Base Excess Determined Within One Hour of Admission Predicts Mortality in Patients with Severe Pelvic Fractures and Severe Hemorrhagic Shock

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Abstract

Background: Unstable pelvic ring fractures with exsanguinating hemorrhages are rare but potentially life-threatening injuries. The aim of this retrospective study was to evaluate whether early changes in acid–base parameters predict mortality of patients with severe pelvic trauma and hemorrhagic shock.

Methods: Data for 50 patients with pelvic ring disruption and severe hemorrhage were analyzed retrospectively. In all patients, the pelvic ring was temporarily stabilized by C-clamp. Patients with ongoing bleeding underwent laparotomy with extra- and/or intraperitoneal pelvic packing, as required. Base excess, lactate, and pH were measured upon admission and at 1, 2, 3, 4, 6, 8, and 12 h postadmission. Patients were categorized as early survivors (surviving the first 12 h after admission) and nonsurvivors. Statistical analysis was performed by Mann–Whitney test; significance was assumed at $p < 0.05$. Receiver operating characteristic curves were generated for early mortality from each acid–base variable.

Results: Sixteen patients (32%) were nonsurvivors due to hemorrhagic shock (n = 13) or severe traumatic brain injury (n = 3). Thirty-four patients were early survivors. Base excess, lactate, and pH significantly discriminated between early survivors and nonsurvivors. Base excess determined 1 h after admission discriminated most strongly, with an area under the receiver operating characteristic curve of 0.915 (95% confidence interval, 0.836–0.993; $p < 0.001$).

Conclusion: Base excess, lactate, and pH discriminate early survivors from nonsurvivors suffering from severe pelvic trauma and hemorrhagic shock. Base excess measured 1 h after admission best predicted early mortality following pelvic trauma with concomitant hemorrhage.

Key Words
Hemorrhage · Base excess · Lactate · pH · Mortality

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Introduction

Traumatic disruption of the pelvic ring is a major cause of life-threatening hemorrhage, mainly due to extensive venous bleeding from the presacral venous plexus. Despite optimal surgical stabilization of the fracture and control of the hemorrhage, early recognition and assessment of the degree of hypoperfusion remains a challenge [1]. While measurements of conventional hemodynamic and hematologic parameters (heart rate, arterial blood pressure, central venous pressure, and hemoglobin/hematocrit) have been shown to be inaccurate for identifying severe hemorrhage and predicting outcome [1–4], indicators of anaerobic metabolism and acidosis, including lactate, pH, and base excess (BE), have been reported as being strongly associated

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with the degree of blood volume change and outcome, and thus have been suggested as end points of resuscitation [5–8].

Admission BE is a well-established marker of injury and has been shown to be a valuable indicator of trauma patients with hemodynamic instability, high transfusion requirements, and a high probability of death [9, 10]. Severity of BE on admission correlated with the incidence of shock-related complications, specifically adult respiratory distress syndrome, renal failure, coagulopathy, and multiple organ failure [5].

Serum lactate is frequently used as a diagnostic marker of hemorrhagic shock and is significantly correlated with poor outcome [1, 8]. In our previous series of 20 multiply injured patients with pelvic ring disruption treated with C-clamp, lactate was a sensitive marker of hemorrhage and allowed early evaluation of the patient's response to shock treatment [1].

Admission to the hospital and admission to ICU are good time-points for predicting posttraumatic outcome based on lactate, pH, and BE values [5, 9, 11]. The question remains as to whether there are other stages during the early resuscitative period where BE, lactate, and pH provide good predictions of posttraumatic outcome.

The present study was designed to analyze the physiologic factors that determine outcome in patients with multiple traumas, focusing on patients with severe pelvic fractures and concomitant hemorrhagic shock. The aim was threefold: (1) to investigate whether the acid–base variables BE, pH, and lactate were associated with mortality following severe pelvic trauma; (2) to identify the acid–base parameter most predictive of mortality; (3) and to evaluate prognostic time-points for early mortality in the early posttraumatic course.

