Use of Different Approaches of Acid-Base Derangement to Predict Mortality in Critically Ill Patients

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Background: *There have been controversial data regarding the application of acid-base analysis based on Stewart methodology to predict clinical outcome in different populations.*
Objective: *To compare predictive ability of the physicochemical approach and the traditional bicarbonate approach of acid-base analysis in critically ill patients in relation to 28-days mortality and to evaluate the use of the physico chemical approach determined by the strong ion gap (SIG) in 1) medical compared to surgical critically ill patients; and 2) sepsis compared to non-sepsis patients.*
Material and Method: *This retrospective cohort study included 410 critically ill patients in the adult medical and surgical intensive care units (ICU) at a tertiary care hospital over a 2-year period. For each patient, values derived from the bicarbonate approaches including anion gap (AG), corrected anion gap (cAG) and lactate and those obtained from the physicochemical approach like SIG were simultaneously computed at ICU admission. The comparison of predictive ability between different approaches was assessed by forward stepwise logistic regression and the area under the receiver operating characteristic (aROC) curves.*
Results: *Of the 410 patents enrolled, 205 (50%) were admitted in the medical ICU and 226 patients (55%) were male. Overall 28-day mortality was 44.6% (183/410). The comparison between medical and surgical patients showed no difference in age (59 vs. 64 yr), APACHE II score (21 vs. 20), presence of sepsis (71% vs. 70%) and 28-day mortality (45% vs. 44%). Acid-base disturbance in non-survivors (n = 183) and survivors (n = 227) determined by pH (7.39 $\pm$ 0.04 vs. 7.41 $\pm$ 0.01), serum bicarbonate (16.0 $\pm$ 6.1 vs. 17.9 $\pm$ 7.4) and $PaCO_2$ (32.4 $\pm$ 13.4 vs. 29.4 $\pm$ 8.2) were comparable. However, non-survivors had higher levels of SIG (9.7 $\pm$ 6.2 vs. 6.4 $\pm$ 5.2) and cAG (27.5 $\pm$ 8.8 vs. 20.3 $\pm$ 8.6) than survivors did. According to a ROC curves, the predictive ability to discriminate between survivors and non-survivors of lactate, cAG, AG and SIG are 0.77, 0.72, 0.68 and 0.67, respectively. Correlations between the SIG and values derived from bicarbonate approach are fair. There was no difference in SIG values between surgical and medical patients with the same severity scores. Sepsis patients (n = 291) had significantly higher SIG than non-sepsis patients (n = 129) did (8.81 $\pm$ 6.38 vs. 5.74 $\pm$ 4.14; p = 0.01).*
Conclusion: *Compared to the traditional approach, an alternative Stewart approach does not provide any greater advantage to predict mortality in the studied population. Because of complex calculation, the usefulness of such approach on the routine clinical practice may be limited.*

Keywords: *Strong ion gap, Prognostic factor, Acid-base disturbance, ICU, Anion gap, Lactate*

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The critically ill patients usually have complex acid-base status derangement, for which the accurate diagnosis is needed for proper management. Formerly, a bicarbonate-based approach was the dominant method used for both diagnosis and treatment. This traditional approach to acid-base status allows explanation and quantification of many disorders of acid-base physiology and is still widely used in clinical practice. However, this approach has been criticized by some as[1] qualitative and not quantitative in nature (1) and (2) incapable of detecting important diagnosis and the complex metabolic disorders, such as those presented in critically ill patients[2-4]. Peter Stewart proposed a different approach to acid-base physiology based upon physicochemical principles[5]. This theory was then modified by Figge including the principals of electroneutrality and the conservation of mass, leading to development of a "new" approach to the diagnosis

