Use of Serum Bicarbonate Measurement in Place of Arterial Base Deficit in the Surgical Intensive Care Unit

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Hypothesis: Serum bicarbonate (HCO₃⁻) measurement may accurately and reliably be substituted for the arterial base deficit (BD) assay in the surgical intensive care unit (ICU).

Design: Retrospective criterion standard analysis.

Setting: Surgical ICU in a tertiary care facility.

Patients: Consecutive sample of non–trauma-related surgical ICU admissions from January 1996 to January 2004 with simultaneously obtained serum HCO₃⁻ and arterial BD levels.

Main Outcome Measures: Correlation between HCO₃⁻ and BD at admission and during the ICU stay; predictive value of serum HCO₃⁻ for significant metabolic acidosis and ICU mortality.

Results: The study included 2291 patients with 26,063 sets of paired laboratory data. The mean±SD age was 52±16 years and mean ICU stay was 5.8±9.8 days. There were 174 ICU deaths (8%). Serum HCO₃⁻ levels showed significant correlation with arterial BD levels both at admission (r=0.85, R²=0.72, P<.001) and throughout the ICU stay (r=0.88, R²=0.77, P<.001). Serum HCO₃⁻ reliably predicted the presence of significant metabolic acidosis (BD > 5) with an area under the receiver operating characteristic curve (AUC) of 0.93 at admission and 0.95 overall (both P<.001), outperforming pH (AUC, 0.80), anion gap (AUC, 0.70), and lactate (AUC, 0.70). The admission serum HCO₃⁻ level predicted ICU mortality as accurately as the admission arterial BD (AUCs of 0.68 and 0.70, respectively) and more accurately than either admission pH or anion gap.

Conclusions: Serum HCO₃⁻ provides equivalent information to the arterial BD and may be used as an alternative predictive marker or guide to resuscitation. Low HCO₃⁻ levels should prompt immediate metabolic acidosis evaluation and management.

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measurement is not routinely performed in all ICU patients, which could result in a failure or delay in the diagnosis of significant acidosis.

The increased concentrations of plasma hydrogen ions with metabolic acidosis are buffered by a variety of homeostatic mechanisms, including plasma bicarbonates (HCO₃⁻). Serum HCO₃ levels have been shown to decrease in a linear fashion with increasing acid loads and theoretically should provide information similar to the arterial BD. In addition, plasma HCO₃ measurement is part of the routine chemistry panel obtained on nearly all ICU admissions, does not require any separate equipment to obtain or perform analysis, and does not require arterial puncture or catheterization. The aims of this study were to examine the degree of correlation between the arterial BD and serum HCO₃ levels, to analyze the accuracy of serum HCO₃ in identifying significant metabolic acidosis, and to compare their ability to predict mortality in a surgical ICU population.

### METHODS

This study was designed as a retrospective criterion standard analysis to compare the use of serum HCO₃ levels with the standard measure of arterial BD in an ICU population. The Los Angeles County Hospital (Los Angeles, Calif) is a large tertiary care facility and level I trauma center with a 16-bed surgical ICU. The study population included all adult (>14 years) patients admitted to the surgical ICU by either the Emergency Non-Trauma Surgery Service or one of the general surgical specialties (Thoracic Foregut, Hepatobiliary, Colorectal, or Vascular) from January 1, 1996, to January 1, 2004. Only patients with an ICU stay longer than 24 hours and adequate laboratory data for analysis were included.

Patients were identified from a prospectively maintained clinical and laboratory database of all surgical ICU admissions. Patients who met the foregoing criteria and had at least 1 simultaneously drawn arterial blood gas determination (with BD) and serum chemistry panel (with HCO₃) were included. Laboratory, demographic, and outcome data for each patient were entered into a computerized spreadsheet. The Simplified Acute Physiology Score II and the Acute Physiology and Chronic Health Evaluation II score at 24 hours after ICU admission were calculated and recorded. The correlation between HCO₃ and BD was assessed by calculation of the Pearson correlation coefficient (r) and the coefficient of determination (R²), and linear regression analysis was used to develop a predictive equation for BD. The predictive ability of HCO₃ and 3 conventional measures (pH, lactate, and anion gap [AG]) of severe metabolic acidosis and mortality were examined by calculating the area under the receiver operating characteristic curve (AUC).

