patients (32%) (recommendation 3, Table 3).

The median temperature at each treatment setting (trauma scene/pre-hospital, ED, OR and ICU) is shown in Figure 1. The mean lowest body core temperature was  $35.5 \pm 1.4^\circ\text{C}$  and for

the patient group that received 2 or more RBC (n= 64; 44.1%), the mean lowest temperature was  $35.1 \pm 1.4^{\circ}\text{C}$ . Control of temperature above  $35^{\circ}\text{C}$  was achieved in 109 patients (75.2%) (recommendation 9, Table 3).

All patients previously treated with vitamin K antagonists all received prothrombin complex concentrate (PCC) (n= 4) (recommendation 18, Table 3). Three patients in the 2014 cohort, who were previously treated with PLT inhibiting drugs, suffered significant intracranial or perisplenic bleeding; one patient (33%) received PLT transfusion (recommendation 19, Table 3), and no patients received desmopressin (recommendation 21, Table 3).

The median lowest haemoglobin was 10.4 g/dL (IQR 8.8 – 12) in the total study population (Table 3) and 10.3 g/dL (IQR 8.8-11.9) in patients who received RBC transfusion.

Haemoglobin levels lower than 7 g/dL occurred in 27 patients (18.6%) (recommendation 10, Table 3) and four of these patients had profound anaemia ( $\text{Hb} < 6\text{g/dL}$ ). The target haemoglobin level (i.e. 7 to 9 g/dL) was achieved in 118 of the 145 patients (81%).

Coagulation parameters of patients with major bleeding are shown in Table 5. Seventeen of the 27 patients (63%) with major bleeding and a fibrinogen level  $< 1.5\text{ g/dL}$ , received FC. FC was not administered to non-bleeding patients with a fibrinogen level  $> 2\text{ g/dL}$  (recommendation 16, Table 3). All patients who had a massive transfusion and who had hypocalcaemia were given intravenous calcium (recommendations 11, Table 3). In 2013, 27 of the 37 patients (73%) with major bleeding received FP; however, for the subgroup of patients who received  $\geq 4\text{ RBC}$ , 7 of the 8 patients (87.5%) received FP (recommendations 12, Table 3). In 2014, 15 of 27 patients (55.6%) with major bleeding received either FP or FC and for the subgroup of patients who received  $\geq 4\text{ RBC}$ , all (15/15) received either FP or FC (recommendation 13, Table 3). The median FP/RBC ratio was 1 (IQR 0.7 -1.5) in patients transfused with FP. In the 10 patients who received massive transfusion, the FP/RBC ratio

was always above 0.5 (recommendation 16, Table 3). Transfused patients (n= 68) had a mean PLT count of  $160 \pm 47 \times 10^9/L$  and 33 (48.5%) received PLT transfusion (Table 6). Three patients with TBI had a PLT count below  $100 \times 10^9/L$ , two of the patients (66.6%) received PLT transfusion (recommendation number 15, Table 3).

TXA was administered to 39 of the 145 patients (26.9%); 15/68 (22%) in 2013 and 24/77 (31%) in 2014. However, only 10 of the 145 patients (6.9%) received TXA within the first 3 hours from injury. Considering only the 2014 patient cohort, the median delay between initiation of trauma management and TXA administration was 135 minutes [IQR 105-175]; only eight of the 24 patients (33%) administered TXA, received TXA prior to hospital admission (recommendation 17, Table 3). Furthermore, the median dose of TXA was lower than recommended (Table 6).

#### *3.4. Bleeding diagnosis and control*

CT body scan was performed on 139 patients (96%) within a median time of 150 min [IQR 118-194]. Two of the six patients without CT body scan had a FAST body echo recorded in their medical chart (recommendation 2, Table 3).

