Characterization of Acidosis in Trauma Patient

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Abstract

Background: Recent data suggest that acidosis alone is not a good predictor of mortality in trauma patients. Little data are currently available regarding factors associated with survival in trauma patients presenting with acidosis. Aims: The aims were to characterize the outcomes of trauma patients presenting with acidosis and to identify modifiable risk factors associated with mortality in these patients. Settings and Design: This is a retrospective observational study of University of Arkansas for Medical Sciences (UAMS) trauma patients between November 23, 2013, and May 21, 2017. Methods: Data were collected from the UAMS trauma registry. The primary outcome was hospital mortality. Analyses were performed using t-test and Pearson’s Chi-squared test. Simple and multiple logistic regressions were performed to determine crude and adjusted odds ratios. Results: There were 532 patients identified and 64.7% were acidotic (pH < 7.35) on presentation: 75.9% pH 7.2–7.35; 18.5% pH 7.0–7.2; and 5.6% pH ≤ 7.0. The total hospital mortality was 23.7%. Nonsurvivors were older and more acidotic, with a base deficit >8, Glasgow Coma Scale (GCS) ≤ 8, systolic blood pressure ≤ 90, International Normalized Ratio (INR) >1.6, and Injury Severity Score (ISS) >15. Mortality was significantly higher with a pH ≤ 7.2 but mortality with a pH 7.2–7.35 was comparable to pH > 7.35. In the adjusted model, pH ≤ 7.0, pH 7.0–7.2, INR > 1.6, GCS ≤ 8, and ISS > 15 were associated with increased mortality. For patients with a pH ≤ 7.2, only INR was associated with increased mortality. Conclusions: A pH ≤ 7.2 is associated with increased mortality. For patients in this range, only the presence of coagulopathy is associated with increased mortality. A pH > 7.2 may be an appropriate treatment goal for acidosis. Further work is needed to identify and target potentially modifiable factors in patients with acidosis such as coagulopathy.

Keywords: Acidosis, arterial blood gas, base deficit, pH, trauma

Introduction

The presence of acidosis in trauma patients on presentation to the emergency department has been viewed as a poor prognostic factor dating back three decades to the early descriptions of the “lethal triad” of acidosis, coagulopathy, and hypothermia.[1,2] However, recent data suggest that acidosis (pH ≤ 7.2) alone is not very good at predicting mortality in trauma patients.[3] It has been observed that trauma patients presenting with severe acidosis (pH ≤ 7.0) may still survive.[4,5]

In 1995, it was first reported that as many as 30% of trauma patients presenting with a pH ≤ 7.0 survived, a finding that has been confirmed in a recent study.[4,5] Survivors with severe acidosis tended to be less severely injured and have less neurologic dysfunction. However, the small number of patients presenting with this degree of acidosis made it difficult to draw conclusions regarding factors associated with survival in patients with severe acidosis.[1,2] In another recent study, a revised “lethal triad” criteria, which included fibrin/fibrinogen degradation products, base excess, and core body temperature, were found to be better at predicting mortality than the classic “lethal triad” criteria.[3] Few data are currently available regarding factors associated with survival and nonsurvival in trauma patients presenting with acidosis.

In the current study, our objectives were twofold: first, to characterize trauma patients presenting by the severity of acidosis and second, to identify potentially modifiable risk factors associated with mortality in trauma patients with acidosis.

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**METHODS**

**Study setting**
The University of Arkansas for Medical Sciences (UAMS) is a tertiary care university teaching hospital with a total of 405 adult patient beds. UAMS is an American College of Surgeons Verified Level 1 Trauma Center.

**Study design**
The study was a retrospective observational cohort study. Data on trauma patients presenting to UAMS between November 23, 2013, and May 21, 2017, were extracted from the UAMS Trauma Registry. Patients were included if all of the following data were available at the time of presentation: arterial blood gas (ABG) pH, International Normalized Ratio (INR), base deficit (BD), Glasgow Coma Scale (GCS), Injury Severity Score (ISS), penetrating or blunt mechanism of injury, and systolic blood pressure (SBP). Baseline demographics were collected.