Patients and Methods

From January 1996 until December 2007, 50 multiply injured patients were enrolled in this retrospective study. Inclusion criteria were admission to our level I trauma center within 24 h of injury, an injury severity score (ISS) of ≥17 points, and an unstable pelvic ring fracture according to the AO classification (AO B1/2, C1/2/3) [12]. Patients were excluded if they suffered from penetrating injuries and if they had received sodium bicarbonate ($NaHCO_3$) within the first hour after admission or more than 100 ml of $NaHCO_3$ during the initial resuscitation.

All patients were treated according to the advanced trauma life support (ATLS®) guidelines. Ultrasound of the abdomen [focused assessment sonogram in trauma (FAST)] was performed on arrival in the emergency room. Further assessments included plain radiographs of the chest and pelvis. Concomitant brain, chest, and/or abdominal injuries were evaluated by computed tomography (CT) scan if the patient was hemodynamically stable. In 21 patients (42%), CT scan could not be performed before emergency treatment because of initial severe hemorrhagic shock. In all patients, dislocation of the pelvic ring was immediately reduced and maintained by external fixation using a pelvic C-clamp. In patients with persistent hemodynamic instability due to ongoing hemorrhage, laparotomy and extra- and/or intraperitoneal packing or even additional resuscitative thoracotomy were performed.

BE (mmol/l), lactate (mmol/l), and pH were measured upon admission to our hospital and thereafter at 1, 2, 3, 4, 6, 8, and 12 h after admission. Other data collected included demographics, mechanism of injury, pelvic fracture pattern, blood transfusion requirements, and injury severity using the abbreviated injury score (AIS) for each body area, thereby calculating the ISS. Severity of hemorrhagic shock at admission was defined according to the ATLS® guidelines [13]. For this study, we defined classes I and II as mild or moderate hemorrhage and classes III and IV as severe hemorrhage. Mean acute physiology and chronic health evaluation (APACHE) II score was determined for each patient upon arrival.

Blood samples were analyzed with the ABL blood gas analyzer (Radiometer, http://www.radiometer.com). BE was calculated based on hemoglobin, pH, and pCO_2, using an integrated algorithm of the blood gas analyzer.

This retrospective analysis was approved by the local ethics committee; the requirement for written informed consent was waived.

Patients were categorized as early survivors (surviving the first 12 h after admission) and nonsurvivors (death within 12 h after admission). The groups were compared using the chi-square test or Fisher's exact test for dichotomous variables and the Mann–Whitney test for continuous variables. Differences were considered significant at $p < 0.05$. Receiver operating characteristic (ROC) curves were constructed to analyze each variable's discriminating power for predicting mortality, and the areas under each ROC curve were compared. The SPSS software package (SPSS 13.0, SPSS Inc., Chicago, IL, USA) was used to perform all statistical analyses.

Results

During the 12-year period, 50 patients [24 (48%) males and 26 (52%) females] who met the predefined inclu-

Table 1. Characteristics of early survivors and nonsurvivors with pelvic ring disruption and concomitant severe hemorrhage. (AIS: Abbreviated injury score; ISS: injury severity score; GCS: Glasgow coma scale; APACHE: acute physiology and chronic health evaluation; SD: standard deviation).

	All patients (n = 50)	Early survivors (n = 34)	Nonsurvivors (n = 16)	p Value
Age (years), mean ± SD	44.7 ± 17.9	45.2 ± 18.0	43.7 ± 18.3	0.60
Age ≥ 55	31.9% (15)	35.5% (11/31)	25.0% (4)	0.53
Males	48.0% (24)	44.1% (15)	56.3% (9)	0.55
AIS head ≥ 3	38.0% (19)	32.4% (11)	50.0% (8)	0.35
AIS chest ≥ 3	62.0% (31)	55.9% (19)	75.0% (12)	0.23
AIS abdomen ≥ 3	76.0% (38)	70.6% (24)	87.5% (14)	0.29
AIS extremity ≥ 3	60.0% (30)	58.8% (20)	62.5% (10)	1.00
ISS (mean ± SD)	41.7 ± 11.2	39.7 ± 12.4	45.9 ± 6.6	0.06
ISS ≥ 25	90.0% (45)	85.3% (29)	100.0% (16)	0.16
GCS ≤ 8	59.1% (26/44)	44.8% (13/29)	86.7% (13/15)	0.01
APACHE II, mean ± SD	21.6 ± 9.5	17.7 ± 8.5	30.1 ± 5.1	< 0.001

sion criteria were included in this study. Traffic accident was the most common mechanism of trauma (n = 26, 52%); the majority were motor vehicle accidents (n = 11, 22%), motorcycle or bicycle accidents (n = 7, 14%), or pedestrians (n = 8, 16%). Sixteen patients (32%) suffered severe injuries after a fall from a great height; ten of these were suicide attempts.