The three patients who suffered from pelvic ring disruption and who had haemorrhagic shock did not undergo pelvic ring closure (recommendation 5, Table 3). Tourniquet was used at the trauma scene in three patients who were considered to have life-threatening bleeding from open extremity injuries. However, it was not possible to assess whether other patients with extremity injuries had an indication for tourniquet use. Surgery was performed within the first 24 hours for 77 patients, including 20 patients for bleeding control (Table 6). Another 11 patients had angio-embolisation for bleeding control (Table 6). Whether any

attempts were made to shorten the time between trauma and bleeding control could not be assessed.

### *3.5. Other interventions*

Arterial blood gases were available in all ventilated patients (n= 103). Patients tended to initially have hypercapnia (median PaCO<sub>2</sub> 47 mmHg, IQR 42-55) and then hypocapnia (median PaCO<sub>2</sub> 33.5 mmHg, IQR 29-37). Normocapnia was achieved in only one of the 31 ventilated patients in 2014 (recommendation 1, Table 3). Ventilator setting and tidal volume could not be analysed because of missing data.

Data for mechanical thromboprophylaxis was available for 68 of the 77 patients in the 2014 cohort; 67 (98.5%) of the assessable cases received mechanical thromboprophylaxis (recommendation 20, Table 3).

### *3.6. Summary of compliance with the European trauma guidelines*

Of the 21 recommendations that could be assessed in this study, a good level of compliance was identified for nine recommendations (i.e. applied to ≥80% of cases), inconsistent compliance for six recommendations (i.e. applied to 50 to 79% of cases), and compliance was poor for six recommendations (i.e. applied in <50% of cases) (Table 3). The inconsistently applied recommendations included those related to early diagnosis of coagulopathy (68.9% compliance), achievement of normothermia (75.2% compliance), the administration of FC in patients with major bleeding and low fibrinogen level (63% compliance), achievement of target MAP in patients with major bleeding (with and without TBI) (55.5% compliance), and PLT transfusion to maintain target PLT counts (67% compliance). The six recommendations for which compliance was poor included the use of pelvic ring in patients with haemorrhagic shock and pelvic ring disruption (0% compliance;

total of 3 cases), the early administration of TXA (18% compliance), achievement of normocapnia in mechanically ventilated patients (3% compliance; total of 31 cases), early measurement of base deficit or lactate (32% compliance), and PLT transfusion or desmopressin administration in patients with major bleeding or ICH in patients treated with PLT inhibiting drugs (33% and 0% compliance respectively; total of 3 cases).

## **Discussion**

In our referral trauma centre, nine of 21 assessable recommendations of the European trauma guidelines were consistently applied, while the other recommendations were either inconsistently (n=6) or poorly (n=6) applied. Identified target areas for improvement included early diagnosis and treatment of coagulopathy, achievement of haemodynamic control and ventilation management. When managing patients with severe trauma, efforts must be taken to include early determination of fibrinogen level and lactate and/or base deficit for the diagnosis of coagulopathy and early administration of the appropriate dose of TXA. Optimisation of ventilation settings to achieve normal PCO<sub>2</sub> and optimisation of haemodynamic parameters in the presence of TBI and/or major bleeding are important areas for improvement.

Several studies have emphasised the positive impact of good compliance with guidelines on patient outcome, highlighting the importance to implement and comply with current trauma guidelines [16] [17]. However, the ETRAUSS survey conducted in 2015 to assess compliance with the European trauma guidelines found many deviations from the recommendations, suggesting a need for improvement [10]. For instance, in this survey, only 38% of the responders targeted a systolic arterial blood pressure between 80 and 90

mmHg in patients in haemorrhagic shock without TBI and only 31% complied with the targeted blood pressure in the presence of TBI. Although, questionnaires capture important information, they may not reflect precisely what is done in practice. To our knowledge, our study is the first observational study to report the level of compliance with the European trauma guidelines in a cohort of trauma patients treated at a single referral trauma centre. Although standard practices can be deduced from recent large observational studies, these studies in the setting of trauma management often focus on blood components ratio and anti-fibrinolytic therapeutics and do not attempt to evaluate other guidelines including haemodynamic recommendations [18-20]. Interventions, including achievement of normothermia and correction of hypocalcaemia have been reported to also play a key role in the prevention of further bleeding in trauma patients [21]. Importantly, observational studies may not analyse the timing of the interventions. In our study, we considered the time of coagulopathy diagnosis and interventions when possible. Fibrinogen level, the earliest biomarker of trauma induced coagulopathy, was measured in 69% of the study cohort within the first 24 hours; however, only 63% of patients with active bleeding and fibrinogen deficit were administered FC [22]. It is unclear why some patients did not receive FC despite having overt deficiency.