Severe metabolic acidosis was defined as a BD greater than 5. The AG was calculated with the following formula:

\[
AG = (Na + K) - (Cl + HCO₃)
\]

where Na indicates the level of sodium; K, of potassium; and Cl, of chloride. Linear variables are reported as the mean value ± 1 SD and AUC with 95% confidence intervals. All statistical analysis was performed with SPSS 12.0 for Windows (SPSS Inc, Chicago, Ill), and statistical significance was set at P<.05. This study was reviewed and approved with waiver of informed consent by the hospital’s institutional review board.

### RESULTS

Among 7241 surgical ICU admissions, 2291 patients (32%) were identified who met the inclusion criteria and had adequate laboratory data for analysis. These patients had a total of 26,063 sets of simultaneously obtained paired laboratory data, including an arterial blood gas and serum chemistry panel with serum HCO₃. The patient demographics are shown in Table 1. The majority of patients (56%) were admitted to the Emergency Non-Trauma Surgery Service for major abdominal surgery or disease. There were 174 deaths in the ICU, for an overall ICU mortality rate of 8%.

Table 2 shows the mean relevant laboratory values for the study population, for both the ICU admission laboratory studies only and for the entire ICU stay. There was a mean BD of 1.9 at ICU admission, which improved to 0.1 for the ICU stay. Similarly, the mean HCO₃ level at admission was 19.8 mEq/L, with improvement to a mean of 23.9 mEq/L for the ICU stay. Correlation and regression analysis demonstrated a very strong correlation between the arterial BD and the simultaneously measured serum HCO₃ levels. Figure 1 shows the strong linear correlation between the arterial BD and serum HCO₃ levels.

### Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2291</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>52.3 ± 16.1</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1393 (61)</td>
</tr>
<tr>
<td>Female</td>
<td>898 (39)</td>
</tr>
<tr>
<td>Mechanical ventilation, No. (%)</td>
<td>1634 (71)</td>
</tr>
<tr>
<td>SAPS II, mean ± SD</td>
<td>16.8 ± 8.8</td>
</tr>
<tr>
<td>APACHE II, mean ± SD</td>
<td>21.8 ± 9.7</td>
</tr>
<tr>
<td>ICU LOS, mean ± d</td>
<td>5.8 ± 9.8</td>
</tr>
<tr>
<td>Reason for ICU admission, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal</td>
<td>1289 (56)</td>
</tr>
<tr>
<td>Vascular</td>
<td>420 (18)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>218 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>364 (16)</td>
</tr>
<tr>
<td>ICU mortality, No. (%)</td>
<td>174 (8)</td>
</tr>
</tbody>
</table>

### Table 2. Mean Laboratory Values at ICU Admission and During ICU Stay*

<table>
<thead>
<tr>
<th>Laboratory Measure</th>
<th>ICU Admission (n = 2291)</th>
<th>All Values (n = 26 063)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>pH</td>
<td>7.37 ± 0.08</td>
<td>7.39 ± 0.07</td>
</tr>
<tr>
<td>BD</td>
<td>1.9 ± 4.1</td>
<td>0.1 ± 4.1</td>
</tr>
<tr>
<td>HCO₃, mEq/L</td>
<td>19.8 ± 5.8</td>
<td>23.9 ± 4.1</td>
</tr>
<tr>
<td>Anion gap</td>
<td>16 ± 4.5</td>
<td>14.7 ± 4.8</td>
</tr>
<tr>
<td>Lactate, mg/dL</td>
<td>28.8 ± 29.7</td>
<td>26.1 ± 30.6</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.1 ± 1.0</td>
<td>1.4 ± 1.7</td>
</tr>
</tbody>
</table>

Abbreviations: BD, base deficit; HCO₃, serum bicarbonate; ICU, intensive care unit.

*SI conversion factors: To convert creatinine to micromoles per liter, multiply by 88.4; lactate to millimoles per liter, multiply by 0.111. *Values are mean ± SD.
correlation between the BD and serum HCO₃ level drawn at the time of ICU admission, with a correlation coefficient of 0.85 ($R^2 = 0.72$, $P < .001$). This linear relationship was retained throughout the early resuscitation period and for the entire ICU stay, with a correlation coefficient of 0.88 ($R^2 = 0.77$, $P < .001$) for all ICU laboratory measures obtained during the study period. The regression equation derived from this analysis allows prediction of the arterial BD from the serum HCO₃ level by the following formula:

$$BD = 21.5 - (0.79 \times HCO_3).$$

From this equation, 2 important cutoff points for clinical use would be a serum HCO₃ level of 22 mEq/L, which equates a BD of 0, and a serum HCO₃ level of 18 mEq/L, which equates to a BD of 5.

