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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serum chemistry panel (with HCO₃) were included. Labora-
taneously drawn arterial blood gas determination (with BD) and
tients who met the foregoing criteria and had at least 1 simul-
cal and laboratory database of all surgical ICU admissions. Pa-
tients with an ICU stay longer than 24 hours and adequate labo-
Vascular) from January 1, 1996, to January 1, 2004. Only pa-
tials admitted to the surgical ICU by either the Emergency
Care facility and level I trauma center with a 16-bed surgical
ces County Hospital (Los Angeles, Calif) is a large tertiary
rinary, demographic, and outcome data for each patient were en-
te calculation of the Pearson correlation co-
ance analysis was used to develop a predictive equa-
tion for BD. The predictive ability of HCO₃ and 3 conventional
measures (pH, lactate, and anion gap [AG]) of severe meta-
bolic 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 con-
ent 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 pa-
tients had a total of 26,063 sets of simultaneously ob-
tained paired laboratory data, including an arterial blood
gas and serum chemistry panel with serum HCO₃. The
patient demographics are shown in Table 1. The ma-
ority of patients (56%) were admitted to the Emergency
Non-Trauma Surgery Service for major abdomi-
nal 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 labo-atory 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 regres-
sion analysis demonstrated a very strong correlation be-
tween the arterial BD and the simultaneously measured
serum HCO₃ levels. Figure 1 shows the strong linear

### METHODS

This study was designed as a retrospective criterion standard
analysis to compare the use of serum HCO₃ levels with the stand-
ard measure of arterial BD in an ICU population. The Los An-
geles 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) pa-
tients admitted to the surgical ICU by either the Emergency
Non-Trauma Surgery Service or one of the general surgical spe-
cialty services (Thoracic Foregut, Hepatobiliary, Colorectal, or
Vascular) from January 1, 1996, to January 1, 2004. Only pa-
tients with an ICU stay longer than 24 hours and adequate labo-
ratory data for analysis were included.

Patients were identified from a prospectively maintained clini-
cal and laboratory database of all surgical ICU admissions. Pa-
tients who met the foregoing criteria and had at least 1 simulta-
aneously drawn arterial blood gas determination (with BD) and
serum chemistry panel (with HCO₃) were included. Labora-
tory, demographic, and outcome data for each patient were en-
tered 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 cal-
culated and recorded. The correlation between HCO₃ and BD
was assessed by calculation of the Pearson correlation co-
efficient (r) and the coefficient of determination (R²), and lin-
ear regression analysis was used to develop a predictive equa-
tion for BD. The predictive ability of HCO₃ and 3 conventional
measures (pH, lactate, and anion gap [AG]) of severe meta-
bolic acidosis and mortality were examined by calculating the
area under the receiver operating characteristic curve (AUC).

### 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>15.6 ± 8.8</td>
</tr>
<tr>
<td>APACHE II, mean ± SD</td>
<td>21.8 ± 9.7</td>
</tr>
<tr>
<td>ICU LOS, mean ± d, d</td>
<td>5.8 ± 9.8</td>
</tr>
<tr>
<td>Reason for ICU admission, No. (%)</td>
<td>1289 (56)</td>
</tr>
<tr>
<td>Abdominal</td>
<td>420 (18)</td>
</tr>
<tr>
<td>Vascular</td>
<td>218 (10)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>364 (16)</td>
</tr>
<tr>
<td>Other</td>
<td>174 (8)</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II score; ICU, intensive care unit; LOS, length of stay; SAPS II, Simplified Acute Physiology Score II.

### 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>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 ± 3.8</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.

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correlation between the BD and serum HCO3 level drawn at the time of ICU admission, with a correlation coefficient of 0.85 (R²=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 (R²=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 × HCO3).