The reasons for poor compliance of various other recommendation are also unclear and might be due to several factors, depending on the particular recommendation. Some recommendations are not supported by high levels of evidence. For instance, administration of desmopressin in patients treated with PLT inhibiting drugs is not supported by strong evidence and was removed from the 2013 edition of the European trauma guidelines. Non-administration of TXA may have been due to misdiagnosis of the patient's haemostatic

condition, educational issues or the absence of a trauma checklist or trauma alert system at the time of the study.

### *Strengths and limitations*

A major strength of our study was the comprehensive review of all medical and nursing charts generated within the first 24 hours following trauma injury, including at the trauma scene, ED, OR and ICU. This compilation of data resulted in a very precise and complete dataset that allowed accurate assessment of all recommendations of the European trauma guidelines evaluable retrospectively as well as the time that specific interventions occurred during trauma management. Furthermore, this study was conducted in a major regional academic referral trauma centre that serves a large catchment area.

However, our study had some limitations. It was a retrospective study and consequently some guidelines could not be assessed. In addition, because it was a single-centre study, the results may not be generalisable. Some recommendations were applicable to only a few patients, limiting the accuracy of assessment of compliance and making it difficult to draw definitive conclusions. However, to minimise bias, all consecutive eligible trauma cases were included in the analysis and, at the planning phase of the study, each recommendation in the guidelines was carefully considered for feasibility to be accurately assessed. Major bleeding was defined by the requirement for RBC transfusion based on the ISTH definition, which is not specific to the trauma setting; however, in the relatively young patient cohort in this study, transfusion of at least two RBC units within 24 hours would likely reflect substantial acute bleeding. Although the ISTH definition is not specific to trauma, it considers patients who may benefit from the application of the European trauma guidelines in order to reduce bleeding and avoid the need for further transfusion. More than half of

the study cohort did not require blood transfusion, which suggests that some of the recommendations were less relevant to their specific treatment plan. However, compliance was assessed only in the subgroup of patients where the recommendations were relevant and should have been applied. Although the European trauma guidelines have been recently updated, recommendations evaluated in our study remain in the 2016 version of the guidelines [9]. Finally, some interpretations may have been biased, as non-achievement of targets may not mean non-compliance with recommendation for some guidelines. For instance, the absence of records of ventilator settings and patient ventilation parameters limited the determination of whether hypocapnia was related to spontaneous breathing or ventilator settings.

#### *Study implications and future research*

Our study provides a snapshot of how the European trauma guidelines have been applied in our hospital and allow the identification of areas for practice improvement, including 1) earlier determination of fibrinogen level, base deficit and/or lactate in all severely injured trauma patients to allow prompt identification of coagulopathy, 2) pre-hospital TXA administration with appropriate dose and fibrinogen replacement, when necessary, for earlier coagulopathy treatment, 3) better control of arterial blood pressure based on the presence or not of TBI in patients with major bleeding, and 3) better control of PCO<sub>2</sub> in ventilated patients.

Further research is warranted, including repeat of the study on the trauma cohort since 2015. This would provide comparison of results and identify the impact of any recent changes in trauma management, such as the implementation of checklists and algorithms to

improve compliance with the guidelines and the introduction of new technologies or procedures.

## 5. Conclusion

We retrospectively assessed the compliance with the European trauma guidelines in a major referral trauma centre. Less than half of the assessable recommendations were consistently applied. Opportunities for improvement in trauma management practice were identified, in particular related to early diagnosis and treatment of trauma coagulopathy and interventions to minimise worsening of brain damage in TBI patients. Our study demonstrated a feasible approach that could be adopted by trauma centres to review and audit the level of compliance with the European trauma guidelines.