**Outcomes**
The primary outcome measure was hospital mortality.

**Statistical analysis**
Data were presented as mean ± standard deviation or median with the 25th and 75th percentiles. Analyses were performed using t-test or Pearson’s Chi-squared test. Simple and multiple logistic regressions were performed to determine crude and adjusted odds ratios. The logistic model was adjusted for age, race, sex, mechanism, pH, BD, SBP, INR, GCS, and ISS. The variables used in the model were those identified as significantly associated with mortality in the univariate analysis, as well as basic demographic data such as age, sex, race, and mechanism of injury. The variables in the model are consistent with what have been used in other studies of acidosis.[4,5] Data analyses were performed using JMP Pro 13 (JMP Statistical Discovery from SAS, Cary, NC, USA).

**RESULTS**

**Population and demographics**
A total of 532 patients were included in the study [Figure 1]. The characteristics of the study population are displayed in Table 1. Approximately two-third of the patients had some degree of acidosis (pH < 7.35), of these patients, 75.9% had a pH between 7.2 and 7.35, 18.6% had pH between 7.0 and 7.2, and 5.5% had a pH ≤ 7.0. The mean base deficit was −4.6 with almost 25% of patients having a base deficit ≥−8.0. Most patients suffered a blunt mechanism of injury.

**Mortality**
The mortality among the study population was 23.7%, of which 5.6% occurred in the emergency room. The characteristics of survivors versus nonsurvivors are displayed in Table 2. Nonsurvivors were older and more acidic and were also more likely to have more severe metabolic acidosis (base deficit ≥−8), worse neurologic status (GCS ≤ 8), hypotension (SBP ≤ 90), coagulopathy (INR > 1.6), and more severe injury (ISS > 15).

**Acidosis and mortality**
We observed that patients with pH ≤ 7.2 had a statistically significant increase in mortality as compared to patients with a pH > 7.2 (51.8% vs. 18.5%, P < 0.001). This was particularly so for patients with a pH ≤ 7.0 who had a mortality of 79.0%. On the other hand, survival for patients with a pH between 7.2 and 7.35 was comparable to those patient with a pH > 7.35 (19.5% vs. 17.1%, P = 0.621).

Patients with a base deficit ≥−8 were associated with a statistically significantly higher mortality as compared to patients with a base deficit <−8 (36.4% vs. 19.6%, P < 0.001). On the other hand, patients with more severe metabolic acidosis (base deficit ≥−8) were less likely to die if their pH was > 7.2 than if the pH was ≤ 7.2 (18.0% vs. 52.9%, P < 0.001).

**Multivariate analysis**
In the logistic model of mortality, acidosis (pH ≤ 7.2) was associated with an almost 4-fold increase in the odds of mortality, while severe acidosis (pH ≤ 7.0) was associated with an almost 25-fold increase in the odds of mortality [Table 3]. On the other hand, for those patients presenting with a between pH 7.2 and 7.35, the odds of mortality were no greater than for patients presenting with a normal pH (>7.35). Other variables associated with mortality were neurologic status (GCS ≤ 8), coagulopathy (INR > 1.6), and injury severity (ISS > 15). Neither base deficit nor SBP was significantly associated with mortality in the adjusted model.

In the logistic model of mortality including only patients with a pH ≤ 7.2, only coagulopathy (INR > 1.6) was associated...
with increased odds of mortality [Table 4]. For those patients with a pH 7.2–7.35, neurologic status (GCS ≤ 8), coagulopathy (INR > 1.6), and injury severity (ISS > 15) were associated with increased odds of mortality [Table 5].

**Discussion**

We observed that trauma patients presenting with acidosis (pH ≤ 7.2) have greater odds of mortality, particularly with severe acidosis (pH ≤ 7.0), who have 25-fold greater odds of mortality than trauma patients without acidosis. However, even in the severe acidosis group, some patients do survive. On the other hand, trauma patients with more moderate, or compensated, acidosis (pH 7.2–7.35) have odds of mortality no greater than those without acidosis (pH > 7.35) on presentation. For those patients with a pH ≤ 7.2, coagulopathy (INR > 1.6) increased the odds of mortality.

