



# Trauma-induced coagulopathy upon emergency room arrival: still a significant problem despite increased awareness and management?

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## Abstract

**Purpose** Over the last decade, the pivotal role of trauma-induced coagulopathy has been described and principal drivers have been identified. We hypothesized that the increased knowledge on coagulopathy of trauma would translate into a more cautious treatment, and therefore, into a reduced overall incidence rate of coagulopathy upon ER admission.

**Patients and methods** Between 2002 and 2013, 61,212 trauma patients derived from the TraumaRegister DGU® had a full record of coagulation parameters and were assessed for the presence of coagulopathy. Coagulopathy was defined by a Quick's value < 70% and/or platelet counts < 100,000/μl upon ER admission. For each year, the incidence of coagulopathy, the amount of pre-hospital administered i.v.-fluids and transfusion requirements were assessed.

**Results** Coagulopathy upon ER admission was present in 24.5% of all trauma patients. Within the years 2002–2013, the annual incidence of coagulopathy decreased from 35 to 20%. Even in most severely injured patients (ISS > 50), the incidence of coagulopathy was reduced by 7%. Regardless of the injury severity, the amount of pre-hospital i.v.-fluids declined during the observed period by 51%. Simultaneously, morbidity and mortality of severely injured patients were on the decrease.

**Conclusion** During the 12 years observed, a substantial decline of coagulopathy has been observed. This was paralleled by a significant decrease of i.v.-fluids administered in the pre-hospital treatment. The reduced presence of coagulopathy translated into decreased transfusion requirements and mortality. Nevertheless, especially in the most severely injured patients, posttraumatic coagulopathy remains a frequent and life-threatening syndrome.

**Keywords** Coagulopathy · Resuscitation · Haemorrhage · Trauma · Mortality

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Matthias Fröhlich and Manuel Mutschler contributed equally to this work.

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## Introduction

Uncontrolled haemorrhage still accounts for 50% of all trauma-related deaths within the first 48 h after hospital admission [1, 2] and is still the primary cause of potentially preventable deaths following severe injury [3]. The scenario is often exaggerated by the presence of accompanying haemostatic perturbations, which are present upon emergency room (ER) admission in 20–60% of all cases depending on the definition [4–7].

Over the past decade, increasing awareness of the potentially evolving trauma-induced coagulopathy (TIC), triggered by a multitude of both clinical and basic research initiatives, resulted in the recognition of the TIC as an own clinical entity [6, 8]. The current concept of the TIC is summarized in Fig. 1. This concept distinguishes endogenous from exogenous components: (1) an acute traumatic coagulopathy (ATC), which occurs early and is not accessible to

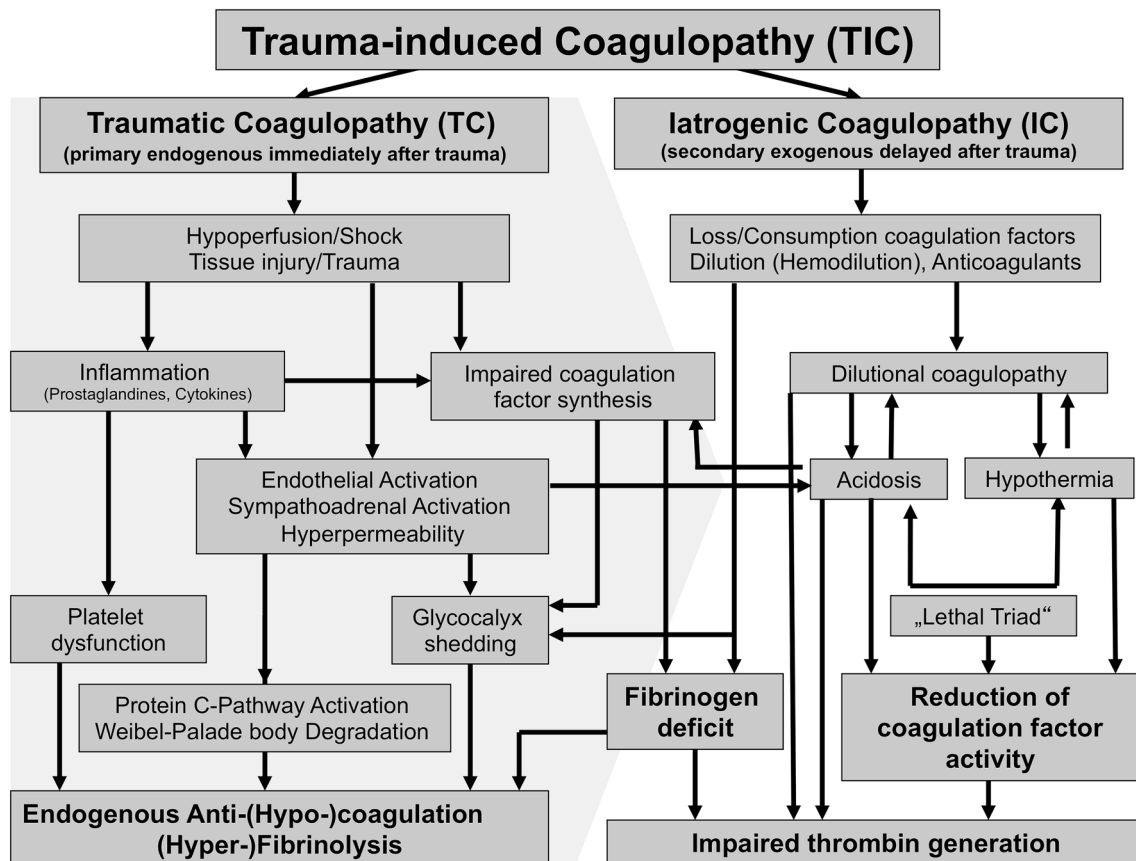


Fig. 1 The current concept of the coagulopathy of trauma (modified according to [31])