## Disclosure of interest

The authors declare that they have no competing interest related to this work.

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None

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**Table 1**

Recommendations in the 2010 and 2013 versions of the European Trauma Guidelines that were not evaluable in this study [7,8].

Recommendation number		Description of Recommendation
Version 2010	Version 2013	
1	1	minimise the time between injury and operation in bleeding patients needing urgent surgery
2	2	appropriate use of tourniquet
3	4	physician clinical assessment of the extent of bleeding and injuries
5, 8	5, 6, 8	whether bleeding control when urgently required was immediate or not
10	10	whether clinicians transfused on haematocrit only
14 - 17	18, 20 -22	whether peritoneal packing, topical haemostatic agents, angiography for haemostasis and damage control surgery were applied when indicated
-	32	management of patients treated with oral anti-Xa agent
28	33	use of recombinant activated coagulation factor VII
31	-	use of anti-thrombin III
-	35 - 37	implementation of checklist and measures to increase adherence to the guidelines

**Table 2**

Patients and trauma characteristics.

Variable	All patients	Patients admitted in	Patients admitted in
	2013 and 2014	2013	2014
	n = 145	n = 68	n = 77

Age, years, mean $\pm$ SD	42.8 $\pm$ 19.6	42.9 $\pm$ 19.2	42.7 $\pm$ 20.1
Gender, male, n (%)	106 (73.1)	51 (75)	55 (71.4)
BMI > 30kg/m <sup>2</sup> , mean $\pm$ SD	6 $\pm$ 4.1	2 $\pm$ 2.9	4 $\pm$ 5.2
- Comorbidities <sup>a</sup>			
- Chronic cardio-vascular, n (%)	12 (8.3)	4 (5.9)	8 (10.4)
Chronic respiratory disease, n (%)	11 (7.5)	5 (7.3)	6 (7.8)
- Mental health disorders, n (%)	20 (13.8)	9 (13.2)	11 (14.3)
Habitus			
- Chronic alcohol abuse, n (%)	17 (11.7)	9 (13.2)	8 (10.4)
- Current smoker, n (%)	18 (12.4)	11 (16.2)	7 (9.1)
Transfer from another hospital, n (%)	43 (29.7)	24 (35.3)	19 (24.7)
Score SAPS II, median [IQR]	34 [21 - 47]	34 [23 - 46]	35 [21 - 48]
Score SOFA, median [IQR] <sup>b</sup>	7 [3 - 10]	7 [3 - 11]	6,5 [3 - 10]
Score ISS, median [IQR]	34 [25 - 41]	33,5 [27 - 42]	34 [24 - 41]
Injuries			
- Blunt injury, n (%)	144 (99.3)	67 (98.5)	77 (100)
- Penetrating injury, n (%)	1 (0.7)	1 (1.5)	0
Trauma kinetic <sup>c</sup>			
- Low, n (%)	11 (7.9)	2 (3.1)	8 (10.7)
- Intermediate, n (%)	16 (11.5)	8 (12.7)	8 (10.7)
- High, n (%)	112 (80.6)	53 (84.2)	59 (78.6)
Glasgow score at the trauma scene, median [IQR]	13 [7 - 15]	14 [7 - 15]	13 [8.8 - 15]
Glasgow score at the ED admission, median [IQR] <sup>d</sup>	11 [3 - 15]	12 [3 - 15]	11 [3 - 15]
ALS head > 3, n (%)	66 (45.5)	30 (44.1)	36 (46.8)
ALS thorax > 3, n (%)	29 (20)	11 (16.2)	18 (23.4)