We then assessed the accuracy and reliability of serum HCO₃ level for the identification of significant metabolic acidoses (BD $> 5$) and compared this with other conventional measures of acidosis such as pH, anion gap, and lactate. The serum HCO₃ level reliably and accurately identified the presence of a significant acidosis, with an AUC of 0.93 (95% confidence interval, 0.92-0.94; $P < .001$) for the ICU admission laboratory studies and 0.95 (95% confidence interval, 0.94-0.96; $P < .001$) for the entire data set (Figure 2). The serum HCO₃ significantly outperformed the other conventional acid-base measures examined, including the arterial pH (AUC, 0.80), serum anion gap (AUC, 0.70), and arterial lactate (AUC, 0.70).

The study laboratory values were then analyzed for their ability to predict ICU mortality. Nonsurvivors were older, had a higher Simplified Acute Physiology Score II and Acute Physiology and Chronic Health Evaluation II score, and demonstrated significant differences in pH, anion gap, HCO₃, BD, and lactate at the time of ICU admission compared with survivors (Table 3). The receiver operating characteristic curves for mortality prediction demonstrated that the serum HCO₃ performed as well as the arterial BD, with AUCs of 0.68 and 0.70 (both $P < .001$), respectively (Figure 3). Both measures outperformed the admission arterial pH (AUC, 0.61) and serum anion gap (AUC, 0.59) for predicting ICU deaths. Analysis of the entire data set demonstrated that BD and HCO₃ level maintained similar predictive power throughout the ICU stay, with an AUC of 0.64 for BD and 0.63 for serum HCO₃ level (both $P < .001$).

The diagnosis and management of major disturbances in acid-base homeostasis are a routine aspect of caring for critically ill or injured patients across all medical and surgical specialties. Acute changes in pH can produce significant alterations in the physical and electrochemical functions from the cellular to the organ and system levels. Metabolic acidosis remains one of the more concerning acid-base disturbances in the acutely ill surgical patient, as it often reflects ongoing tissue or organ...
hypoperfusion, which can result in organ failure or death if not promptly corrected. Multiple techniques to identify the presence of acidosis and/or tissue hypoperfusion have been studied and used, including systemic markers such as the arterial BD, anion gap, lactate, and mixed venous oxygen saturation, as well as tissue- or organ-specific measures such as gastric tonometry and transcutaneous oxygen or carbon dioxide monitoring. Although there is ongoing debate about the relative merits of each measure, the ideal marker would be easily obtained and analyzed, provide accurate and reliable clinical information, and be cost-effective.

The arterial BD remains one of the most commonly used markers in the ICU both to diagnose the presence of metabolic acidosis and to guide resuscitation or therapy. Although an elevated BD is often taken as a surrogate marker for lactic acidosis in the perioperative or acute illness setting, a variety of mechanisms contribute to metabolic acidosis and to guide resuscitation or therapy. Although infrequent, other complications associated with arterial puncture or catheterization can range from minor hematoma formation to devastating ischemia and limb loss. Patient factors such as obesity, diminutive arteries, and hypovolemia may make obtaining an adequate specimen difficult or impossible. In addition, processing of the arterial sample requires specialized equipment for collection, storage, and analysis, with resultant increase in costs to the hospital and patient. The substitution of an easily measured value from a venous sample, such as the serum HCO3, would overcome most of these drawbacks if it provided clinical information equivalent to the arterial BD.