Overall mortality was 40.0% (n = 20). Thirty-four patients (68.0%) survived the first 12 h after admission (early survivors), four of whom died 12 ± 7 days after admission due to multiple organ failure (n = 3) or severe head injury (n = 1). Sixteen patients (32.0%) succumbed to their injuries within 12 h of admission (nonsurvivors), three of whom died due to severe head injury and 13 of whom died due to severe hemorrhagic shock. The basic demographics of early survivors and nonsurvivors, as well as the clinical and laboratory parameters of the two groups, are presented in Tables 1 and 2, respectively.

Injury Pattern and Initial Surgical Management

Analysis of the pelvic fractures showed 8 Type B fractures and 42 Type C fractures according to the AO classification (Table 3) [12]. Associated injuries included head injuries [n = 28 (56%), AIS 3.4 ± 1.3], chest injuries [n = 31 (62%), AIS 3.4 ± 0.6], intra-abdominal injuries [n = 40 (80%), AIS 4.3 ± 0.6], extremity injuries [n = 40 (80%), AIS 2.9 ± 0.7], and spine injuries [n = 14 (28%), AIS 2.7 ± 1.1]. The most commonly injured intra-abdominal organs were the liver (n = 11, 22%), the spleen (n = 9, 18%), the bladder (n = 8, 16%), and the urethra (n = 4, 8%).

Table 2. Clinical and laboratory parameters and fluid administration in patients with pelvic ring disruption and concomitant severe hemorrhage. (SBP: Systolic blood pressure; MAP: mean arterial pressure; HR: heart rate; PRBC: packed red blood cells; FFP: fresh frozen plasma; SD: standard deviation).

	All patients (n = 50)	Early survivors (n = 34)	Nonsurvivors (n = 16)	p Value
Hemoglobin (g/dl) at admission (mean ± SD)	7.4 ± 3.1	8.6 ± 2.9	4.9 ± 2.0	< 0.001
Hematocrit (%) at admission (mean ± SD)	22.2 ± 9.1	25.6 ± 8.4	15.0 ± 6.0	< 0.001
Prothrombin time (%) (mean ± SD)	55.5 ± 26.6	66.5 ± 23.4	34.1 ± 18.5	< 0.001
SBP (mmHg) at admission (mean ± SD)	109.5 ± 29.8	117.3 ± 25.2	90.4 ± 32.1	0.002
MAP (mmHg) at admission (mean ± SD)	76.6 ± 22.4	83.0 ± 18.8	58.6 ± 22.7	0.001
HR at admission (mean ± SD)	104.2 ± 21.0	100.2 ± 17.5	110.4 ± 27.7	0.02
Crystalloid solution administration from injury until 1 h after admission (l) (mean ± SD)	2.9 ± 1.9	2.7 ± 1.5	3.4 ± 2.4	0.42
Colloid solution administration from injury until 1 h after admission (l) (mean ± SD)	2.6 ± 1.8	2.1 ± 1.5	3.7 ± 1.8	0.001
PRBC administration within 1 h after admission (Units) (mean ± SD)	4.7 ± 5.4	2.6 ± 3.9	8.5 ± 5.9	< 0.001
FFP administration within 1 h after admission (Units) (mean ± SD)	1.1 ± 1.9	0.8 ± 1.6	1.6 ± 2.3	0.20

Table 3. Type of pelvic fractures according to the AO classification in 50 patients with pelvic ring disruption.