treatment, and (2) an iatrogenic coagulopathy (IC), which is associated with haemodilution, acidosis and hypothermia as a sequel of resuscitation during the initial pre-hospital and early in-hospital phase of care [6, 9–11]. The deleterious effects of haemodilution and resulting factor depletion include impaired protease cascade activation, impaired thrombin production, reduced platelet function and dysfunctional fibrinogen utilisation [12, 13].

In trauma patients, captured in the TraumaRegister DGU® database, coagulopathy was present in more than 40% of the patients who had received more than 2000 ml and in more than 70% of the patients who had received more than 4000 ml of fluid during their pre-hospital phase of care [6]. Within the so-called “vicious cycle”, haemodilution is a central component, which may further aggravate the TIC (Fig. 1). Besides the preservation of a normal body temperature, the amount of resuscitation fluids given during the pre-hospital treatment is the driver of IC that can be easily influenced. Therefore, the current European guideline on management of major bleeding and coagulopathy following trauma recommends a restricted volume replacement strategy [14].

In the present study, we hypothesized that over 12 years of time, there should have developed an increased awareness of TIC and its association with the amount of i.v.-fluids during the pre-hospital phase of trauma care. Consequently, this development should result into a reduced overall incidence rate of haemostatic disorders upon ER admission. Therefore, we have analysed datasets from trauma patients derived from the TraumaRegister DGU® over 12 years of time for their presence of coagulopathy upon ER admission and have compared the incidence with their fluid resuscitation rates during the pre-hospital phase of care.

## Patients and methods

### The TraumaRegister DGU®

The TraumaRegister DGU® of the German Trauma Society (Deutsche Gesellschaft für Unfallchirurgie, DGU) was founded in 1993. The aim of this multi-centre database is an pseudonymised and standardized documentation of severely injured patients.

Data are collected prospectively in four consecutive time phases from the site of the accident until discharge from hospital: (1) pre-hospital phase, (2) ER and initial surgery, (3) intensive care unit and (4) discharge. The documentation includes detailed information on demographics, injury pattern, comorbidities, pre- and in-hospital management, course on intensive care unit, relevant laboratory findings including data on transfusion and outcome of each individual. The inclusion criterion is admission to hospital via ER with subsequent ICU/ICM care or reaching the hospital with vital signs and death before admission to ICU.

The infrastructure for documentation, data management, and data analysis is provided by the AUC—Academy for Trauma Surgery (AUC—Akademie der Unfallchirurgie GmbH), a company affiliated to the German Trauma Society. The scientific leadership is provided by the Committee on Emergency Medicine, Intensive Care and Trauma Management (Sektion NIS) of the German Trauma Society. The participating hospitals submit their data pseudonymised into a central database via a web-based application. Scientific data analysis is approved according to a peer review procedure established by Sektion NIS.

The participating hospitals are primarily located in Germany (90%) but a rising number of foreign hospitals of other countries contribute data as well (at the moment from Austria, Belgium, Finland, Luxembourg, Slovenia, Switzerland, The Netherlands, and the United Arab Emirates). Currently, approx. 33,000 cases from more than 600 hospitals are yearly entered into the database.

Participation in TraumaRegister DGU® is voluntary. For hospitals associated with TraumaNetzwerk DGU®, however, the entry of at least a basic dataset is obligatory for reasons of quality assurance.

The presented study is in line with the publication guidelines of the TraumaRegister DGU® and registered as TR-DGU project 2012-042.

## Patients

In this study, datasets of multiple injured patients that had been entered in the TraumaRegister DGU® between 2002 and 2013 were analysed. Criteria for inclusion into this study were age  $\geq 16$  years and primary admission to a TraumaRegister DGU® affiliated hospital. From a total of 98,896 identified patients, 74,641 had a full record of coagulation parameters (prothrombin time and platelets counts) and were screened for the presence of coagulopathy. 61,212 patients met the remaining inclusion criteria. Demographics, injury pattern and vital signs were assessed as present upon ED arrival. The administration of blood products was used as a surrogate for blood loss. Massive transfusion (MT) was defined as administration of  $\geq 10$  packed red-blood-cells (pRBC) during early clinical course from ED to ICU

admission. The presence of coagulopathy was compared to the volume of resuscitation fluids.

## Definition of coagulopathy

Coagulopathy was defined by the presence of abnormal coagulation parameters like prothrombin time in percent activity (Quick's value)  $< 70\%$  and/or platelet counts  $< 100,000/\mu\text{l}$  upon ER admission [6, 7, 11, 15]. The prothrombin time either can be expressed in Quick-% (70–130% = normal [11]) or as international normalized ratio (INR). Unfortunately, the TraumaRegister DGU® did not document the INR at the beginning of the observation period but started documentation in 2009. Therefore, all analysis had to be based on the Quick's value, which was recorded throughout the entire study period. Approximately, a Quick's value of 70% equates to an INR of 1.4 [6, 11].

