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Comparison of Base Deficit and Vital Signs as Criteria for Hemorrhagic Shock Classification in Children with Trauma

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Purpose: Base deficit (BD) is superior to vital signs in predicting trauma outcomes in adults. The authors aimed to compare BD and vital signs as criteria for the four-tiered hemorrhagic shock classification in children with trauma.

Materials and Methods: We retrospectively reviewed the data of 1046 injured children who visited a Korean academic hospital from 2010 through 2018. These children were classified separately based on BD (class I, BD ≤2.0 mmol/L; II, 2.1–6.0 mmol/L; III, 6.1–10 mmol/L; and IV, ≥10.1 mmol/L) and vital signs (<13 years: age-adjusted hypotension and tachycardia, and Glasgow Coma Scale; 13–17 years: the 2012 Advanced Trauma Life Support classification). The two methods were compared on a class-by-class basis regarding the outcomes: mortality, early transfusion (overall and massive), and early surgical interventions for the torso or major vessels.

Results: In total, 603 children were enrolled, of whom 6.6% died. With the worsening of BD and vital signs, the outcome rates increased stepwise (most $p<0.001$; only between surgical interventions and vital signs, $p=0.035$). Mortality more commonly occurred in BD-based class IV than in vital signs-based class IV (58.8% vs. 32.7%, $p=0.008$). Early transfusion was more commonly performed in BD-based class III than in vital signs-based class III (overall, 73.8% vs. 53.7%, $p=0.007$; massive, 37.5% vs. 15.8%, $p=0.001$). No significant differences were found in the rates of early surgical interventions between the two methods.

Conclusion: BD can be a better predictor of outcomes than vital signs in children with severe hemorrhagic shock.

Key Words: Acid-base balance, child, classification, shock, hemorrhagic, lactic acid, wounds and injuries

INTRODUCTION

In 2018, the American College of Surgeons Committee on Trauma recommended base deficit (BD), in addition to vital signs, as a criterion for the hemorrhagic shock classification in adults.[1,2] In children, owing to a large physiologic reserve for shock, hypotension rarely manifests until a 45% blood loss.[3] This feature suggests the low diagnostic utility of blood pressure measurement in the early phase of shock. Hypotension and tachycardia are variably defined by age groups, and tachycardia is readily affected by emotional stress. Contrary to these drawbacks of vital signs, BD is associated with pediatric trauma mortality.[4-7] This association indicates the need for validation of the adult BD-based hemorrhagic shock classification in children, which has not been performed to the authors' best knowledge.

However, the clinical implications of BD may be less prominent in children than in adults. This speculation is based on children's lower incidence of major trauma and post-injury multiorgan failure, and a more robust oxygen uptake.[8,9] Therefore, the authors hypothesized that in pediatric trauma, BD-based classification is more strongly associated with outcomes compared to vital signs-based classification, despite the gap

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between the two methods being narrower than that observed in adult trauma. Based on this perspective, we aimed to compare BD and vital signs as the criteria for the four-tiered hemorrhagic shock classification in children with trauma.

MATERIALS AND METHODS

Study design and setting

This retrospective study was a planned secondary analysis of pediatric trauma dataset-based studies,[10-12] which were conducted at a Korean academic hospital trauma center, equivalent to a level 1 trauma center in the United States. Despite the partial overlap in the study population, this current study differs from the previous ones in terms of the topics and implications (Supplementary Table 1, only online). Approximately 16000 trauma patients visit the trauma bay or emergency department annually, with about 100 pediatric trauma team activations. The study was approved by the Institutional Review Board with a waiver for informed consent (IRB no. AJIRB-MED-MDB-19-473).

In the trauma center, children are managed according to the contemporary Advanced Trauma Life Support guidelines. All children, except those with trivial injury, undergo blood tests. As a marker for shock, BD is usually measured using venous blood gas analysis within the initial hours of admission. These children are generally hospitalized at the intensive care unit. Transfusion, surgery or angioembolization is performed at the discretion of the attending trauma surgeons. Since 2007, we have maintained a 0.5–1:1 ratio of fresh frozen plasma to packed red blood cells. In 2015, a massive transfusion protocol was implemented at the center.