	All patients (n = 50)	Early survivors (n = 34)	Nonsurvivors (n = 16)	p Value
Type B	16.0% (8)	8.8% (3)	31.3% (5)	0.09
B1	12.0% (6)	2.9% (1)	31.1% (5)	0.01
B2	4.0% (2)	5.9% (2)	0% (0)	1.00
Type C	84.0% (42)	91.2% (31)	68.8% (11)	0.09
C1	44.0% (22)	47.1% (16)	37.5% (6)	0.56
C2	4.0% (2)	2.9% (1)	6.3% (1)	0.54
C3	36.0% (18)	41.2% (14)	25.0% (4)	0.35

According to the ATLS® classification, 29 patients (58%) were in severe hemorrhagic shock (class III and IV) and 21 patients (42%) were in mild or moderate hemorrhagic shock (class I and II) at admission. All of the nonsurvivors presented with severe hemorrhagic shock, compared to 13 patients in the early survivor group (100 vs. 38%; $p < 0.001$). To control hemorrhage, C-clamp was applied in all patients, with a mean time to C-clamp application of 72.4 ± 58.0 min after admission to the hospital. Due to persistent hemodynamic instability, 41 patients (82%) underwent additional crash laparotomy, with pelvic packing in 35 patients (70%). In 11 patients (22%), the aorta had to be cross-clamped for hemodynamic stabilization. Twenty-two patients (44%) required repair of intra-abdominal and/or urogenital organ lesions during emergency surgery. Seven patients (14%) required additional resuscitative thoracotomy.

Figure 1 shows the pelvic X-ray and kinetics of BE, lactate, and pH in a 42 year-old male early survivor who was injured in a traffic accident as a bicyclist. The patient sustained a pelvic ring injury of type C3.1 (Figure 1a) and additional rupture of the small bowel and colon, severe retroperitoneal bleeding, and fractures of the lower leg and forearm (ISS 45). On admission, the patient was in severe hemorrhagic shock. The pelvis was immediately reduced and stabilized by C-clamp, followed by laparotomy, intestinal resection without anastomosis, symphysis cerclage, and extraperitoneal packing (Figure 1b). Figure 1c shows the laboratory parameters of this patient for the first 12 h after admission. Within the first 2 h after admission, BE decreased to –18.5 mmol/l. However, after 6 h of resuscitation with aggressive surgical bleeding control, BE, lactate, and pH improved markedly.

Changes in BE, pH, and Lactate in Early Survivors vs. Nonsurvivors

Base excess, pH, and lactate levels of early survivors and nonsurvivors measured at different time points (0, 1, 2, 3, 4, 6, 8, and 12 h after admission) are presented in Figure 2. All acid–base variables discriminated significantly between early survivors and nonsurvivors at each time point measured ($p < 0.05$). Within 6 h of admission, BE, pH, and lactate values of the early