## Statistical analysis

All data were analysed using SPSS 21 (IBM, Chicago, IL, USA). Data are shown as mean  $\pm$  standard deviation (SD) for continuous variables or percentages (%) for categorical variables. Clinical data were compared using the Chi<sup>2</sup>-test for categorical variables and the Mann–Whitney *U* test for continuous variables. Formal statistical testing displaying a time-dependent trend was avoided since due to the large sample size even minor differences would result in highly significant results, which could mislead to over-interpretation. The clinical relevance of differences over time has to be carefully interpreted [16]. For all statistical analyses, a probability of less than 0.05 was considered to be statistically significant.

## Results

General characteristics of all patients included are summarized in Table 1 describing the demography, injury pattern and patient's state upon ED admission. During the 12 years observed, the injury severity declined according to a steady reduction of the ISS and NISS. Since more minor injuries were recorded, the general severity of haemorrhagic shock decreased as demonstrated by the base excess. Consequently, ICU and overall in-hospital lengths of stays (LOS), as well as times on ventilator declined dramatically (Table 2).

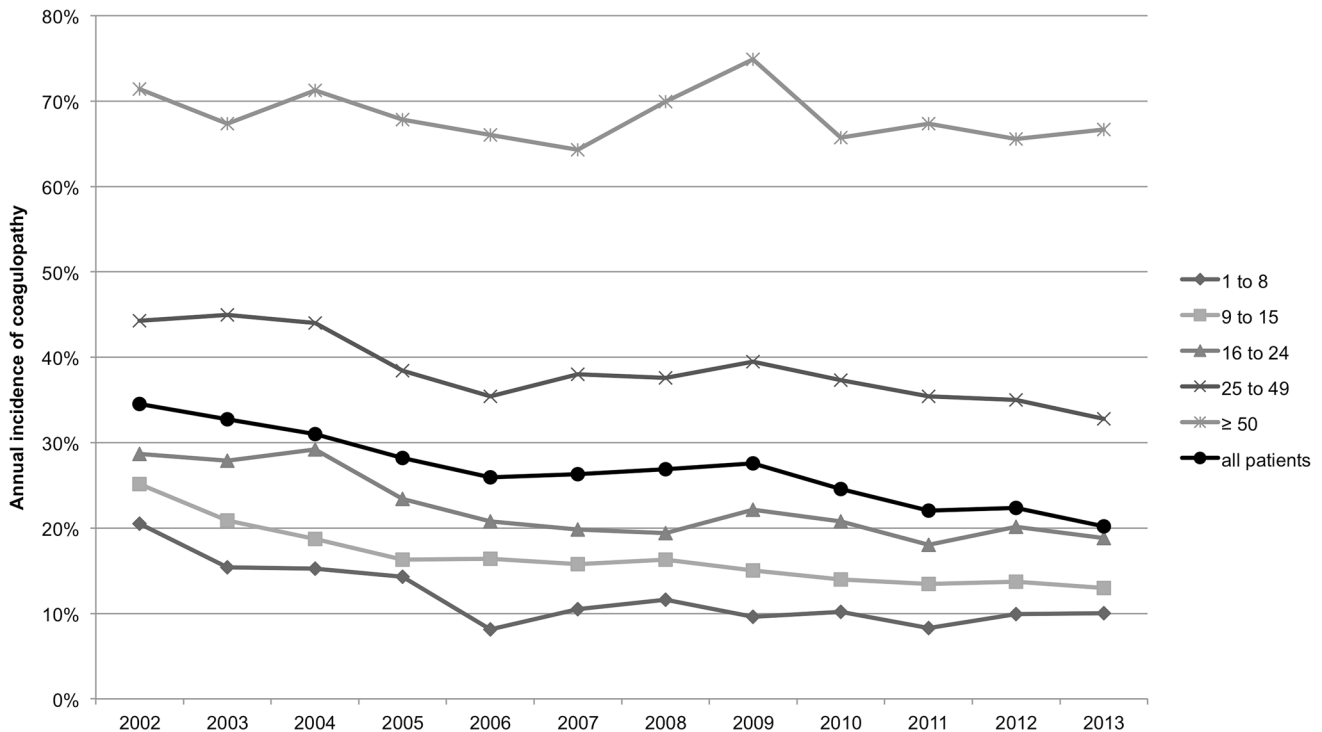
Coagulopathy upon ER admission appeared in 24.5% (14,999/61,212 of all trauma patients included). Within the years 2002–2013, the incidence of TIC decreased continuously from 35% in 2002 to 20% in 2013 (Fig. 2), reflecting a significant overall decline of 41.5%. However, with respect to injury severity, the incidence decreased less pronounced. While incidence halved in minor injured patients up to an