Study population

All consecutive children (<18 years) with trauma who visited the center and underwent assays for admission BD from 2010 through 2018 were included in this study. The exclusion criteria were unavailability of data on BD, environmental injury or poisoning, being dead on arrival, transfer to other centers, and transfer to our center after transfusion, surgery or angioembolization performed elsewhere.

Two criteria for classification: admission BD versus vital signs

Children were classified based on their BD as follows: class I, BD ≤2.0 mmol/L; II, 2.1–6.0 mmol/L; III, 6.1–10.0 mmol/L; and IV, ≥10.1 mmol/L.[1] For class-by-class comparison of the BD- and vital signs-based classifications (e.g., mortality rates between BD- and vital signs-based classes IV), the children were separately classified based on combined vital signs. For this purpose, the population was dichotomized at 13 years or older given the physiologic similarity with adults. Children aged 13–17 years were classified as per the 2012 Advanced Trauma Life Support hemorrhagic shock classification for adults.[13] For those younger than 13 years, we modified an existing classification system that uses systolic blood pressure, heart rate, and the Glasgow Coma Scale (GCS).[1] Due to the variable ranges of vital signs per age group, we used age-adjusted hypotension and tachycardia,[3] and GCS (Supplementary Table 2, only online).

Data collection

All consecutive children with trauma undergoing assays for BD were identified by searching electronic medical records for the International Classification of Diseases, 10th Revision codes for trauma, excluding environmental injury and poisoning. This query was cross-referenced against the institutional code for BD. The charts were then reviewed primarily by two authors (YK and JHK) using a standardized form. Any disagreement was discussed with the chief investigator.

Clinical findings included age, sex, transfer to the center, age-adjusted hypotension and tachycardia, and GCS. If GCS was unavailable, the AVPU scale was converted.[14] Severe traumatic brain injury (TBI; Abbreviated Injury Scale ≥3[1]) was noted due to its impact on pediatric mortality, even at low BD values.[10] Laboratory findings were BD, hemoglobin, and coagulopathy (an International Normalized Ratio >1.2).[15] As trauma scores, we employed the Injury Severity Score (ISS), Revised Trauma Score, and Pediatric Trauma Score.

The outcomes included in-hospital mortality, 24-hour transfusion [overall and massive (≥10 units of packed red blood cells in 24 hours)], and 24-hour surgical interventions (surgery and angioembolization) for the torso or major vessels.

Statistical analysis

Data are presented as means with standard deviations or medians with interquartile ranges for continuous variables, and as numbers and percentages for categorical ones. Analyses of variance or Kruskal-Wallis tests were performed to detect the overall differences across the four classes. If significant, t tests or Mann-Whitney U tests were used for pairwise comparisons. Chi-square tests for trend were performed to see increasing trends of the outcomes over the classes. For class-by-class comparison, we used logistic regressions with generalized estimating equations to account for within-subject correlations. A p value <0.05 was considered significant. Bonferroni-corrected p values are presented for multiple comparisons. We used SPSS for Windows ver. 25.0 (IBM Corp., Armonk, NY, USA) and R Statistical Software, ver. 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Clinical features and outcomes

Of 1046 eligible children, 603 were included in this study (Fig. 1). Their baseline features are outlined in Table 1. In-hospital