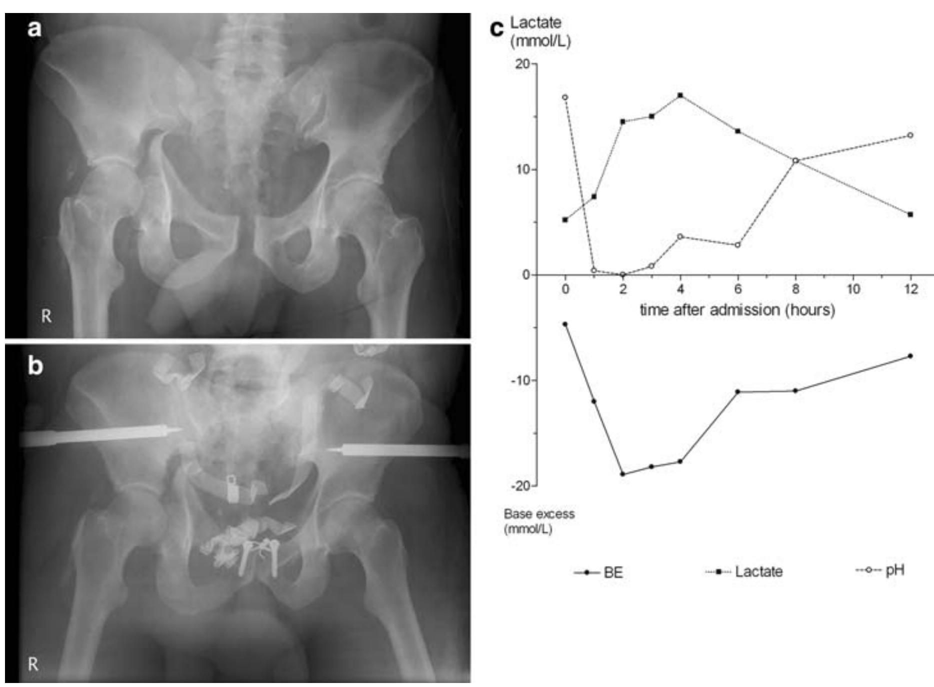

Figure 1. a) A 42-year-old male patient with bilateral vertical shear injury (type C3.1), severe retroperitoneal bleeding, rupture of the small bowel and colon, and fractures of the lower leg and forearm. X-ray of the pelvis at admission shows bilateral vertical shear injury. b) Postoperative X-ray of the pelvis after initial pelvic stabilization with C-clamp, cerclage of symphysis, and extraperitoneal packing. c) Temporal profile of changes in base excess (BE: mmol/l), lactate (mmol/l), and pH in this patient during the early posttraumatic period.

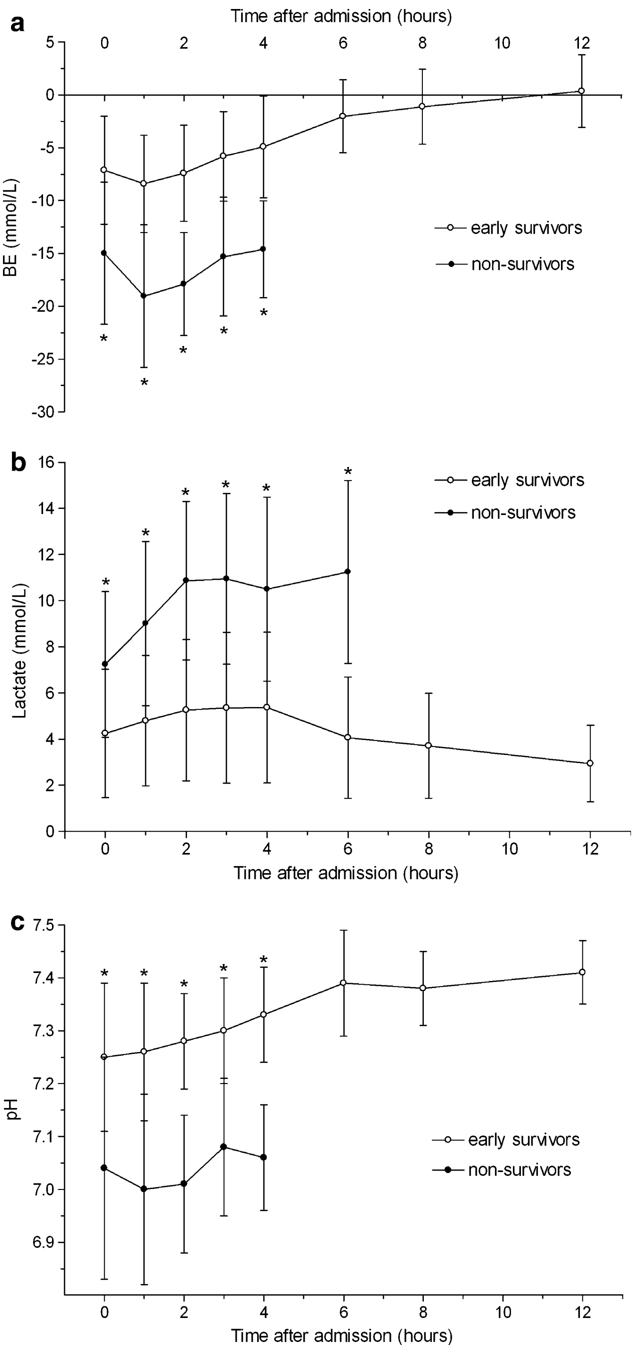

Figure 2. Laboratory parameters in 50 patients with pelvic ring disruption and concomitant severe hemorrhage. a) Base excess (BE: mmol/l), b) lactate (mmol/l), and c) pH (mean ± standard deviation) in arterial blood at admission and at 1, 2, 3, 4, 6, 8 and 12 h post-admission. Patients who survived the first 12 h after admission (early survivors; n = 34) were compared with patients who died in the early posttraumatic period (nonsurvivors; n = 16). *$p < 0.05$ early survivors versus nonsurvivors, Mann–Whitney test.

