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The impact of severe traumatic brain injury on a novel base deficit- based classification of hypovolemic shock

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Abstract

Background: Recently, our group has proposed a new classification of hypovolemic shock based on the physiological shock marker base deficit (BD). The classification consists of four groups of worsening BD and correlates with the extent of hypovolemic shock in severely injured patients. The aim of this study was to test the applicability of our recently proposed classification of hypovolemic shock in the context of severe traumatic brain injury (TBI).

Methods: Between 2002 and 2011, patients ≥ 16 years in age with an $AIS_{head} \geq 3$ have been retrieved from the German TraumaRegister DGU[®] database. Patients were classified into four strata of worsening BD [(class I (BD ≤ 2 mmol/l), class II (BD > 2.0 to 6.0 mmol/l), class III (BD > 6.0 to 10 mmol/l) and class IV (BD > 10 mmol/l)] and assessed for demographic and injury characteristics as well as blood product transfusions and outcomes. The cohort of severely injured patients with TBI was compared to a population of all trauma patients to assess possible differences in the applicability of the BD based classification of hypovolemic shock.

Results: From a total of 23,496 patients, 10,201 multiply injured patients with TBI ($AIS_{head} \geq 3$) could be identified. With worsening of BD, a consecutive increase of mortality rate from 15.9% in class I to 61.4% in class IV patients was observed. Simultaneously, injury severity scores increased from 20.8 (± 11.9) to 41.6 (± 17). Increments in BD paralleled decreasing hemoglobin, platelet counts and Quick's values. The number of blood units transfused correlated with worsening of BD. Massive transfusion rates increased from 5% in class I to 47% in class IV. Between multiply injured patients with TBI and all trauma patients, no clinically relevant differences in transfusion requirement or massive transfusion rates were observed.

Conclusion: The presence of TBI has no relevant impact on the applicability of the recently proposed BD-based classification of hypovolemic shock. This study underlines the role of BD as a relevant clinical indicator of hypovolaemic shock during the initial assessment in respect to haemostatic resuscitation and transfusion requirements.

Keywords: Trauma, Shock, Classification, Vital signs, Base deficit, Transfusion, Traumatic brain injury

Background

Uncontrolled haemorrhage is still responsible for the half of all trauma-related deaths within the first 48 hours after hospital admission [1-3]. This underlines the pivotal role of the early recognition and treatment of hypovolaemia in acute trauma care. The Advanced Trauma

Life Support (ATLS) proclaims for the initial evaluation of circulatory depletion four classes of hypovolemic shock based upon an estimated blood loss in percent and corresponding vital signs [4]. However, recent analyses on data of multiple injured patients derived from the TraumaRegister DGU[®] and the TARN (Trauma Audit and Research Network) database indicated that the current ATLS classification of hypovolemic shock displays substantial deficits in the initial assessment of multiply injured trauma patients [5-8].

Based on these observations, we developed and validated a new classification of hypovolemic shock on the

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physiological shock marker base deficit (Table 1) [9]. The defined four strata of worsening BD indicated the acute presence of hypovolemic shock related to the need for haemostatic resuscitation, transfusion requirement, laboratory findings and outcomes [9]. This new classification of hypovolemic shock predicted transfusion requirements and mortality even more appropriately than the current ATLS classification of hypovolemic shock [9].

More than 40% of all trauma patients captured in the TraumaRegister DGU® sustain a combination of injuries including severe traumatic brain injury (TBI) [8]. Together with hemorrhage, TBI is the leading cause of death in multiply injured trauma patients [1-3,10] and the coincidence of TBI and hemorrhage has been associated with an even worse overall morbidity and mortality [11]. Several studies have shown that TBI may impair cardiovascular compensation to acute blood loss [12-16]. In detail, it has been demonstrated that the autonomic response to haemorrhage is disturbed in the presence of TBI and the physiological response to acute blood loss, like hypotension or the modification of vascular tone may be impaired or delayed [14,15,17]. Yuan and colleagues even demonstrated that TBI may suppress spontaneous hemodynamic recovery from hemorrhage and also impede the efficacy of fluid resuscitation [12,18]. Additionally, traditional vital signs like heart rate (HR), systolic blood pressure (SBP), shock index (SI) and Glasgow Coma Scale may be affected, indicating that current assessment strategies, like the ATLS classification of hypovolemic shock, have to be used with caution [8,14,19].