There are few published data examining the utility of using the serum HCO3 to provide information equivalent to the arterial BD in the ICU. In patients with chronic acidosis undergoing dialysis, serum HCO3 levels have been demonstrated to correlate with nutritional status, hospitalization rates, and mortality. In a large series of patients with septic shock, serum HCO3 levels demonstrated a moderate correlation with the degree of lactic acidosis but were not directly compared with BD. Eachempati et al performed the only study to date that has objectively described the relationship between simultaneously measured arterial BD and serum HCO3 levels, which served as the impetus for this study. They found a strong linear correlation between the 2 measures ($r=0.91$, $R^2=0.83$) in a mixed trauma and surgical ICU population, and derived a regression equation to predict the BD from a known HCO3 level. Although they demonstrated a high degree of overall correlation, they did not analyze the performance of the serum HCO3 in the most clinically important area, identifying or excluding a significant metabolic acidosis. In addition, inclusion of a more homogeneous population (trauma) with a more mixed group of patients (nontrauma surgical) could po-
tentially overestimate the degree of correlation and utility of serum HCO₃⁻ in the nontrauma patients.

Our results do demonstrate a strong linear correlation between these 2 measures in a nontrauma surgical ICU population, with correlation coefficients only slightly weaker (r=0.88 vs 0.91 and R²=0.77 vs 0.83) than those reported by Eachempati et al.² Our receiver operating characteristic curves for prediction of significant acidosis and mortality also demonstrate that serum HCO₃⁻ measurement provides nearly identical information as arterial BD in this patient population, both at the time of ICU admission and throughout the ICU stay. The serum HCO₃⁻ level also provided better diagnostic and prognostic information than other conventional measures, such as the arterial pH and the serum anion gap.

This study has several limitations. Although a strong and reliable relationship was found between the 2 main study variables in the entire population, there may have been unidentified subgroups of patients in whom this relationship may have been altered or even invalid. Measurement of the arterial BD is only one of several major indications for arterial puncture or catheterization in the ICU population, and adoption of this practice would potentially decrease but would not eliminate the need for arterial puncture. Because of the nature of this retrospective review, we are unable to comment on the percentage of patients in this study who had other indications for arterial catheterization, such as hemodynamic or respiratory instability. Although we have identified several local complications from arterial manipulation in these patients, including hand ischemia, our database did not track the overall number or type of arterial-related complications.

In conclusion, these results indicate that the serum HCO₃⁻ determination may be safely and reliably substituted for measurement of arterial BD in the surgical ICU patient. Potential advantages of this approach include increased patient comfort, avoidance of complications associated with arterial puncture and cannulation, and cost savings in terms of both time and equipment. These data should also improve the understanding that low serum HCO₃⁻ levels accurately identify metabolic acidosis and should prompt immediate evaluation and potential interventions.

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Previous Presentation: This paper was presented at the 76th Annual Meeting of the Pacific Coast Surgical Association; February 20, 2005; Dana Point, Calif; and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

REFERENCES

Steven C. Stain, MD, Nashville, Tenn: Dr Martin and his colleagues at USC have presented a series of 2291 nontrauma patients admitted to their surgical ICU with more than a 24-hour length of stay between 1996 and 2004. This retrospective analysis assessed the correlation of venous HCO3 levels with arterial BD at admission and during the ICU stay and concluded that venous HCO3 levels reliably predict the presence of significant metabolic acidosis with BDs of greater than 5. Furthermore, the venous HCO3 levels were more predictive than pH, anion gap, and lactate. Finally, the venous measurement predicted ICU mortality as accurately as the admission arterial BD and more accurately than either the admission pH or anion gap.

It would seem intuitive that patients with low venous HCO3 levels would have arterial BDs, as the BD is calculated from measured values including HCO3, albeit arterial HCO3. And while I agree with the basic conclusion of the manuscript that the values, venous HCO3, and BD must correlate, I find myself asking what types of ICU patients would have an isolated venous HCO3 level measured. By that I mean those patients without the need for arterial blood gas or lactate level. In my practice patients with moderately severe reduced HCO3 on a chemistry panel generally have other signs of hypoperfusion such as tachycardia, oliguria, or even hypotension. Generally they respond to fluid challenges evident by proven clinical rather than laboratory values. Those who do not respond often end up having invasive monitoring.

Those on ventilators generally have arterial blood gases obtained, and many centers now have arterial blood gas analyzers that routinely report lactate with the arterial blood gas results. The trauma literature is replete with reports of the value of lactate as an end point of acute resuscitation.