Table 4. Areas under the receiver operating characteristic curves and confidence intervals for acid–base variables at admission and 1 h postadmission in 50 patients with pelvic ring disruption and concomitant severe hemorrhage. (BE: Base excess; AUC: area under the curve; CI: confidence interval).

	AUC	95% CI	p Value
BE at admission	0.856	0.751–0.961	< 0.001
BE 1 h after admission	0.915	0.836–0.993	< 0.001
Lactate at admission	0.784	0.651–0.917	0.001
Lactate 1 h after admission	0.825	0.705–0.944	< 0.001
pH at admission	0.804	0.671–0.938	< 0.001
pH 1 h after admission	0.905	0.819–0.992	< 0.001

survivor group improved, while the values for the nonsurvivor group remained deranged or even deteriorated.

Relationship Between BE, pH, and Lactate on Hospital and ICU Admission

Severely decreased BE at hospital and ICU admission was associated with significantly increased lactate levels and significantly reduced pH values ($p < 0.05$).

Predicting Mortality Based on BE, pH, and Lactate Levels

ROC areas and 95% confidence intervals (CIs) determined for BE, pH, and lactate at admission and 1 h after admission are shown in Table 4. All of these descriptors were significantly associated with mortality. The ROC curve for BE 1 h after admission had the greatest area under the curve (AUC, 0.915; 95% CI, 0.836–0.993; $p < 0.001$; Figure 3). A sensitivity of 70% and a specificity of 100% were associated with a BE cut-off point of –9.35 mmol/l. When the BE cut-off point was decreased to –20.5 mmol/l, the sensitivity increased to 100% and the specificity decreased to 50%. In logistic regression analysis, none of the other acid–base variables contributed significantly to predicting mortality as compared to BE values determined 1 h after admission.

Discussion

The patients analyzed in this study represent a unique and relatively rare subset of severely injured patients presenting with traumatic pelvic ring disruption and severe hemorrhagic shock. Managing these patients is a diagnostic and therapeutic challenge for every trauma

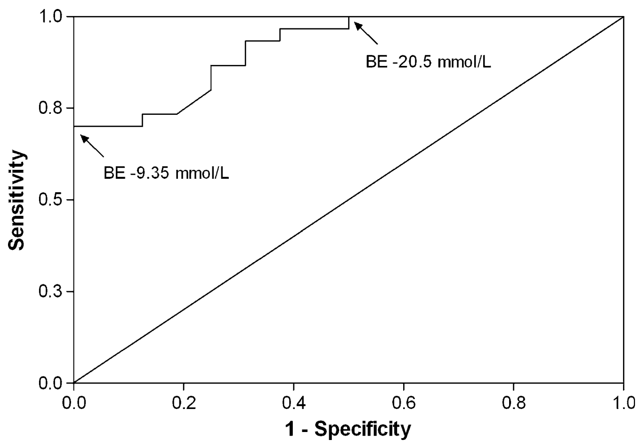

Figure 3. Receiver operating characteristic (ROC) curve for base excess (BE) 1 h after admission. The *diagonal line* corresponds to a test that is sensitive or specific just by chance. The area under the curve is 0.915.

team. Early identification of those patients more likely to require aggressive resuscitative efforts with surgical bleeding control represents the centerpiece of treatment for these patients [1]. Several studies have examined the prognostic significance of acid–base variables, such as pH, HCO_3, BE, lactate concentrations, and anion gap to predict survival or death in multiply injured patients [4, 9, 14–16]. Each of these markers has been shown to have predictive value, although each has its own shortcomings.