Therefore, the aim of this study was to test the applicability of the novel BD-based classification of hypovolemic shock in the context of severe traumatic brain injury (TBI).

Methods

The TraumaRegister DGU® of the German Trauma Society

The TraumaRegister DGU®, founded in 1993, is the official trauma registry of the German Trauma Society. Details of this registry have been published *in extenso* elsewhere [5,8,9,20]. To date, datasets from approximately > 450 hospitals have been entered into the database. The TraumaRegister DGU® captures all severe trauma patients, who are either admitted to the hospital via the emergency department (ED) with subsequent admission to an intensive care unit (ICU)/intermediate

care unit (IMC) or reach the hospital with vital signs and die prior to ICU/IMC admission. The TraumaRegister DGU® is approved by the review board of the German Trauma Society (DGU) and is in compliance with the institutional requirements of its members. Furthermore, all data analyses have been approved by the review board of the “Sektion NIS” of the German Trauma Society.

Data analyses

Datasets of multiple injured patients entered into the TraumaRegister DGU® between 2002 and 2011 were analyzed. Inclusion criteria were age ≥ 16 years, primary admission, and complete datasets for base deficit upon admission blood gas analysis in the emergency department. Severe traumatic brain injury was defined by an $AIS_{head} \geq 3$ (abbreviated injury scale) as previously described [21-23]. Based on these criteria, 10,201 patients with severe TBI could be identified and were classified into four strata of worsening BD according to the recently proposed classification of hypovolemic shock (Table 1) [9]. Assessments included demographics, injury patterns and vital signs as present upon ED arrival. Additionally, therapeutic interventions such as administration of blood products, intravenous fluids and vasopressors were analyzed. The assessment of mortality was performed by analyzing the overall in-hospital mortality. Massive transfusion (MT) was defined by the administration of ≥ 10 blood products between ED arrival and ICU admission. Coagulopathy was defined by a Quick's value $\leq 70\%$, which is equivalent to an international normalized ratio (INR) of approximately 1.3 [22,24]. For the evaluation of the applicability of the novel BD-based classification in the context of severe TBI, patients with an $AIS_{head} \geq 3$ were classified according to their BD at ED admission and compared to both, an unselected cohort of all trauma patients derived from the TraumaRegister DGU® as well as to patients without a significant TBI (no TBI). Subsequently, transfusion requirements within the different cohorts were assessed.

Statistical methods

Data are shown as mean \pm standard deviation (SD) for continuous variables or percentages (%) for categorical variables. GCS is displayed as median and interquartile ranges (IQR). For continuous variables, normal distribution was excluded using the Shapiro-Wilk test. To detect differences between the four groups of worsening BD a

Table 1 The BD-based classification of hypovolemic shock [9]

	Class I	Class II	Class III	Class IV
Shock	none to minimal	mild	moderate	severe
BD at admission (mmol/l)	≤ 2	> 2.0 to 6.0	> 6.0 to 10.0	> 10.0
Need for blood products	watch	consider	act	Be prepared for massive transfusion

Abbreviations: BD base deficit.

Kruskal-Wallis test was performed. Categorical variables were analyzed accordingly with the Chi-square test. For all statistical analyses, a probability of less than 0.05 was considered to be statistically significant. All data were analyzed using IBM SPSS (IBM SPSS 19, Chicago, USA).