From this equation, 2 important cutoff points for clinical use would be a serum HCO3 level of 22 mEq/L, which equals 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 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.21,23,36,37 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...
Figure 3. Receiver operating characteristic curves comparing the prediction of intensive care unit mortality by the serum bicarbonate (HCO₃) level and the arterial base deficit (BD).

hypoperfusion, which can result in organ failure or death if not promptly corrected.²⁵⁻²⁷ 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,²⁸ anion gap,²⁹ lactate,³⁰ and mixed venous oxygen saturation,³¹ as well as tissue- or organ-specific measures such as gastric tonometry,³² sublingual capnometry,³³ and transcutaneous oxygen or carbon dioxide monitoring.³⁴ 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 in the surgical ICU.³⁴⁻³⁶ Thus, while the level of serum lactate appears to be a more specific predictor of ICU and hospital mortality,³⁵⁻³⁶ the arterial BD remains a more sensitive measure of the overall degree of metabolic acidosis from all causes.²³ In trauma patients, several series have demonstrated that the admission BD is predictive of hospital mortality and morbidity and that normalization of the BD during the initial resuscitation correlates with improved outcomes.⁶⁻²⁸⁻⁴⁰⁻⁴⁲

The BD has also been used extensively in other medical and surgical ICU populations. In a series of 104 patients with acute pancreatitis, Sanchez-Lozada et al²⁷ reported that the admission arterial BD predicted disease severity with a sensitivity of 71% and mortality with a sensitivity of 100%. Takeuchi et al¹⁰ found that the BD predicted the presence of intestinal gangrene in a series of patients with small-bowel obstruction and that the absolute level of BD correlated with the size of the necrotic segment of bowel. Other series have demonstrated that BD independently predicts perioperative mortality after ruptured abdominal aortic aneurysm repair,⁸ predicts mortality and the development of multiple organ dysfunction after thermal injury,⁹ and correlates with the ICU length of stay after cardiac surgery.⁴¹ In a study of 438 patients undergoing elective noncardiac surgery, Bennett-Guerrero et al²⁵ found that BD independently predicted postoperative complications and increased length of stay (P = .008), whereas standard variables such as heart rate, blood pressure, temperature, and urine output did not. In addition, the BD has been shown to be superior to other conventional measures of acidosis, such as the arterial pH or the serum anion gap.²⁸⁻⁴¹⁻⁴⁴

Our data confirm that nonsurvivors in a surgical ICU population have significant BD elevations, that both the admission and serially obtained BDs are predictive of ICU mortality, and that the BD clearly outperforms other measures such as pH and anion gap.

Although the arterial BD has demonstrated utility for diagnosis, for prognosis, and as a guide to therapy, there are several drawbacks to its use. The main drawbacks involve the need for arterial puncture (single or multiple) or arterial catheterization. In an audit of patients undergoing arterial puncture, 49% recalled pain levels greater than 5 of 10, and 49% were poorly informed regarding the procedure.⁴⁵ Although infrequent, other complications associated with arterial puncture or catheterization can range from minor hematoma formation to devastating ischemia and limb loss.⁷⁻¹⁰ 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.⁴⁶ 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.⁴⁷⁻⁴⁸ 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.³⁸ Eachempati et al¹² 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, R² = 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 $R^2=0.77$ vs 0.83) than those reported by Eachempati et al. 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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Correspondence: Matthew J. Martin, MD, Department of Surgery, Los Angeles County Hospital + USC Medical Center, 1200 N State St, Room 10-750, Los Angeles, CA 90033 (docmartin2@yahoo.com).

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.

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Steven C. Stain, MD, Nashville, Tenn: Dr Martin and his colleagues at USC have presented a series of 2291 nontrauma pa-
tients 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 con-
cluded that venous HCO3 levels reliably predict the presence of significant metabolic acidosis with BDs of greater than 5. Fur-
thermore, 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 arte-
rial 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 mea-
sured values including HCO3, albeit arterial HCO3. While I agree with the basic conclusion of the manuscript that the valu-
es, venous HCO3, and BD, must correlate, I find myself ask-
ing 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 severely reduced HCO3 on a chem-
istry 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 ob-
tained, and many centers now have arterial blood gas analyz-
ers that routinely report lactate with the arterial blood gas re-
sults. 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 be-
lieve that venous HCO3 is preferable to serial lactate determi-
nations to guide their fluid resuscitations? All of the patients in the current study had arterial blood gases obtained, and that inclusion criterion was part of the study design. What propor-
tion 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 really 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 un-
measured 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 be-
 tween 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?

Stain also asked if we believe that the reported correla-
tions 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.