**Table 1** Basic characteristics and injury severity of all patients included upon ER admission ( $n=61,212$ )

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>Demographics</b>												
<i>n</i> (total, %)	1857 (3%)	1897 (3%)	1839 (3%)	2228 (4%)	3035 (5%)	4458 (7%)	4668 (8%)	4643 (8%)	6310 (10%)	8702 (14%)	10,156 (17%)	11,419 (19%)
Male ( <i>n</i> , %)	1369 (74%)	1411 (74%)	1331 (72%)	1628 (73%)	2230 (73%)	3301 (74%)	3412 (73%)	3274 (72%)	4462 (72%)	6294 (73%)	7322 (72%)	8125 (71%)
Age (years; mean $\pm$ SD)	43.5 $\pm$ 19.9	43.8 $\pm$ 19.5	43.6 $\pm$ 19.4	43.9 $\pm$ 19.3	44.6 $\pm$ 19.8	44.3 $\pm$ 19.7	46.1 $\pm$ 20.2	46.9 $\pm$ 20.3	47.7 $\pm$ 20.5	28.2 $\pm$ 20.5	49.1 $\pm$ 20.4	49.6 $\pm$ 20.7
Blunt trauma ( <i>n</i> , %)	1767 (95%)	1785 (94%)	1725 (94%)	2094 (94%)	2844 (94%)	4226 (95%)	4450 (95%)	4189 (95%)	5673 (95%)	7814 (95%)	9297 (95%)	10,428 (95%)
<b>Injury severity</b>												
ISS (points; mean $\pm$ SD)	22.0 $\pm$ 13.6	22.3 $\pm$ 14.1	20.9 $\pm$ 13.6	22.1 $\pm$ 14.0	22.6 $\pm$ 14.2	22.4 $\pm$ 13.9	22.6 $\pm$ 14.0	22.0 $\pm$ 13.4	20.6 $\pm$ 13.7	19.8 $\pm$ 13.6	19.2 $\pm$ 13.3	17.9 $\pm$ 12.7
NISS (points; mean $\pm$ SD)	26.8 $\pm$ 13.6	26.8 $\pm$ 14.1	25.9 $\pm$ 15.7	27.2 $\pm$ 16.7	27.6 $\pm$ 16.6	27.6 $\pm$ 16.5	28.1 $\pm$ 17.0	27.6 $\pm$ 13.4	25.7 $\pm$ 13.7	24.6 $\pm$ 13.6	24.1 $\pm$ 13.1	22.5 $\pm$ 12.7
RISC II (points; mean $\pm$ SD)	13.3 $\pm$ 22.9	14.0 $\pm$ 24.3	12.4 $\pm$ 22.6	14.1 $\pm$ 24.5	14.7 $\pm$ 25.0	13.5 $\pm$ 23.7	15.3 $\pm$ 26.0	13.4 $\pm$ 24.6	12.3 $\pm$ 23.4	11.2 $\pm$ 22.9	11.4 $\pm$ 22.9	10.5 $\pm$ 22.1
TASH score (points; mean $\pm$ SD)	6.9 $\pm$ 5.1	7.0 $\pm$ 5.3	6.7 $\pm$ 5.2	6.3 $\pm$ 5.1	6.4 $\pm$ 5.1	6.4 $\pm$ 5.1	6.2 $\pm$ 5.0	5.5 $\pm$ 4.9	5.1 $\pm$ 4.7	4.7 $\pm$ 4.6	4.8 $\pm$ 4.7	4.2 $\pm$ 4.3
<b>Vital signs</b>												
SBP at ED (mmHg; mean $\pm$ SD)	124 $\pm$ 27	123 $\pm$ 30	125 $\pm$ 29	123 $\pm$ 29	123 $\pm$ 30	126 $\pm$ 30	126 $\pm$ 30	127 $\pm$ 30	128 $\pm$ 30	129 $\pm$ 29	130 $\pm$ 30	132 $\pm$ 30
HR at ED (beats/min; mean $\pm$ SD)	90 $\pm$ 19	90 $\pm$ 21	89 $\pm$ 20	89 $\pm$ 20	89 $\pm$ 21	89 $\pm$ 20	89 $\pm$ 20	88 $\pm$ 20	88 $\pm$ 20	87 $\pm$ 20	88 $\pm$ 20	88 $\pm$ 20
GCS at ED (points; mean $\pm$ SD)	7.9 $\pm$ 5.6	8.2 $\pm$ 5.6	8.7 $\pm$ 5.6	8.6 $\pm$ 5.6	8.6 $\pm$ 5.6	8.8 $\pm$ 5.6	9.1 $\pm$ 5.6	9.4 $\pm$ 5.6	9.9 $\pm$ 5.5	10.4 $\pm$ 5.4	10.7 $\pm$ 5.3	11.0 $\pm$ 5.2
<b>Laboratory findings</b>												
Base excess (mmol/l; mean $\pm$ SD)	-3.2 $\pm$ 4.8	-3.4 $\pm$ 4.3	-3.4 $\pm$ 4.8	-3.8 $\pm$ 4.8	-3.4 $\pm$ 5.2	-3.1 $\pm$ 4.6	-3.2 $\pm$ 4.9	-2.6 $\pm$ 4.4	-2.2 $\pm$ 4.9	-2.1 $\pm$ 4.5	-2.3 $\pm$ 4.7	-2.0 $\pm$ 4.6
Haemoglobin (g/dl; mean $\pm$ SD)	11.5 $\pm$ 3.0	11.8 $\pm$ 2.7	11.8 $\pm$ 2.7	12.0 $\pm$ 2.7	12.1 $\pm$ 2.7	12.2 $\pm$ 2.7	12.2 $\pm$ 2.6	12.4 $\pm$ 2.7	12.6 $\pm$ 2.7	12.8 $\pm$ 2.4	12.8 $\pm$ 2.4	13.1 $\pm$ 2.2
Thrombocytes (tsd/ul; mean $\pm$ SD)	205 $\pm$ 84	202 $\pm$ 78	201 $\pm$ 81	207 $\pm$ 78	210 $\pm$ 76	213 $\pm$ 78	212 $\pm$ 78	213 $\pm$ 80	215 $\pm$ 83	218 $\pm$ 76	218 $\pm$ 80	220 $\pm$ 78
Quick's value (s; mean $\pm$ SD)	78.9 $\pm$ 23.6	78.5 $\pm$ 22.0	79.9 $\pm$ 22.8	80.5 $\pm$ 22.5	81.6 $\pm$ 22.1	82.7 $\pm$ 22.8	81.8 $\pm$ 23.4	81.0 $\pm$ 22.7	82.2 $\pm$ 21.7	84.1 $\pm$ 22.0	83.5 $\pm$ 22.5	85.2 $\pm$ 21.8
aPTT (seconds; mean $\pm$ SD)	35.0 $\pm$ 18.5	30.9 $\pm$ 22.2	36.5 $\pm$ 28.9	34.3 $\pm$ 18.1	34.2 $\pm$ 18.2	33.0 $\pm$ 17.2	33.8 $\pm$ 19.1	33.2 $\pm$ 18.6	32.3 $\pm$ 16.2	31.1 $\pm$ 16.4	31.1 $\pm$ 16.3	30.1 $\pm$ 14.6
Lactate (mmol/l; mean $\pm$ SD)	2.99 $\pm$ 2.51	2.92 $\pm$ 2.54	2.89 $\pm$ 2.71	3.84 $\pm$ 5.23	4.29 $\pm$ 7.12	3.91 $\pm$ 6.83	3.22 $\pm$ 4.40	3.21 $\pm$ 5.86	4.04 $\pm$ 8.03	2.95 $\pm$ 4.49	3.03 $\pm$ 4.12	3.15 $\pm$ 4.94