Results

Characteristics of the four classes of hypovolemic shock in TBI patients

A total of 23,496 patients from the TraumaRegister DGU® were identified for further analysis. Out of these, 10,201 (43.4%) patients presented with severe TBI defined by an AIS_{head} ≥ 3. General demographics and trauma mechanism for the four classes of hypovolemic shock are shown in Table 2. Worsening of BD category was associated with an increased injury severity score (ISS 25.8 ± 11.9 in class I to 41.6 ± 17.0 in class IV). Through the classes I to IV, this was paralleled by an increased incidence of sepsis (7.5% to 14.1%) and multiple organ failure (18% to 44.4). Overall in-hospital mortality increased from 15.9% in class I patients to 61.4% in class IV patients (Table 3). No relevant tachycardia was observed in any group and a substantial hypotension was found in class IV patients only. Patients with a BD > 10.0 mmol/l (class IV) were coagulopathic (Table 4) and presented with significantly decreased haemoglobin levels (9.4 ± 3.2 g/dl)

and platelet counts (177 ± 93 tsd/μl) compared to class I patients (haemoglobin 12.6 ± 2.3 g/dl; platelet counts 208 ± 72 tsd/μl).

Fluid resuscitation and transfusion requirement in correlation to increasing BD category are demonstrated in Table 5. Patients of class I received 1.5 ± 6 blood units, whereas class IV patients received 15.1 ± 22 blood units until ICU admission. The average transfusion ratio between packed red blood cells (pRBC's) and fresh frozen plasma (FFP's) was almost 1:1 within all groups. Likewise, observed and predicted transfusion requirements were concordant as the number of blood products transfused paralleled increased TASH (Trauma-Associated Severe Hemorrhage) scores.

Comparison of transfusion requirement between multiply injured patients with TBI and all trauma patients classified according to the BD-based classification of hypovolemic shock

In multiply injured patients with TBI, an increase in BD category was associated with a progressively increasing transfusion requirement (Figure 1). The percentage of patients who received ≥ 1 blood unit during early ED resuscitation increased from 14% in class I to 64% in class IV (Figure 1A), while simultaneously massive transfusion rates increased stepwise from 5% in class I to 42% in

Table 2 Patients classified by BD (classes I to IV): demographics, injury mechanism and severities as well as outcome parameters

	Class I	Class II	Class III	Class IV
	BD ≤ 2.0 (none to minimal)	BD > 2.0 to 6.0 (mild)	BD > 6.0 to 10.0 (moderate)	BD > 10.0 (severe)
Demographics				
n (total, %)	4369 (42.8)	3658 (35.9)	1404 (13.8)	770 (7.5)
Male (n, %)	3211 (73.9)	2636 (72.6)	982 (70.5)	523 (68.2)
Age (years; mean ± SD)	50.9 (21.4)	46.4 (21)	45.6 (20.6)	46.2 (20.3)
Blunt trauma (n, %)	4121 (97.3)	3467 (96.8)	1332 (96.2)	703 (93.1)
Injury severity				
ISS (points; mean ± SD)	25.8 (11.9)	30.2 (13.6)	35.2 (15.9)	41.6 (17.0)
AIS Thorax ≥ 3 points (n, %)	1476 (33.8)	1642 (44.9)	742 (52.8)	486 (63.1)
AIS Abdomen ≥ 3 points (n, %)	236 (5.4)	395 (10.8)	270 (19.2)	199 (25.8)
AIS Pelvis/Extremities ≥ 3 points (n, %)	650 (14.9)	892 (24.4)	469 (33.4)	305 (39.6)
Outcome				
Mortality (n, %)	696 (15.9)	805 (22)	502 (35.8)	473 (61.4)
Hospital LOS (days; mean ± SD)	18.1 (17.8)	21.7 (25)	20.8 (24.8)	16 (29.1)
ICU (days; mean ± SD)	10.8 (12.2)	13.5 (13.8)	14 (15.9)	11.1 (16.8)
Ventilator days (days; mean ± SD)	7.3 (10.4)	9.7 (11.8)	10.5 (13.1)	9.1 (14.4)
MOF (n, %)	694 (18)	876 (26.8)	389 (32.6)	256 (44.4)
Sepsis (n, %)	296 (7.5)	428 (12.5)	194 (15.8)	83 (14.1)

(n = 10,201; p < 0.001 for all parameters).