Lactate is a commonly used serum marker for diagnosing shock and monitoring resuscitation in trauma patients [1, 17, 18]. During hemorrhage with impaired tissue oxygen delivery, anaerobic metabolism is increased, resulting in increased lactate concentrations [18]. In addition, decreased blood flow during hemorrhage results in decreased delivery of lactate to the liver and kidneys, thereby attenuating lactate clearance [19]. Initial and serial lactate levels have been shown to be reliable indicators of morbidity and mortality following trauma [1, 17, 20]. In a recent study by Smith et al. [11], lactate, BE, and a combination of the two were good predictors of morbidity and mortality in critically ill patients. In addition, decreased lactate clearance has been shown to be an important predictor of mortality. A retrospective analysis of 95 surgical ICU patients documented a stepwise increase in hospital mortality with increasing time to normal lactate levels (≤ 2.0 mmol/l) [20]. In our study group, nonsurvivors had significantly higher lactate levels at admission and during resuscitation as compared to early survivors. However, we did not specifically analyze the mechanism of hyperlactemia. Patients in the present study received a mean of 2.6 l of crystalloid solutions from the time of injury until 1 h after admission, representing an exogenous source of plasma lactate. Furthermore, we did not document hepatic and renal lactate clearance in these patients. Further studies investigating hepatic perfusion and function using, e.g., the noninvasive liver function monitoring system "LiMON" (Pulsion Medical Systems, Munich, Germany), based on the clearance of intravenously injected indocyanine green, could help to estimate the influence of decreased lactate elimination on hyperlactemia in patients with severe hemorrhage [21].

BE provides an indirect estimation of global tissue acidosis due to impaired tissue perfusion [8, 17, 18]. Multiple studies in trauma patients have demonstrated the ability of an initial negative BE to predict the severity of hemorrhagic shock. Davis et al. stratified the extent of negative BE into three categories: mild (–3 to –5 mEq/l), moderate (–6 to –9 mEq/l), and severe (–10 mEq/l or less). Based on these subgroups, the authors observed a significant correlation between admission BE and transfusion requirements within the first 24 h and the risk of posttraumatic organ failure or death [5]. Similarly, Rixen et al. found that BE values measured at hospital and ICU admission were significantly prognostic of hemodynamic stability, the need for blood transfusions and fluid administration, and mortality. The predicted mortality for a BE level of –6.0 mmol/l at hospital admission was 25% [9]. Our data are in line with previously published studies showing that a significantly deranged BE correlates with poor outcome. BE demonstrated the strongest association with early hospital mortality as compared to pH and lactate. However, while admission BE and BE at ICU admission have already been shown to be prognostically significant time points [5, 9, 11], our statistical analysis revealed that BE determined 1 h after hospital admission is an additional and significant time-point for predicting mortality in severely injured patients with pelvic ring disruption and concomitant severe hemorrhage. Furthermore, 1 h after admission might be the optimal time-point for estimating the severity of the traumatic insult and the response to shock treatment.

In the present study, both lactate and BE significantly discriminated between early survivors and nonsurvivors. However, arterial BE had a markedly better correlation with mortality than did lactate in ROC analysis. This difference in the ability of BE and lactate to predict the severity of hemorrhagic shock and subsequently to predict the risk of mortality is explained by the fact that BE is influenced by all H^+ ions released into the extracellular fluid. BE buffers H^+ ions stemming from hypoxic lactic acid production as well as other sources, such as increased ATP hydrolysis during hemorrhagic shock [22]. Thus, BE is useful for estimating and monitoring the extent of bleeding, reflecting the adequacy of therapy for trauma-induced oxygen deficit.

Interestingly, nonsurvivors in our study received a remarkably high amount of colloid solution during the initial resuscitation. Colloids have been recommended in a number of resuscitation guidelines and intensive care management algorithms in the early 1990s [23, 24]. However, besides their plasma expanding properties, artificial colloids exert an anticoagulant effect, potentially leading to increased bleeding [9, 25]. Also, dextrans have been shown to be effective in preventing postoperative venous thrombosis and pulmonary embolism [26]. Previous examinations of Trumble et al. and de Jonge et al. found that hydroxyethyl starch was associated with increased postoperative blood loss [25, 27]. Due to the retrospective nature of the present investigation, the specific colloids administered remain uncertain. Nevertheless, the administration of colloids may have contributed to increased transfusion requirements and detrimental outcome.

In summary, metabolic correlates of ischemic metabolism in terms of decreased BE, increased lactate, and reduced pH provide a means of predicting mortality in trauma patients with pelvic ring injury and severe hemorrhage. BE determined within 1 h of admission appears to be the best immediate predictor. Its value at admission and at 1 h after admission may help to guide early and aggressive therapy for trauma- and concomitant hemorrhage-induced tissue hypoxia in multiply injured trauma patients with pelvic ring injury and severe hemorrhage.

Conflict of interest statement

The authors declare that there is no actual or potential conflict of interest in relation to this article.

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