Our findings are consistent with prior reports of acidosis in trauma patients being associated with increased mortality, whether measured by pH, lactate, or base deficit. The single best measure of acidosis either as a marker for resuscitation or a marker for prognosis has been debated. Base deficit has been shown to be a better predictor of outcome than pH, while lactate has been reported to be a better predictor of outcome than base deficit. Recently, it has been suggested that sucinate may be the most sensitive marker for severe shock. We did not have lactate levels available for our population, thus our analysis was restricted to pH and base deficit as measures of acidosis. In contrast to pH, while patients with a base deficit ≤ –8 had a significantly higher mortality, a base deficit ≥ –8 was not associated with significantly increased odds of mortality in the adjusted logistic models. While the reason why base deficit was not associated with significantly increased odds of mortality in the adjusted logistic models is not completely clear, it may be because the cutoff of ≤ –8 was too conservative. We selected a base deficit of ≥ –8 because it was the 75th percentile value in our population and because a base deficit ≥ –8 was associated with increased morbidity and mortality in other studies. Had we chosen a lower value reflecting more severe metabolic acidosis, we may have been able to identify a population with a higher mortality. However, there were

| Table 1: Characteristics of the study population |
|-----------------------------------------------|
| **Characteristics**                           | **Summary measure (n=532)** |
| Age (years) (SD)                             | 42.6 (18.8)                |
| Sex (percentage male)                        | 76.3                       |
| Race (%)                                      |                           |
| White                                         | 68.0                       |
| Black or African-American                    | 27.1                       |
| Other race                                    | 4.9                        |
| Mortality (percentage dead)                  | 23.7                       |
| ED mortality (%) (SD)                        | 1.3                        |
| Mechanism of injury (%)                      |                           |
| Penetrating                                   | 19.9                       |
| Blunt                                         | 80.1                       |
| Mean SBP (mmHg) [SD]                         | 72.3 (33.2)                |
| SBP ≤90 (mmHg)                                | 14.7                       |
| Median total hospital days (25th, 75th)       | 8 (3, 16)                  |
| Median total ICU days (25th, 75th)            | 4 (2, 10)                  |
| Median total ventilatory days (25th, 75th)    | 3 (1, 7)                   |
| ISS >15                                       | 66.7                       |
| GCS ≤8                                        | 66.0                       |
| Mean INR (SD)                                 | 1.5 (3.0)                  |
| INR >1.6                                      | 10.0                       |
| Mean ABG pH (SD)                              | 7.30 (0.13)                |
| ABG pH ≤7                                     | 3.6                        |
| 7.0–7.2                                       | 12.0                       |
| 7.2–7.35                                     | 49.1                       |
| >7.35                                        | 35.3                       |
| Mean ABG BD (SD)                              | –4.6 (6.7)                 |
| ABG BD ≤–8                                    | 24.2                       |
| >–8                                           | 75.8                       |

| Table 2: Characteristics of patients by mortality |
|-----------------------------------------------|
| **Characteristic**                           | **Alive (n=406)** | **Dead (n=126)** | **P** |
| Age (years)                                  | 40.7 | 48.5 | <0.001† |
| Sex (percentage male)                        | 77.1 | 73.8 | 0.449*  |
| Race (%)                                      |     |     |       |
| White                                         | 67.2 | 70.6 | 0.389† |
| Black or African-American                    | 28.3 | 23.0 |       |
| Other race                                    | 4.4  | 6.4  |       |
| Mechanism of injury (%)                      |     |     |       |
| Penetrating                                   | 19.7 | 20.6 | 0.819* |
| Blunt                                         | 80.3 | 79.4 |       |
| Mean SBP (mmHg) (%                           | 125.1| 113.3| 0.004† |
| SBP ≤90 (mmHg) (%)                           | 11.3 | 25.4 | <0.001† |
| Mean total hospital days                      | 13.5 | 4.9  | <0.001† |
| Mean total ICU days                           | 7.4  | 4.8  | <0.001† |
| Mean total ventilatory days                   | 5.4  | 4.5  | 0.143† |
| ISS >15 (%)                                   | 60.1 | 88.1 | <0.001* |
| GCS ≤8 (%)                                    | 62.1 | 78.6 | <0.001* |
| Mean INR (%)                                  | 1.5  | 2.5  | <0.001† |
| INR >1.6 (%)                                  | 3.9  | 29.4 | <0.001* |
| Mean ABG pH (%)                               | 7.31 | 7.24 | <0.001† |
| ABG pH ≤–7                                    | 1.0  | 11.9 | <0.001* |
| 7.0–7.2                                       | 8.9  | 22.2 |       |
| 7.2–7.35                                      | 51.7 | 40.5 |       |
| >7.35                                         | 38.4 | 25.4 |       |
| Mean ABG BD (%)                               | –4.0 | –6.5 | 0.003† |
| ABG BD (%) ≤–8                                | 20.2 | 37.3 | <0.001* |
| >–8                                           | 79.8 | 62.7 |       |