Abbreviations: ISS injury severity score, AIS abbreviated injury scale, LOS length of stay, ICU intensive care unit, MOF multiple organ failure.

Table 3 Patients classified by BD (classes I to IV): traditional vital signs as presented at ED admission and at scene

	Class I BD ≤ 2.0 (none to minimal)	Class II BD > 2.0 to 6.0 (mild)	Class III BD > 6.0 to 10.0 (moderate)	Class IV BD > 10.0 (severe)
Vital signs				
SBP at ED (mmHg; mean ± SD)	132.3 (28.6)	124.3 (30)	113.2 (32.4)	95.7 (40.9)
HR at ED (beats/min; mean ± SD)	84.3 (18.4)	88.7 (21.6)	95.3 (23.4)	96.5 (32.9)
GCS at ED (points; median, IQR)	3 (3–14)	3 (3–8)	3 (3–3)	3 (3–3)
Intubation rate [pre-hospital] (n; %)	2306 (54.5)	2563 (71.9)	1116 (81.4)	674 (89.2)

(n = 10,201; p < 0.001 for all parameters).

Abbreviations: SBP systolic blood pressure, HR heart rate, GCS Glasgow coma scale, ED Emergency Department.

class IV (Figure 1B). However, substantial and clinical relevant differences between patients who sustained TBI and the general trauma population were not observed within the four classes of hypovolemic shock based on BD. Similar results were seen when multiply injured patients with TBI were compared to a cohort of severely injured patients without TBI (Figure 1A and B). Only in group IV, patients without TBI had a slightly higher overall transfusion requirement. However, the clinical relevance of this finding remains questionable.

Discussion

The aim of this study was to test the applicability of the recently proposed classification of hypovolemic shock based on BD in multiple injured patients who have sustained severe traumatic brain injury.

Previous studies have demonstrated that base deficit detects the presence of hypovolemic shock and correlates with the need for haemostatic resuscitation, transfusion requirements, laboratory findings as well as mortality rates. In times of point-of-care testing, BD is available within minutes after ED admission [25]. Recent research provides evidence that the assessment of BD is a more useful approach to quantify the extent of hypovolemic shock than the estimation of blood loss, the extent of volume resuscitation or traditional vital signs such as HR and SBP [9,26-29] and may help to distinguish major from minor trauma [30]. The four classes of hypovolemic

shock based on BD has been compared and validated against the ATLS classification of hypovolaemic shock. ATLS serves as a standard protocol for the initial assessment and treatment of severely injured trauma patients and has been widely implemented over the past decades. In this analysis, the BD-based classification has been shown to predict transfusion requirements and mortality more appropriately than the current ATLS classification of hypovolemic shock [9].

The present study focused on TBI patients with an AIS_{head} ≥ 3. Within this group of patients, worsening of BD category was associated with an increased injury severity and mortality, which is in accordance with several previous analyses [9,31-34] and has been also observed in pediatric and elderly trauma populations [35-38]. As expected, mortality rates across the four classes of hypovolemic shock were higher in multiple injured patients with TBI. In particular, 15.9% of class I and 22% of class II patients died within hospital stay and therefore nearly doubled mortality compared to our previous analysis on a general trauma population [9]. These findings are substantiated by Tremblay and colleagues who demonstrated that mortality increases with successive increase in base deficit but is also highly dependent on injury pattern. In TBI patients, mortality was markedly higher at a given BD than in patients suffering from stab wounds or lacerations [39]. Furthermore, in young trauma patients without TBI, a 25% mortality rate was observed at a BD

Table 4 Patients classified by BD (classes I to IV): laboratory findings

	Class I BD ≤ 2.0 (none to minimal)	Class II BD > 2.0 to 6.0 (mild)	Class III BD > 6.0 to 10.0 (moderate)	Class IV BD > 10.0 (severe)
Laboratory findings				
Haemoglobin (g/dl; mean ± SD)	12.6 (2.3)	11.8 (2.5)	10.7 (2.9)	9.4 (3.2)
Thrombocytes (tsd/μl; mean ± SD)	208 (72)	204 (70)	188 (73)	177 (93)
Quick's value (%; mean ± SD)	84 (20.9)	77.8 (22.8)	68.2 (25.0)	54.7 (26.6)
aPTT (seconds; mean ± SD)	30.7 (11)	33.9 (16.3)	41.9 (26.6)	61.8 (42.8)

(n = 10,201; p < 0.001 for all parameters).