AIS abdomen > 3, n (%)	35 (24.1)	16 (23.5)	19 (24.7)
AIS extremities > 3, n (%)	33 (22.8)	19 (27.9)	14 (18.2)
Lowest MAP in patients with TBI, mean $\pm$ SD <sup>e</sup>	63 $\pm$ 15	70 $\pm$ 15	65 $\pm$ 13
Lowest SBP in patients without TBI, mean $\pm$ SD <sup>f</sup>	90 $\pm$ 22	89 $\pm$ 21	91 $\pm$ 24
Major bleeding, n (%)	64 (44.1)	37 (54.4)	27 (35.1)
Patients requiring vasopressors, n (%)	82 (56)	43 (63.2)	39 (50.7)
Patients requiring invasive MV, n (%)	82 (56)	38 (55.9)	44 (57)
Hospital LOS, days, median [IQR]	25 [13 - 48]	24,5 [13 - 4.3]	22 [10 - 48]
Hospital mortality, n (%) <sup>g</sup>	17 (11.7)	11 (16.2)	6 (7.8)
Time to death, days, median [IQR]	3,5 [2 - 7]	5 [2 - 13.5]	3 [1.25 - 4]

P value was higher than 0.05 for all comparisons between both study periods.

BMI: Body Mass Index; SAPS II: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure assessment; ISS: Injury Severity Score; AIS: Abbreviated Injury Scale; LOS: Length of stay.

<sup>a</sup>Data were available in 134 patients (65 in 2013 and 69 in 2014)

<sup>b</sup>Data were available in 144 patients (68 in 2013 and 76 in 2014)

<sup>c</sup>Data were available in 139 patients (63 in 2013 and 75 in 2014)

<sup>d</sup>Data were available in 144 patients (68 in 2013 and 76 in 2014)

<sup>e</sup>Data were available in 85 patients in the sub-group of suspected TBI (88 patients) : 42 in 2013 and 43 in 2014

<sup>f</sup>Data were available in 42 patients in the sub-group of patients without suspected TBI (45 patients) : (24 in 2013 and 18 in 2014)

<sup>g</sup>Death occurred in the first 24 hours for one patient.

**Table 3**

Compliance with the recommendations of the European trauma guidelines.

Nb	Recommendations	Compliance (%)
1	Initial normo-ventilation with low tidal volume. Target PaCO <sub>2</sub> = 37-41 mmHg <sup>a</sup>	1/31 (3)
2	Whole body CT for hemodynamically stable patients in case of high risk mechanism of injury or suspected torso trauma	130/130 (100)
3	Serum Lactate or base deficit measurements to estimate/monitor the extend of bleeding and shock <sup>b</sup>	46/145 (32)
4	Early, repeated and combined measures of PT, aPTT, Fg and PLT to detect post traumatic coagulopathy; the only measures of PT and aPTT are not sufficient <sup>b</sup>	100/145 (68.9)
5	Patients pelvic ring disruption in haemorrhagic shock undergo immediate pelvic ring closure and stabilisation	0/3 (0)
6	Target systolic blood pressure of 80 to 90 until <sup>a</sup> (to 100 until <sup>c</sup> ) major bleeding has stopped in patients without TBI	35/46 (76)
7	In presence of TBI and major bleeding: target MAP ≥ 80 mmHg <sup>a</sup>	10/18 (55.5)
8	Crystalloids be applied initially to treat bleeding trauma patients	138/145 (95.2)
9	Early applications of measures to reduce heat loss and warm hypothermic patient to achieve normothermia	109/145 (75.2)
10	Target Hb of 7 to 9 g/dL	118/145 (81)
11	Ionised calcium to be monitored and maintained in the normal ranges when massive transfusion	9/9 (100)
12	Early transfusion of FP when major bleeding <sup>c</sup>	7/8 (87.5)
13	Early transfusion of FP or Fg when major bleeding <sup>a</sup>	15/15 (100)
14	If further plasma is administered suggested FP:RBC ratio of at least 1:2	28/28 (100)
15	Platelet transfusion to maintain platelet count > 50 000/mm <sup>3</sup> , or >100 000/mm <sup>3</sup> when active bleeding and /or TBI	2/3 (67)
16	Administration of fibrinogen concentrate or cryoprecipitate when active	17/27 (63)