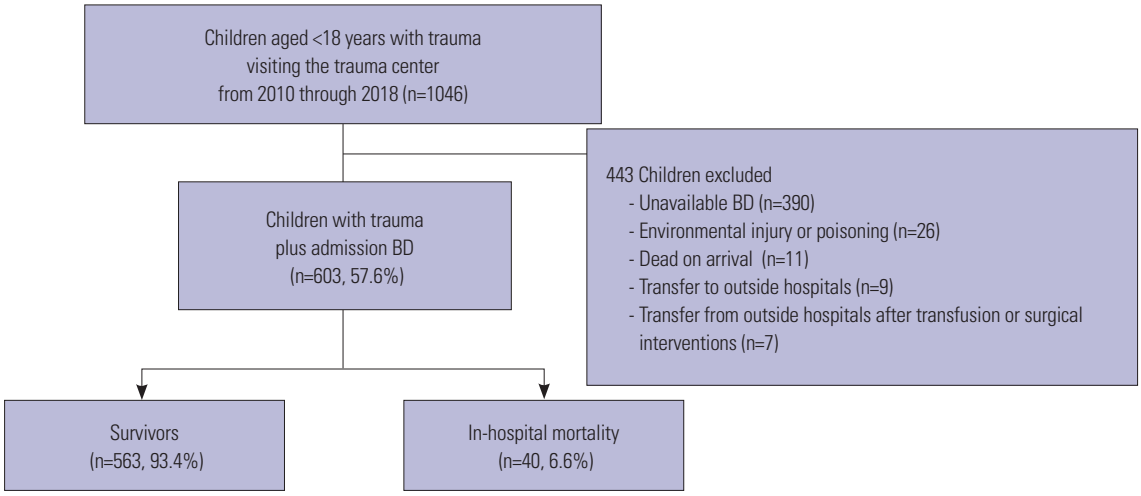

Fig. 1. Flowchart for the selection of study population. BD, base deficit.

Table 1. Baseline Characteristics of the Study Population (n=603)

Age (yr)	13.0 (7.0–16.0)
Girls	141 (23.4)
Transfer to the center	256 (42.5)
Age-adjusted hypotension	29 (4.8)
Age-adjusted tachycardia	181 (30.0)
GCS	15.0 (13.0–15.0)
Severe TBI	127 (21.1)
BD (mmol/L)	3.1 (1.4–5.3)
Hb (g/dL)	12.6±2.1
Coagulopathy*	105 (18.0)
ISS	16.0 (9.0–25.0)
RTS	7.28±1.07
PTS	8.4±3.0
IH mortality	40 (6.6)
TF, overall†	241 (40.0)
TF, massive†	88 (14.6)
SI, torso-vessels†	81 (13.4)

GCS, Glasgow Coma Scale; TBI, traumatic brain injury; BD, base deficit; Hb, hemoglobin; ISS, Injury Severity Score; RTS, Revised Trauma Score; PTS, Pediatric Trauma Score; IH, in-hospital; TF, transfusion; SI, surgical intervention. The values are expressed as mean±standard deviation, median (interquartile range), or number (%).
*The denominator was 582, representing the number of children undergoing assays for the International Normalized Ratio, †Performed within the initial 24 hours.

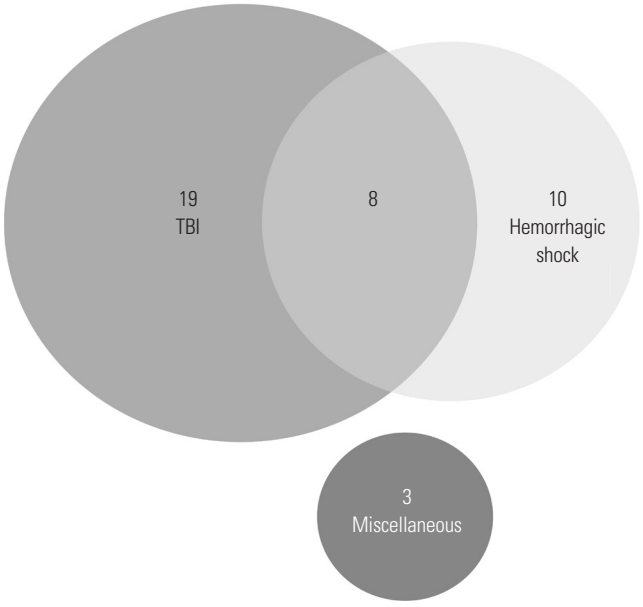

Fig. 2. Venn diagram showing the causes of death. Of the 40 non-survivors, 19 had isolated TBIs, 8 had both TBIs and hemorrhagic shock, 10 had isolated hemorrhagic shock, and 3 had miscellaneous causes (airway obstruction, cardiac contusion, and sepsis, respectively). Therefore, TBI was the leading cause [27 (68%)]. The isolated TBI-related non-survivors (n=19) had a lower median base deficit than in the hemorrhagic shock-related ones (n=18) [7.1 mmol/L (interquartile range, 4.4–9.5) vs. 15.8 mmol/L (9.3–22.4), p<0.001]. TBI, traumatic brain injury.

mortality, 24-hour overall transfusion, massive transfusion, and surgical interventions for the torso or major vessels were observed in 6.6%, 40.0%, 14.6%, and 13.4% of the children, respectively. The median intervals from accident to arrival at the center and that from arrival to BD assay were 2 hours (interquartile range, 1.0–4.0) and 37.5 minutes (17.0–186.0), respectively. Pedestrian collision and TBI were the most common injury mechanism (Supplementary Table 3, only online) and cause of mortality (Fig. 2), respectively. The isolated TBI-related non-survivors had a lower median BD than hemorrhagic shock-related ones (Fig. 2).