Abbreviations: aPTT activated partial thromboplastin time.

Table 5 Patients classified by BD (classes I to IV): haemostatic and fluid resuscitation

	Class I BD ≤ 2.0 (none to minimal)	Class II BD > 2.0 to 6.0 (mild)	Class III BD > 6.0 to 10.0 (moderate)	Class IV BD > 10.0 (severe)
Transfusion requirements				
All blood products/units (n; mean ± SD)	1.5 (6)	4.2 (11.5)	9.4 (17.5)	15.1 (22)
pRBC transfusions/units (n; mean ± SD)	1.1 (3.4)	2.6 (5.8)	5 (8.4)	8.1 (10.9)
FFP transfusions/units (n; mean ± SD)	0.8 (3.1)	2.3 (11.6)	4.1 (7.4)	6.2 (10)
TC transfusion/units (n; mean ± SD)	0.1 (0.5)	0.3 (1.1)	0.6 (1.8)	0.9 (1.8)
TASH Score (points; mean ± SD)	3.1 (3.1)	5.6 (4.0)	10.0 (5.0)	13.5 (5.3)
IV fluids at ED (ml; mean ± SD)	1498 (1531)	2143 (2075)	2573 (2404)	2964 (2564)
Vasopressors at ED (n; %)	888 (21.9)	1233 (36.1)	690 (52.3)	549 (75.8)

(n = 10,201; p < 0.001 for all parameters).

Abbreviations: pRBC packed red blood cells, FFP fresh frozen plasma, TC thrombocyte concentrate, TASH Trauma-associated severe hemorrhage score, i.v. intravenous, ED Emergency Department.

level of 15 mmol/l. In contrast, TBI patients showed same mortality rates already at a BD level of 8 mmol/l [33].

In the present study, increasing BD was associated with signs of hemodynamical instability and laboratory alterations such as drops in hemoglobin levels and platelet counts. Approximately one out of four patients in class III and IV presented coagulopathic at ED arrival which is in accordance to a previous analysis on isolated traumatic brain injuries by Wafaisade and colleagues [22]. Furthermore, BD correlated with an increasing overall amount of transfused blood units and with an increasing risk of ongoing hemorrhage as reflected by increasing TASH (trauma-associated severe hemorrhage) score values. These observations are supported by several studies demonstrating an association between increasing BD and the increased need for blood product transfusions as well as increasing amounts of i.v. fluids [9,31,32,39].

In order to further assess the applicability of the BD-based classification of hypovolemic shock in the context of severe TBI, multiple injured patients who sustained also brain injury were compared to a cohort of all trauma

patients. As there has been no gold standard introduced yet to assess hypovolaemic shock including blood loss in trauma which triggers therapeutic measures and interventions, the authors have decided to analyze and compare for transfusion requirements as a well-established surrogate for hypovolaemia. Both, the percentage of patients who received ≥ 1 blood product as well as the percentage of patients who received massive transfusions were increasing throughout the groups I to IV. However, a relevant difference between both patient cohorts was not observed at all. In a second step, severely injured patients with TBI were also compared to a cohort of multiply injured trauma patients without any significant TBI. Only in group IV, a slight difference in transfusion requirements between both groups was observed. However, the clinical relevance of this finding remains questionable. These results are substantiated by an analysis on 131 patients with isolated head injury, demonstrating that TBI does neither alter BD levels nor reliably predicts the presence of TBI [23]. Therefore, the authors concluded that in patients with isolated head injury an increase of BD should lead to a