**Table 2** Early treatment, transfusion requirements and outcome of all patients included upon ER admission (*n* = 61,212)

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>Pre-hospital treatment</b>												
IV fluids at scene (ml; mean ± SD)	1510 ± 1070	1480 ± 1054	1391 ± 974	1337 ± 952	1237 ± 894	1289 ± 909	1194 ± 911	1055 ± 798	969 ± 705	876 ± 655	819 ± 626	738 ± 610
Pre-hospital crystalloids (ml; mean ± SD)	1088 ± 721	1097 ± 698	<b>1013 ± 669</b>	<b>983 ± 637</b>	<b>962 ± 607</b>	968 ± 607	911 ± 665	834 ± 559	805 ± 510	764 ± 493	749 ± 480	729 ± 529
Pre-hospital colloids (ml; mean ± SD)	636 ± 524	691 ± 512	<b>578 ± 497</b>	<b>569 ± 504</b>	543 ± 423	498 ± 467	474 ± 443	312 ± 427	247 ± 364	178 ± 324	145 ± 297	73 ± 218
Tranexamic acid ( <i>n</i> ; %)	na	na	na	na	na	na	na	60 (1.6%)	97 (1.8%)	202 (2.4%)	466 (4.9%)	729 (6.8%)
Intubation rate ( <i>n</i> ; %)	986 (56%)	982 (54%)	896 (51%)	1109 (51%)	1452 (49%)	2123 (49%)	2071 (46%)	1895 (43%)	2336 (38%)	2815 (33%)	3019 (31%)	3001 (27%)
<b>Transfusion requirements</b>												
pRBC transfusions/units ( <i>n</i> ; mean ± SD)	4.9 ± 8.4	5.7 ± 8.5	5.0 ± 8.9	4.1 ± 7.2	4.2 ± 7.4	3.3 ± 6.5	3.3 ± 6.9	1.8 ± 5.2	1.5 ± 5.5	1.0 ± 3.8	1.1 ± 4.1	0.7 ± 3.1
FFP transfusions/units ( <i>n</i> ; mean ± SD)	3.0 ± 5.8	3.8 ± 7.6	3.7 ± 12.5	3.4 ± 7.0	4.5 ± 7.4	2.8 ± 5.9	3.2 ± 7.4	1.4 ± 4.5	1.1 ± 4.4	0.7 ± 3.3	0.8 ± 3.5	0.5 ± 2.7
TC transfusion/units ( <i>n</i> ; mean ± SD)	0.4 ± 2.4	0.3 ± 0.9	0.3 ± 1.3	0.4 ± 2.2	0.4 ± 1.3	0.3 ± 1.4	0.3 ± 1.2	0.2 ± 0.8	0.1 ± 0.6	0.1 ± 0.7	0.1 ± 0.8	0.1 ± 0.6
<b>Outcome</b>												
Mortality ( <i>n</i> ; %)	295 (15.9%)	297 (16%)	256 (14%)	320 (14%)	388 (13%)	505 (11%)	617 (13%)	614 (13%)	728 (12%)	901 (10%)	1134 (11%)	1171 (10%)
Hospital LOS (days; mean ± SD)	25.2 ± 28.0	26.1 ± 31.9	23.5 ± 29.1	23.3 ± 28.0	21.9 ± 26.9	21.1 ± 22.9	19.8 ± 21.6	18.8 ± 23.8	17.7 ± 20.2	16.4 ± 19.4	16.4 ± 19.6	15.4 ± 18.3
ICU LOS (days; mean ± SD)	11.1 ± 13.9	11.4 ± 14.3	9.9 ± 12.7	10.3 ± 12.5	9.7 ± 13.2	10.1 ± 12.6	9.5 ± 12.3	7.9 ± 11.0	7.5 ± 11.4	6.7 ± 10.7	6.6 ± 10.6	6.2 ± 10.8
Ventilator days (days; mean ± SD)	7.7 ± 12.0	7.6 ± 12.4	6.5 ± 11.3	6.7 ± 10.8	6.5 ± 11.4	6.6 ± 11.0	6.1 ± 10.5	4.9 ± 8.8	4.8 ± 9.4	3.9 ± 8.4	3.7 ± 7.9	3.3 ± 8.0
MOF ( <i>n</i> ; %)	168 (12.1%)	246 (15.1%)	235 (14.6%)	360 (17.8%)	494 (17.8%)	711 (17.6%)	762 (18.3%)	527 (13.0%)	558 (10.7%)	598 (8.1%)	720 (8.5%)	617 (6.5%)
Sepsis ( <i>n</i> ; %)	143 (9.4%)	133 (8.0%)	116 (6.9%)	182 (8.8%)	231 (8.2%)	346 (8.4%)	362 (8.4%)	246 (6.1%)	289 (5.6%)	392 (5.4%)	449 (5.3%)	403 (4.3%)