The children aged 5 years or younger tended to have a higher median BD compared to older children, without differences in GCS, rate of severe TBI, and ISS (Supplementary Table 4, only online). In contrast, the older children more frequently underwent 24-hour massive transfusion and surgical interventions.

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Table 2. Base Deficit-Based Classification

Variable	Class I (n=198)	Class II (n=291)	Class III (n=80)	Class IV (n=34)	*p* value
Age (yr)*	14.0 (8.0–16.0)	12.0 (6.0–16.0)	12.5 (4.3–16.0)	6.5 (3.0–15.0)	0.002
GCS	15.0 (15.0–15.0)	15.0 (13.0–15.0)	12.0 (7.0–15.0)	6.5 (3.8–10.3)	<0.001
Severe TBI	50 (25.3)	45 (15.5)	32 (40.0)	0 (0)	<0.001
Hb (g/dL)†	13.3±1.8	12.6±1.9	11.5±2.1	11.3±3.7	<0.001
Coagulopathy‡	28 (15.2)	29 (10.2)	27 (33.8)	21 (63.6)	<0.001
ISS§	12.0 (5.5–20.0)	13.0 (9.0–22.0)	24.0 (13.0–29.0)	34.0 (25.0–44.0)	<0.001
RTS§	7.65±0.53	7.46±0.77	6.52±1.37	5.32±1.74	<0.001
PTS	9.7±2.2	8.7±2.5	6.0±3.1	3.9±2.9	<0.001

GCS, Glasgow Coma Scale; TBI, traumatic brain injury; Hb, hemoglobin; ISS, Injury Severity Score; RTS, Revised Trauma Score; PTS, Pediatric Trauma Score.
The values are expressed as mean±standard deviation, median (interquartile range), or number (%).
*Significant only between class I and class II, and between class I and class IV, †Not significant between class III and class IV, ‡The denominators were 184, 285, 80, and 33 in the order of columns, §Not significant between class I and class II.

Table 3. Vital Signs-Based Classification

Variable	Class I (n=313)	Class II (n=97)	Class III (n=95)	Class IV (n=98)	*p* value
Age (yr)*	12.0 (7.0–16.0)	14.0 (8.0–16.0)	10.0 (4.0–15.0)	15.0 (7.8–16.3)	0.001
GCS	15.0 (15.0–15.0)	15.0 (15.0–15.0)	12.0 (10.0–13.0)	6.0 (4.0–7.3)	<0.001
Severe TBI	63 (20.1)	18 (18.6)	26 (27.4)	20 (20.4)	0.419
Hb (g/dL)†	13.0±1.7	12.9±2.1	11.9±2.3	12.0±2.8	<0.001
Coagulopathy‡	28 (9.4)	9 (9.5)	19 (20.4)	49 (50.5)	<0.001
ISS§	9.0 (5.0–17.0)	11.0 (5.0–19.3)	22.0 (16.0–29.0)	29.0 (22.0–38.0)	<0.001
RTS§	7.80±0.17	7.77±0.15	7.14±0.53	5.23±1.16	<0.001
PTS	10.0±1.9	9.2±1.9	7.3±2.1	3.8±2.0	<0.001

GCS, Glasgow Coma Scale; TBI, traumatic brain injury; Hb, hemoglobin; ISS, Injury Severity Score; RTS, Revised Trauma Score; PTS, Pediatric Trauma Score.
The values are expressed as mean±standard deviation, median (interquartile range), or number (%).
*Significant only between class I and class IV, between class II and class III, and between class III and class IV, †Not significant between class I and class II, and between class III and class IV, ‡The denominators were 297, 95, 93, and 97 in the order of columns, §Not significant between class I and class II.