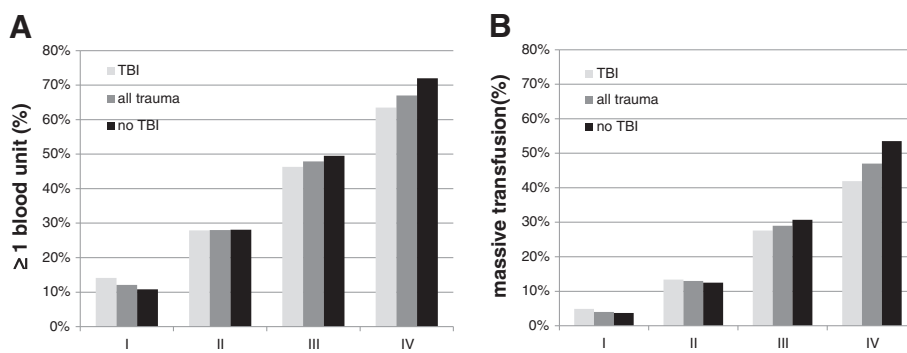


Figure 1 Transfusion requirements in multiply injured patients with TBI, all trauma patients and multiply injured trauma patients without TBI. A) Percent of patients with ≥ 1 blood product. (n = 23,496); **B)** Percent of patients with massive transfusion (≥ 10 blood units until ICU admission). (n = 23,496). Abbreviations: TBI: traumatic brain injury.

careful assessment of extracranial injuries as the underlying reason for hypoperfusion and hence the raise in BD.

Some limitations of the present study have to be acknowledged. First, this analysis is a retrospective study of trauma registry data with all the shortcomings associated with such an analysis. Second, not every ED is equipped with point-of-care testing. Consequently, BD values may not be available within the first minutes after ED admission. Further prospective clinical trials should be conducted to assess the accuracy of the proposed classification of hypovolemic shock in the clinical setting. But in spite of these restrictions, we are confident that determination of base deficit, as proclaimed in the BD based classification of hypovolemic shock, is a useful clinical tool to early risk-stratify patients who are in a state of hypovolemic shock and in need for early blood product transfusions, also in patients who sustained traumatic brain injury.

Conclusions

Our recently proposed classification of hypovolemic shock based on admission base deficit has been tested for its applicability in a large cohort of multiple injured patients with accompanying TBI. Within the four classes of hypovolemic shock (class I to IV), no clinical relevant differences in transfusion requirement in multiple injured patients with TBI and all trauma patients was observed. Consequently, this study underlines the role of BD as a relevant clinical indicator of hypovolaemic shock during the initial assessment and as a guide for transfusion requirements also in patients with traumatic brain injury.

Abbreviations

AI: Abbreviated injury scale; ATLS: Advanced Trauma Life Support; BD: Base deficit; DGU: Deutsche Gesellschaft für Unfallchirurgie (German Trauma Society); ED: Emergency Department; FFP: Fresh frozen plasma; GCS: Glasgow coma scale; HR: Heart rate; ICU: Intensive care unit; INR: International normalized ratio; IQR: Interquartile ranges; ISS: Injury severity score; i.v.: Intravenous; LOS: Length of stay; MOF: Multiple organ failure; MT: Massive transfusion; PC: Platelet concentrate; POCT: Point of care testing; pRBC: Packed red blood cells; PT: Prothrombin time; SBP: Systolic blood pressure; TARN: Trauma Audit and Research Network; TASH: Trauma-associated severe hemorrhage score; TBI: Traumatic brain injury.

Competing interests

The authors declare that they have no competing interests. This is an unfunded study.

Authors' contributions

MMutschler contributed to study design, acquisition of data, interpretation and recording of paper. UN and BB contributed to analysis and interpretation of data and revision of the article. TB, AW, CP and TP contributed to study design and revision of the article. MMaegele contributed to study conception and design, acquisition of data, analysis and interpretation of data, and revision of the article. All authors read and approved the final manuscript.

The TraumaRegister DGU

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