†t-test, *Pearson’s Chi-squared test. ED: Emergency department, ISS: Injury Severity Score, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, ABG pH: Arterial blood gas pH, BD: Base deficit, ICU: Intensive care unit
only a small numbers of patients with base deficits much greater than 8, which would have limited our ability to draw meaningful conclusions from this cohort.

Our findings suggest that patients with less severe acidosis (pH > 7.2) are less likely to die. The ability of patients to respiratory compensate may be an important factor in explaining this finding, which is supported by an earlier study of severe acidosis in which lower pCO_2 was found to be associated with a better prognosis. The potential importance of compensation is suggested by our finding that a
Our data suggest that treatment of acidosis should be directed toward those patients with a pH < 7.2. Further, the data also support a pH goal of >7.2 for resuscitation. However, the question remains how best to intervene. It has been suggested that bicarbonate therapy for acidosis is not only ineffective in improving outcome, but may in fact increase mortality.[14] Similarly, there is little data supporting the efficacy of bicarbonate therapy in patients with lactic acidosis.[15,16] In fact, bicarbonate can cause increase in intracellular pH as well as increase in lactic acid production.[17] The improved outcomes we observed in patients with less severe or uncompensated acidosis suggest that efforts directed toward lowering pCO₂, including early initiation of mechanical ventilation, should be considered. It may be that using better markers of acidosis to guide resuscitation, such as succinate, may be important moving forward.[10]

Interestingly, in the cohort of acidic patients with a pH ≤ 7.2, we found that coagulopathy as measured by INR was the only variable associated with increased odds of mortality. This is in contrast to patients with less severe acidosis (pH 7.2–7.35) where neurologic status and severity of injury are also associated with increased odds of mortality. While coagulopathy is a major component of the classic “lethal triad,” the use of INR as a measure of coagulopathy in trauma patients has been questioned.[13] Endo et al. have suggested a revision of the “lethal triad” that uses fibrinolytic markers rather than INR as the measure of coagulopathy.[2] We did not have other markers of hemostasis available for our analysis, however, given our findings, markers reflecting hemostasis or coagulopathy may provide therapeutic goals in the treatment of trauma patients presenting with acidosis.

There are several limitations inherent to this retrospective study that warrant mention. A large number of patients in the trauma registry were excluded because of the absence of critical values, in particular an ABG at presentation. It may be that using better markers of acidosis to guide resuscitation, such as succinate, may be important moving forward.[10]
meaningful statistical results. In particular, we do not have specific information on the subgroup of patients with severe hemorrhage. However, the fact that mechanism of injury (blunt vs. penetrating trauma) was not associated with changes in outcome suggests that the study findings may be applicable to acidosis independent of mechanism, including hemorrhage. Further study of this particular subgroup would be of interest. In addition, we used GCS as a surrogate for neurologic status. However, we recognize that GCS may be affected by factors other than traumatic brain injury. Finally, because this was a retrospective study, we can only describe associations, not determine cause and effect.

**Conclusions**

A pH ≤7.2 is associated with increased odds of mortality. On the other hand, this is not the case for those trauma patients with a pH >7.2 and a pH >7.2 may be an appropriate goal for resuscitation of acidic patients. The ability of patients to compensate for acidosis appears to be important. For those patients with a pH ≤7.2, only the presence of coagulopathy is associated with increased odds of mortality. Therapeutic interventions facilitating the identification and correction coagulopathy in acidic trauma patients should be explored.

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**Conflicts of interest**

There are no conflicts of interest.

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