BD- and vital signs-based classifications

Overall decreases in GCS were noted in both classifications (Tables 2 and 3). Notably, in BD-based class IV, no severe TBI occurred while the rates of TBI were similar across the four vital signs-based classes. As BD and vital signs worsened, the trauma scores also did, except the ISS and Revised Trauma Score between classes I and II in both classifications.

Class-by-class comparison of the two classifications

The occurrence of all outcomes increased stepwise according to worsening BD and vital signs (chi-square tests for trend, most $p<0.001$; only between surgical interventions and vital signs, $p=0.035$).

In class IV, the BD-based classification showed a higher rate of in-hospital mortality than did the vital signs-based method (58.8% vs. 32.7%) (Fig. 3A, Table 4). In class III, the former method showed higher rates of 24-hour transfusions (overall, 73.8% vs. 53.7%; massive, 37.5% vs. 15.8%) (Fig. 3B and C). If a child was classified by BD, the rates of massive transfusion could increase from 5.1% in class I to 67.6% in class IV (c.f., by vital signs, from 3.5% to 52.0%). No significant differences were found in the rates of 24-hour surgical interventions (Fig. 3D).

In classes III and IV, median GCSs were similar between both classifications, but severe TBI more commonly occurred in vital signs-based class IV (0% vs. 20.4%) (Supplementary Table 5, only online). BD-based class III showed consistently worse Revised and Pediatric Trauma Scores than vital signs-based class III (c.f., conflicting findings in the other classes).

DISCUSSION

We found that, between BD and vital signs, BD is more strongly associated with adverse outcomes of pediatric trauma. As both markers worsened, the rates of outcomes increased in a stepwise fashion. However, early transfusion and mortality were more commonly noted in BD-based classes III and IV, respectively, than in the vital signs-based counterparts. In class III, two of the three trauma scores were worse in the BD-based classification. Hence, in children with severe trauma, BD can be used to assess the amount of bleeding and the need for early transfusion and surgical interventions more precisely and promptly than using vital signs.

The features of the study population are consistent with those of children in the 2002–2007 German trauma registry in terms of the median age, as well as the proportions of boys