	bleeding and functional Fg deficit diagnosed by ROTEM or serum Fg<1.5-2g/dL (initial FC dose of 3 to 4g)	
17	Early administration (<3 hours) of Tranexamic acid (1g) in bleeding patients or at high risk of haemorrhage	10/145 (18)
18	Early use of PCC for emergency reversal of vitamin K-dependent oral anticoagulants	4/4 (100)
19	PLT Transfusion if major bleeding or ICH in patients treated with platelet inhibiting drugs <sup>a</sup>	1/3 (33)
20	Mechanical thromboprophylaxis with intermittent pneumatic compression and/or anti-embolic stockings as soon as possible <sup>a</sup>	67/68 (98.5)
21	No desmopressin in routine in bleeding trauma patients, desmopressin could be considered in microvascular bleeding in patient treated with platelet-inhibiting drug	0/3 (0)

<sup>b</sup> Only measures performed at hospital admission were considered as appropriate

<sup>a</sup> Recommendation that belongs only to the 2013 European trauma guidelines

<sup>c</sup> Recommendation that only belong to the 2010 European trauma guidelines

TBI: trauma brain injury; Fg: Fibrinogen; PLT: platelet; PCC: prothrombin complex concentrate; FP: frozen plasma; Hb: Haemoglobin; MAP: mean arterial blood pressure; ICH: intra cranial haemorrhage; PT: prothrombin time; aPTT: activated Partial Thromboplastin Time.

**Table 4**

Haemostasis parameters within the first 24 hours.

Variable	Patients with test performed	All Patients n = 145	Patients with test done n = 68	Patients admitted in 2013 n = 68	Patients with test done n = 77	Patients admitted in 2014 n = 77
<b>Worse value within 24 hours</b>						
Hemoglobin, g/dL	145	10.4 [ 8.8 - 12 ]	68	9.9 [8.375 – 11.4]	77	10,7 [9,5 – 12,4]
PT, %	145	64 [51 - 74]	68	62 [51 - 70.2]	77	69 [50 - 76]
INR	37	1.3 [1.2 - 1.95]	15	1.3 [1.23 - 1.7]	22	1.3 [1.2 - 2.15]
ratio TCA	145	1.19 [1.07 - 1.37]	68	1.21 [1.1 - 1.37]	77	1.17 [1.04 - 1.38]
Fibrinogen, g/L	139	1.9 [1.5 - 2.4]	65	1.8 [1.5 - 2.3]	74	2.10 [1.6 - 2.5]
Ionised Calcium, mmol/L	132	0.93 [0.88 - 0.97]	63	0.93 [0.88 - 0.97]	69	0.93 [0.88 - 0.97]
Platelet count, x10 <sup>9</sup> /L	145	139 [97 - 185]	68	124 [87 - 182]	77	147 [107 - 187]
Base deficit, mmol/L <sup>a</sup>	133	-5 [-8.78 - -2.08]	63	-6.4 [-9.2 - -2.8]	70	-4.2 [-8.7 - -2]
<b>Best value within 24 hours</b>						
Hemoglobin, g/dL	145	13.9 [12.5 – 15.2]	68	13.5 [12.1 – 14.9]	77	14.2 [12.8 - 15.3]
PT, %	45	83 [71 - 94]	68	82 [71 - 94]	77	84 [72 - 93]
INR	37	1.3 [1.1 - 1.6]	15	1.3 [1.07 - 1.6]	22	1.27 [1.1 - 1.6]
ratio TCA	145	0.97 [0.9 - 1.06]	68	0.97 [0.9 - 1.08]	77	0.97 [0.91 - 1.06]
Fibrinogen, g/L	139	2.9 [2.4 - 3.4]	65	2.8 [2.3 - 3.3]	74	2.9 [2.4 - 3.6]
Ionised Calcium, mmol/L	132	0.97 [0.94 - 1.02]	63	0.97 [0.94 - 1.04]	69	0.97 [0.94 - 1.02]
Platelet count, x10 <sup>9</sup> /L	145	244 [204 - 286]	68	244 [198 - 275]	77	241 [210 - 294]
Base deficit, mmol/L <sup>a</sup>	133	-1.1 [-3.5 - 0]	63	-1.35 [-3.53 - 0]	70	-1.1 [-3.2 - 0]

Values are expressed as medians and [interquartile range]

PT: prothrombin time; INR: International Normalised Ratio; TCA: ratio aPTT patient over aPTT reference.