**Fig. 2** Annually incidence rate of coagulopathy in subgroups according to injury severity over the years 2002–2013 (ISS, five groups;  $n=61,212$ ; decrease significant,  $p < 0.001$  for all groups)

ISS of 15, we observed a reduction of 26.0 and 6.7% in the most severely injured subgroups with an ISS of 25–49 and  $\geq 50$ , respectively. Thus in 2013, 67.6% of the patients with an ISS  $\geq 50$  had a TIC.

From 2002 to 2013, the total amount of pre-hospital volumes given, decreased from 1510 ( $\pm 1070$ ) ml to 738 ( $\pm 610$ ) ml reflecting a reduction of 51.1%. Most of this difference was due to a significantly reduced use of colloidal fluids (Table 2). The total amounts of pre-hospital volumes amended to the different subgroups of injury severity are demonstrated in Fig. 3. In detail, the largest reduction ( $-52\%$ ) was observed in patients with an ISS of 16–24. In patients with an ISS  $\geq 50$ , pre-hospital volume resuscitation decreased by 35%. This trend paralleled increasing haemoglobin values upon ER admission ( $11.5 \pm 3.0$  g/dl in 2002 to  $13.1 \pm 2.2$  g/dl in 2013). Since beginning of the documentation in 2009, significantly more trauma patients received Tranexamic acid (TXA). While in 2013, TXA was given in 6.8% of all trauma cases, already 16.3% of coagulopathic patients received an antifibrinolytic therapy.

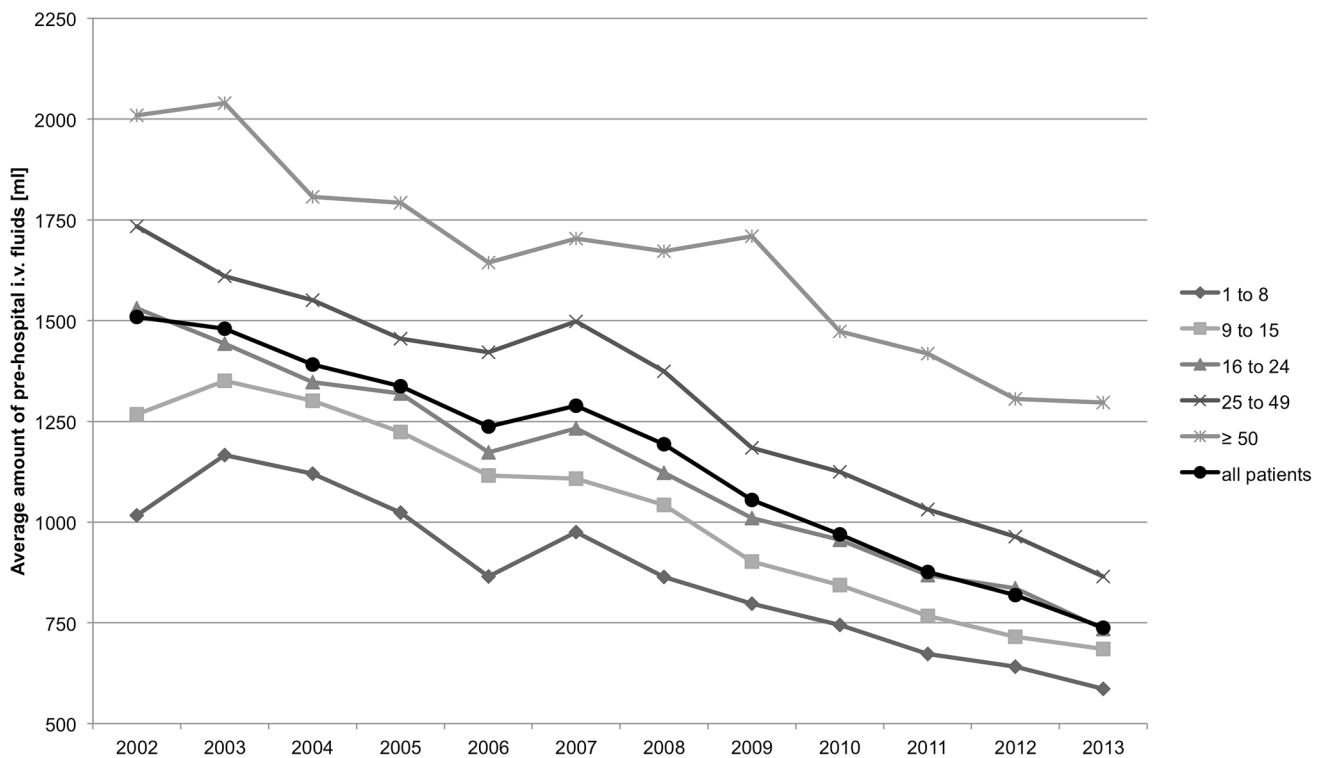
During the observation period, less patients required any blood product or mass transfusion with a remarkable reduction since 2006 (Fig. 4). The declined frequency of TIC was accompanied by a continuous decrease of mortality from 15.9% in 2002 to 10.3% in 2013. Simultaneously, the incidence of sepsis (9.4% in 2002 to 4.3% in 2013) and multiple