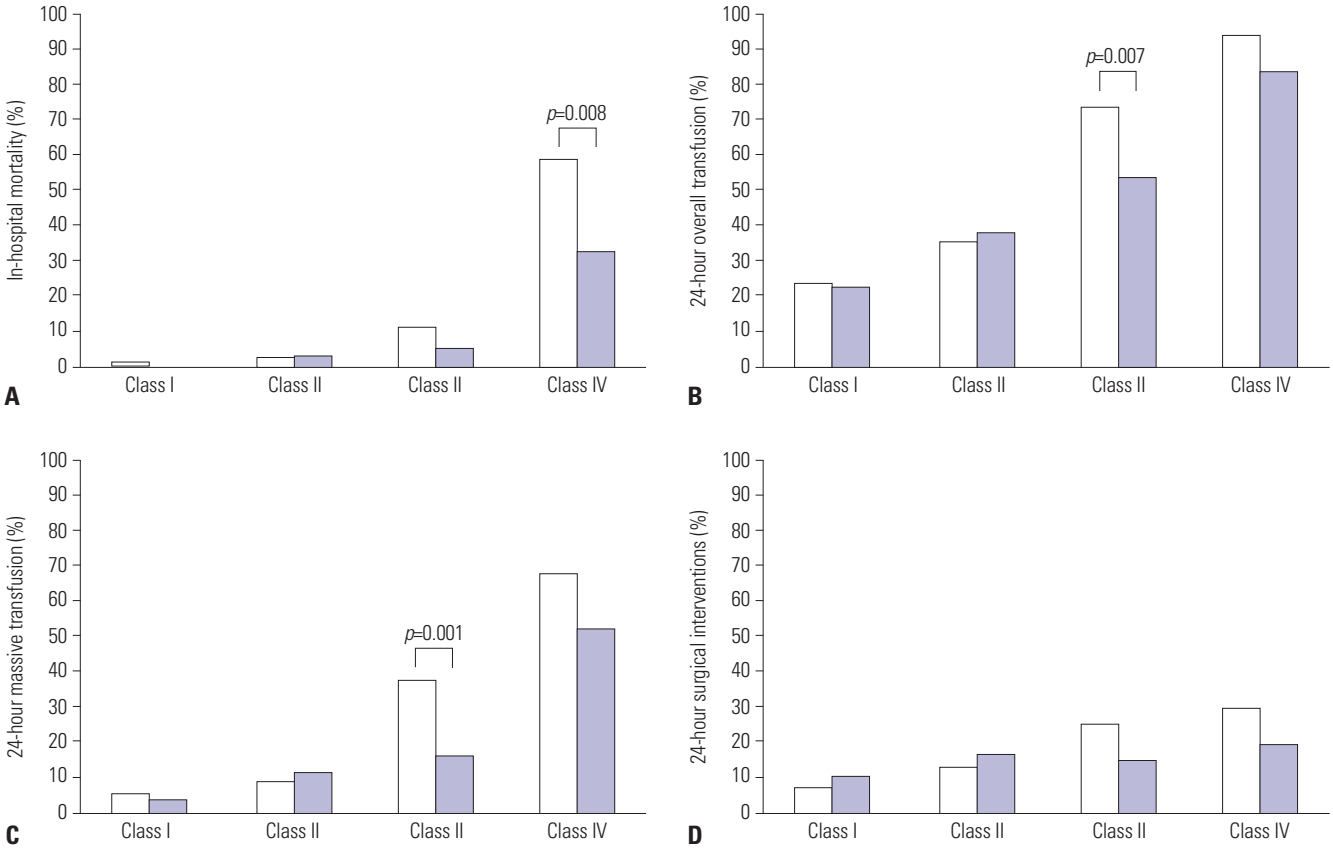

Fig. 3. Class-by-class comparison of the outcomes between the BD (shaded bars)- and vital signs (open bars)-based classifications. (A) In-hospital mortality was more common in BD-based class IV than in vital signs-based class IV (58.8% vs. 32.7%, p=0.008). Twenty-four-hour transfusions were more common in BD-based class III than in vital signs-based class III [overall, 73.8% vs. 53.7%, p=0.007 (B); massive, 37.5% vs. 15.8%, p=0.001 (C)]. (D) No significant differences were found in the rates of 24-hour surgical interventions for the torso or major vessels. BD, base deficit.

Table 4. Class-by-Class Comparison of the Outcomes between the Base Deficit- and Vital Signs-Based Classifications

	Class I			Class II			Class III			Class IV		
	Base deficit (n=198)	Vital signs (n=313)	*p* value*	Base deficit (n=291)	Vital signs (n=97)	*p* value*	Base deficit (n=80)	Vital signs (n=95)	*p* value*	Base deficit (n=34)	Vital signs (n=98)	*p* value*
IH mortality†‡	3 (1.5)	0 (0)	0.082†	8 (2.7)	3 (3.1)	0.082†	9 (11.3)	5 (5.3)	0.155	20 (58.8)	32 (32.7)	0.008
TF, overall‡	47 (23.7)	71 (22.7)	0.783	103 (35.4)	37 (38.1)	0.625	59 (73.8)	51 (53.7)	0.007	32 (94.1)	82 (83.7)	0.144
TF, massive‡	10 (5.1)	11 (3.5)	0.397	25 (8.6)	11 (11.3)	0.420	30 (37.5)	15 (15.8)	0.001	23 (67.6)	51 (52.0)	0.117
SI, torso-vessels‡	14 (7.1)	32 (10.2)	0.228	37 (12.7)	16 (16.5)	0.349	20 (25.0)	14 (14.7)	0.090	10 (29.4)	19 (19.4)	0.227

IH, in-hospital; TF, transfusion; SI, surgical intervention.
The values are expressed as number (%).
*p values are obtained by logistic regressions with generalized estimating equations (Bonferroni-corrected p<0.05), †The regression model was set up by classifying into three classes (I plus II, III, and IV) due to the absence of mortality in vital signs-based class I, ‡Significant associations of increasing outcomes with worsening base deficit (chi-square tests for trend, All p<0.001) and vital signs (p values were <0.001, <0.001, <0.001, and 0.035 in the order of rows).

and penetrating injury. This consistency may reflect the features of children in developed countries without an ongoing war. The median ISS and mortality rate were lower in this study than those in the German and U.S. trauma registries (median ISS, 16 vs. 22[16]; mortality rate, 6.6% vs. 11.6%–14.0%[4,16]).