<sup>a</sup>Data were available in 132 patients (63 in 2013 and 69 in 2014)**Table 5**

Coagulation parameters in patients with major bleeding according to the International Society on Thrombosis and Haemostasis definition.

Variable	Patients with test performed (n, %)	All Patients n = 64
<b>Worse value within 24 hours</b>		
PT, %	64 (100%)	51 [40 ; 59.3]
INR	22 (34%)	1.45 [1.25 ; 1.6]
ratio TCA	64 (100%)	1.36 [1.21 ; 1.56]
Fibrinogen, g/L	64 (100%)	1.55 [1.23 ; 1.83]
Ionised Calcium, mmol/L	62 (97%)	0.9 [0.85 ; 0.95]
Platelet count, x10 <sup>9</sup> /L	64 (100%)	228 [198 ; 275.5]
Base deficit, mmol/L <sup>a</sup>	60 (94%)	- 8.1 [-11.2 ; -4.68]

Values are expressed as medians and [interquartile range]

PT: prothrombin time; INR: International Normalised Ratio; TCA: ratio aPTT patient over aPTT reference.

**Table 6**

Transfusion management within the first 24 hours.

Variables	All patients	Patients admitted in	Patients admitted in
	2013 and 2014 n = 145	2013 n = 68	2014 n = 77
Patients transfused with $\geq 1$ RBC units, n (%)	68 (46.9)	39 (57.4)	29 (37.7)
Number of RBC transfused per patient, median [IQR]	3.5 [2 - 6]	3 [2 - 5.5]	4 [2 - 6]
Massive transfusion, n (%)	10 (6.9)	7 (10.3)	3 (3.9)
Time trauma to RBC transfusion, min, median [IQR]	295 [173 - 530]	388 [180 - 550]	280 [125 - 471]
Patients transfused with FP, n (%)	53 (36.6)	30 (44.2)	23 (30%)
Number of FP transfused per patient, median [IQR]	4 [2 - 8]	5 [2 - 8.8]	4 [3 - 7.5]
Time trauma to-FP transfusion, min, median [IQR]	340 [238 - 533]	420 [235 - 595]	360 [313 - 248]
Patients transfused with PLT, n (%)	33 (22.8)	19 (28)	14 (18.2)
Number of PLT transfused per patient, median [IQR]	1 [1 - 2]	1 [1 - 2]	1.5 [1 - 2]
Patients received tranexamic acid, n (%)	39 (27)	15 (22.1)	24 (31.2)
Tranexamic acid dose/24h, g, median [IQR]	1 [1 - 2]	1 [1 - 2]	1 [1 - 2]
Time to tranexamic acid, minutes, median [IQR]	135 [105 - 175]	173 [120 - 296]	118 [69 - 146]
Patients received fibrinogen concentrate, n (%)	26 (18)	13 (19.1)	13 (16.9)
Fibrinogen concentrate dose, g, median [IQR]	3 [1.5 - 3]	3 [1.5 - 3]	3 [1.5 - 3]
Haemostatic surgery, n (%)	20 (13.8)	10 (14.7)	10 (13)
Haemostatic embolisation, n (%)	11 (7.6)	3 (4.4)	8 (10.4)

RBC: red blood cells; FP: frozen plasma; PLT: Platelets. There were no missing data for these variables.

Figure 1. Patient median temperature (°C) and interquartiles at the four settings (pre-hospital; ED: emergency department; OR: operating room; ICU: intensive care unit). Data were missing for 136 patients in pre-hospital setting, 80 patients in ED, 34 of the 74 patients in OR and 1 patients in ICU