organ failure (12.1% in 2002 to 6.5% in 2013) halved. Regarding patients with coagulopathy upon ER admission, the ISS and NISS stayed stable around 27.8 and 33.7 points, respectively. However, as expected, these coagulopathic patients were in a more profound state of shock, displayed by a lower base excess, received more blood products and required more resources since they had more ventilator days and a prolonged ICU and in-hospital LOS.

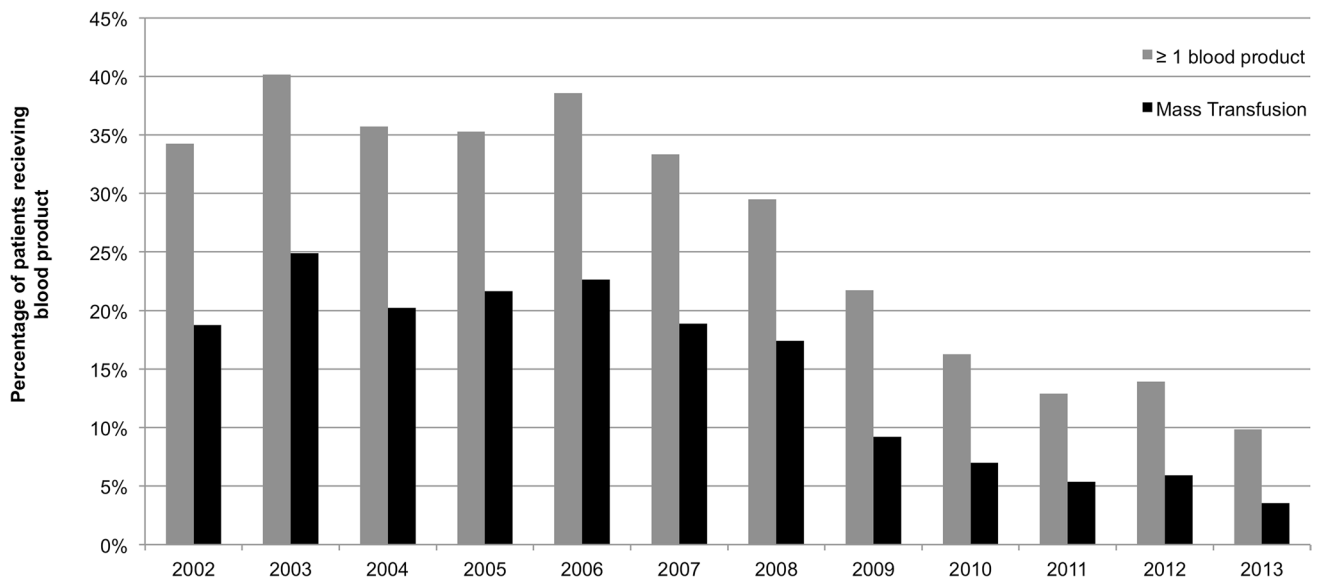
## Discussion

The frequency of haemostatic disorders among trauma patients upon ER admission declined substantially during the observed 12-year period. This occurred in parallel to a reduction of resuscitation fluids given during the pre-hospital treatment. This development might reflect the increased awareness for the role of TIC among pre-hospital health-care-workers. However, TIC remains frequent in most severely injured patients with consequent higher morbidity and mortality.

Coagulopathy upon ER admission was present in approximately one quarter of all trauma patients with an ISS  $\geq 16$ . In 2013, the incidence of coagulopathy even decreased to 20%. The observed overall incidence of coagulopathy appears to be lower compared to previous analyses that described



**Fig. 3** Amount of i.v. fluids administered during the pre-hospital treatment in subgroups according to injury severity (ISS, five groups; decrease significant;  $p < 0.001$  for all groups)



**Fig. 4** Transfusion requirements over the years 2002 to 2013 ( $n = 61,212$ ; decrease significant;  $p < 0.001$ )

for both, blunt and penetrating trauma, TIC to be present in approximately one out of three trauma patients [6, 17]. Depending on the definition of coagulopathy and study design, even a higher incidence was reported [5, 7, 9, 11]. As the injury severity contributes to the development of TIC

[11], different inclusion criteria such as a cut-off in injury severity influences the reported incidence directly (Fig. 2). However, from a prospective cohort study, MacLeod et al. reported with an incidence of 16.3% lower numbers [18]. The difference might be explained as in that study solely a

prolonged prothrombin time (Quick's value) was used for defining coagulopathy while the platelet count was not considered [18].