I have several questions for the authors. Do the authors believe that venous HCO3 is preferable to serial lactate determinations to guide their fluid resuscitations? All of the patients in the current study had arterial blood gas obtained, and that inclusion criterion was part of the study design. What proportion of your ICU patients with more than a 24-hour length of stay did not have an arterial blood gas obtained, and were those excluded from your study? That information is important to estimate how useful your findings are. Why were trauma patients not included? Your group published a paper this month in the Journal of Trauma looking at acid-base derangements of 427 trauma patients. In that manuscript you focused on unmeasured ions, presumably lactate rather than venous HCO3. Do you believe the correlation of HCO3 and BD would be equally applicable in trauma patients?

In the manuscript, 9 of your 11 variables you compared between survivors and nonsurvivors had a P value of less than .001. Will logistic regression of these variables be useful to truly identify which were independently predictive of survival?

Still I enjoyed the paper and the excellent manuscript by Dr Martin and his colleagues.

Richard J. Mullins, MD, Portland, Ore: I want to congratulate Dr Martin on a very nice presentation. Did you determine there was a difference in HCO3 concentration based on where the venous blood gas was obtained? I am assuming most of these were peripheral venous gases, or were there central venous blood samples? Second, you are well aware that there is controversy regarding hyperchloremia as a form of acidemia in the resuscitation of injured patients. At your hospital do you use Ringer lactate or normal saline to resuscitate patients? Did hyperchloremia contribute to the standard error that you show in your linear regression graph? Did you try to use venous HCO3 levels to categorize patients into 3 or 4 groups and find that these groups correlate with the risk of death?

Michael M. Shabot, MD, Los Angeles, Calif: I enjoyed the paper and congratulate the authors. Although the linear analysis and receiver operating characteristic curves were interesting, the standard method of comparing a new test to an established gold standard is the Bland-Altman plot and analysis. I wondered if the authors have done that analysis, which compares the difference from the average at each point of the measurement range. That is the standard method for evaluating a new measurement.

Dr Berner: I would like to thank all of the discussants for their comments and start with Dr Stain’s questions. He asked if we believe that the venous HCO3 is preferable to lactate. The study was designed to answer a different question, so I can’t answer for our own observations. We are not suggesting that the HCO3 is a substitute for the lactate level. Rather, we may use a lactate to figure out the etiology of a patient's acidosis.

It is correct that all the patients in the current study were in the ICU. However, our conclusions may be helpful elsewhere. When you see a patient in the emergency department and somebody has already obtained a venous HCO3 that is low, by using the correlations we have reported, you can use the HCO3 to estimate the BD. There was also a question about how often we had patients in the surgical ICU who did not get arterial blood gas done at almost the same time as the venous bicarbonates were obtained. In our study only about 10% of the HCO3 values were not temporally paired with arterial blood gases. That is not a large part of the time, but it often comes at the beginning of the ICU stay, a time when resuscitation for hypoperfusion is essential.

Dr Stain also asked if we believe that the reported correlation would be likely to hold up in injured patients. Our guess...
is that it would. That is because trauma patients are a more homogeneous group of patients with fewer comorbidities and their major problem is often blood loss.

In regard to the logistic regression analysis that you suggested, we did not do that. We felt that there had been enough studies showing that the BD correlated well with mortality and other outcome measures.

Just one small point: in the equation for the calculation of blood gases, the arterial HCO$_3$ is actually a calculated value, not a measured number.

Dr Mullins, you asked us where these bloods came from. The arterial blood gases for the BDs that we reported were all arterial, and peripheral venous blood was used for the bicarbonates. We usually resuscitate patients with Ringer lactate, but there is some use of normal saline in the emergency department and on Internal Medicine.

Dr Shabot had a question about why we did not do a Bland-Altman analysis to compare the HCO$_3$ and BD measurements. Our understanding is that a Bland-Altman plot would be most appropriate when comparing 2 tests that are trying to measure or quantify the same thing, for instance, comparing 2 methods of estimating a patient’s cardiac output. It is a test to see how close the paired estimates come to each other. This would not be appropriate in our study, as we are comparing 2 distinctly different clinical measurements with different values and scales. Our statisticians believe that the most appropriate test to determine how well each of these measures functions as a test is an analysis of the receiver operating characteristic curves.

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**Announcement**

The Archives of Surgery will give priority review and early publication to seminal works. This policy will include basic science advancements in surgery and critically performed clinical research.