BD has several strengths as a criterion for the shock classification. First, the marker reflects the net acid-base status affected by shock, fluids, and ventilation,[17] providing a practical viewpoint for resuscitation. Second, BD reflects severe shock more simply and precisely than vital signs. For initial assessment, it is complex to combine age-adjusted vital signs; this complexity may lead to underestimation of shock,[18,19] potentially missing some candidates for transfusion or surgery. BD-based classes III and IV respectively showed higher rates of transfusion and a lower rate of TBI [Table 4, Supplementary Table 5 (only online)]. Third, the BD cutoff for class III (6.0

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mmol/L) approximated the relevant values in children, offsetting the arbitrariness of citing the adult value.[1] In pediatric trauma, BD is associated with mortality (≥5–8 mmol/L),[4-7,15] transfusion (≥8 mmol/L),[7] coagulopathy (≥6 mmol/L),[15] intensive care unit care (≥5 mmol/L),[20] 6-month outcomes (≥5 mmol/L),[21] and ISS >15 (≥4.7 mmol/L).[22]

This study indicates a more modest impact of BD on outcomes in children than in adults. Mutschler, et al.[1] showed that adults underwent more frequent transfusion and mortality in BD-based classes II–IV than in the vital signs-based counterparts. In our study, the outcomes more frequently occurred in BD-based classes III and IV. This discrepancy coincides with the lower BD required for achieving a 25% TBI-free mortality rate in children than in adults (11 mmol/L vs. 15 mmol/L).[4,23] Also, a study on the differences in factors for trauma mortality between adults and children showed an exclusive association of a BD >4 mmol/L with adult mortality.[24]

The impact of BD in children is further confounded by TBI, emotional stress, and late presentation. TBI is the leading cause of pediatric trauma mortality. The presence of TBI raised the mortality rate from 5.3% to 21.1% in children with a BD <8 mmol/L,[4] implying its implications even in mild shock. This confounding was also detailed by the low median BD in isolated TBI-related mortality (Fig. 2). In children, pain, fear or anxiety is a source of excess catecholamine that increases lactate production via epinephrine-dependent β2 receptor stimulation.[25,26] This effect may underlie the association of crying with lactic acidosis in toddlers undergoing circumcision[27] and the higher median BD observed in children aged 5 years or younger (Supplementary Table 4, only online). This higher BD may be related to the late presentation of infants and toddlers due to their immature communication skills and nonspecific symptoms.

This study has some notable limitations. First, given the single-center, retrospective design of this study, the results may be limitedly applicable. Second, 42.5% of the population were transferred to our center. This high transfer rate possibly affected the disproportionately large percentage of BD-based class II. Although this feature might act as a selection bias, its effect on the study is likely to be weak because we excluded children who were transferred after transfusion or surgical interventions. Third, due to the lack of relevant records, we pursued the hemorrhage-related outcomes instead of the amount of bleeding. This might hinder the verification of the outcomes predicted by the two criteria. Finally, 37.3% of the eligible population were excluded due to unavailable BD. Yet, this flaw contributed to an inadvertent exclusion of some children with trivial injury.

In conclusion, BD can be a better predictor of outcomes than vital signs in children with severe hemorrhagic shock. For initial assessment of pediatric trauma, emergency physicians and trauma surgeons can measure BD to estimate the amount of bleeding, and to guide early transfusion or surgical interventions.

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AUTHOR CONTRIBUTIONS

Conceptualization: all authors. Data curation: Yura Ko, Jung Heon Kim, Kyungjin Hwang, and Yo Huh. Formal analysis: all authors. Investigation: all authors. Methodology: Yura Ko, Jung Heon Kim, Kyungjin Hwang, and Yo Huh. Project administration: Yura Ko, Jung Heon Kim, and Yo Huh. Resources: Yura Ko, Jung Heon Kim, Kyungjin Hwang, and Yo Huh. Software: Yura Ko, Jung Heon Kim, and Jisook Lee. Supervision: Jisook Lee and Yo Huh. Validation: Yura Ko and Jung Heon Kim. Visualization: Yura Ko, Jung Heon Kim, Jisook Lee, and Yo Huh. Writing—original draft: all authors. Writing—review & editing: all authors. Approval of final manuscript: all authors.

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