Immediately after trauma, endogenous factors such as endothelial damage, hypoperfusion and an early inflammatory response contribute to the development of TIC [5, 11]. Injury pattern and severity determine these endogenous factors. In contrast, exogenous factors such as haemodilution, hypothermia and acidosis are surely implicated by the injury itself, but appear delayed after the trauma and are boosted by external conditions. Among these, especially haemodilution has been identified as one key initiator of TIC patients [6, 9–11]. However, in contrast to endogenous factors, such exogenous threats are potentially avoidable as they might be a result of an inappropriate treatment by the acting health care providers [11, 19].

While previously hypotensive trauma patient received large fluid volumes as early and as rapidly as possible aiming to restore intravascular volume and maintain vital organ perfusion, various studies demonstrated during the observed period, that excessive fluid replacement is associated with increased transfusion requirements and a higher mortality rate [20–22]. Beyond doubt, trauma patients require some fluid replacement to maintain tissue perfusion and avoid high doses of catecholamines. One multicentre study showed that a median pre-hospital fluid administration of 700 ml was associated with an improved survival but did not influence the systolic blood pressure at ER admission [23]. Therefore, the current European guideline of the management of bleeding and coagulopathy following major trauma recommends a restrained fluid resuscitation with a target systolic blood pressure between 80 and 90 mmHg [14]. A recently published analysis from the TR-DGU could demonstrate, that between 2002 and 2012 the amount of volume administered in trauma patients decreased from 1790 to 1039 ml with a striking reduction of colloids from 574 to 169 ml [24]. In contrast to this previous study focusing on volume administration in polytraumatised patients (ISS  $\geq$  16) [24], the presented data show that regardless of the injury severity, the amount of pre-hospital volume administered was reduced continuously. The reduced use of colloidal fluids could as also been seen. In minor injured patients and up to an injury severity of ISS 49, the development of less volume administered was paralleled by a decreasing incidence of TIC. This development and additionally the increasing use of TXA might be an indicator of an increasing awareness of coagulopathy and a result of improved guideline adherence among pre-hospital healthcare personal, being increasingly translated in modified resuscitation strategies.

Regarding endogenous factors, the average injury severity and the proportion of severe abdominal trauma decreased during the observed period. Both factors have been described as independent risk factors for the development

of TIC [11]. However, it is unlikely that the minor altered injury severity and injury pattern contribute decisively to the 41.5% decrease of TIC, which we observed. Considering the most severely injured patients, the decrease was statistically significant but not as pronounced as in less severely injured patients. This trend supports the pivotal role of the injury severity. Therefore, despite all improvements, utmost awareness for the development of TIC is required in the pre-hospital trauma care.

The reduced incidence of coagulopathy was associated with reduced transfusion requirements. The percentage of patients receiving at least one blood product, as well as requiring MT decreased dramatically, which directly affects the outcome after major trauma. It is well known, that coagulopathy and consecutive transfusion of blood products and especially MT are independently associated with various complications such as single or multiple organ failure, sepsis and increased mortality [25–27]. We can clearly reproduce this association in the presented data. Certainly, not only a reduced incidence of coagulopathy but also an improved coagulation management offers advantages for the patient's outcome [28]. Especially the use of thrombelastometry allows an early and valid detection of coagulopathic disorders and the prediction of the need of blood products, which might further improve the therapeutic management [29].

Certain limitations of this investigation have to be acknowledged. This is a retrospective study with all the associated shortcomings, like the introduction of a selection bias, because of selective survival information, incomplete or inaccurate information and dependency on respondents. Therefore, only associations and no causalities can be derived from the underlying data. Still, the TR-DGU enables illustration of consistency or changes in therapy or therapeutically actions. The TraumaRegister DGU® does not capture information about pre-injury medication such as anticoagulant therapy, which could interfere with the assessment of coagulation disorders. With the increasing age of trauma patients, a higher rate of anticoagulants can be assumed. In the TraumaRegister DGU® Quick's value, prothrombin time and platelet counts are documented and available for the definition and analysis of coagulopathy. Unfortunately, the INR was not documented at the beginning of the observation period. Although, these traditional coagulation tests are the basis of current definitions of TIC, these screening tests do not assess the whole coagulation system. Viscoelastic coagulation tests have been identified to be more accurate for the diagnosis of TIC [30]. However, the TraumaRegister DGU® started documenting the execution of viscoelastic testing in 2009, which does not allow a ROTEM based statement on the presence of coagulopathy. Furthermore, not all patients had a full record of coagulation parameters at ER arrival and therefore, some patients had to be excluded from the present analysis.



## Conclusion

Within the years 2002–2013, the incidence of trauma-induced coagulopathy upon ER admission decreased by 41.5%. Simultaneously, the use of pre-hospital i.v.-fluids declined continuously regardless of the injury severity while the use of antifibrinolytic medication increased, which could be an indicator of an increasing awareness of coagulopathy and a result of improved guideline adherence among pre-hospital healthcare personal. The reduced incidence of coagulopathy was associated with decreased transfusion requirements and mortality. Nevertheless, especially in the most severely injured patients, TIC remains a frequent and life-threatening syndrome, which requires utmost awareness in the pre-hospital trauma care.

## Compliance with ethical standards

**Conflict of interest** The authors report no conflict of interest. This is an unfunded study.

**Ethical approval** As this is a retrospective register study, individual formal consent is not required.

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