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and management of acid-base status derangement[6,7]. These techniques are posited as being more sensitive indicators of metabolic disturbance by estimating unmeasured anion concentrations thus encompassing the contribution of the respiratory status ($PaCO_2$), electrolytes and serum albumin abnormalities to the acid-base imbalance. Measures of metabolic disturbance on admission to the intensive care unit have in the past been used to predict patient outcomes[8]. However, there have been some conflicting results regarding whether strong ion gap (SIG), the representative of the physicochemical approach, provide more accuracy in predicting outcome in critically ill patients than the bicarbonate-based approach derivatives, such as corrected anion gap[9]. The disagreement of results from various studies may be caused by both the complexity and the severity of critical care conditions and the difference in studied populations such as surgical or medical patients as well as sepsis and non-sepsis patients[10-13]. The objective of the present study is to compare discriminative ability of physicochemical approach and traditional bicarbonate approach of acid-base status analysis in critically ill patients to predict 28-d mortality. Indeed, we aim to compare the use of the physicochemical approach determined by SIG between patients in medical and surgical intensive care units (ICUs) as well as in sepsis and non-sepsis patients.

Material and Method

This observational study took place in an academic hospital, with separated medical and surgical adult ICUs. After the approval of the local Research and Ethics Committee, the data from 410 consecutive patients admitted during the period of June 2008 to December 2010 were collected retrospectively. Acute Physiology And Chronic Health Evaluation II (APACHE II) was calculated by using the most deranged physiological value within the first 24-hour of ICU admission[14]. Data collection included blood gas analysis, serum electrolytes and albumin measured on a simultaneous blood sample on admission to the intensive care unit. Blood gas analysis was performed using the GEM Premier 3000™ blood gas analyser (GEM®, Life medical equipment, USA) to measure pH and $PaCO_2$. The analyzer underwent daily calibration and quality control checks. Blood was analyzed for Na^+, K^+, Ca^{++}, Cl^-, HCO_3^-, Mg^{++}, PO_4- using ion-selective electrolyte methods. Whereas albumin and lactate were analyzed by the Modular P800 analyser (Hitachi Ltd, Diamond Diagnostic, USA), the anion gap (AG) was calculated using the standard formula and corrected to compensate for abnormal albumin concentrations (corrected anion gap, corrected AG)[15,16]. The strong ion gap (SIG) was computed by subtracting the effective strong ion difference (SID_{eff}) from the apparent strong ion difference (SID_{app}) using previously described equations[6,7]. An AG of greater than 12 mmol/l was considered elevated. A SIG of more than zero represented the presence of unmeasured anions and was considered abnormal. Baseline characteristics, diagnosis and 28-day mortality of the patients were reviewed from the ICU databases.

Statistical analysis

The data was collected and statistical analysis was evaluated with the SPSS version 15.0 (SPSS, Inc, Chicago, Ill). Data are presented as absolute values, percentages, mean and standard deviations (mean $\pm$ SD) or medium and interquartile range (IQR) according to the distribution of the data. A p-value of less than 0.05 was considered significant. Continuous variables were analyzed with the Student's t-test or Mann-Whitney U test method depending on distribution of data. Categorical variables were analyzed with Chi-square test. The acid-base variables derived from the physicochemical approach and the traditional bicarbonate approach which showed significant difference between survivors and non-survivors by univariate analysis were further tested using simple logistic regression analysis. The discriminating ability of various acid-base variables as well as that of the general scoring system (APACHE II) to predict 28-days mortality were assessed by the area under the receiver operator characteristic (aROC) curve. AUC-ROC values were compared according to the method of Hanley and McNeil. An AUC-ROC value of 0.97 to 1.0 indicated excellent, 0.87 to 0.96 indicated very good, 0.76 to 0.87 indicated good and 0.50 to 0.75 indicated no clinical useful value[17]. Correlations between the traditional acid-base approach and the physicochemical approach were assessed by Spearman's and intraclass correlations.

Results

Four hundred and ten patients were enrolled in the present study; 226 were male and 194 patients were female. Half of cases admitted in the medical ICU and the remaining admitted in the surgical ICU. The demographic data according to the ICU type are presented in Table 1. There were no statistically significant differences in baseline characteristics, degree of

severity of illness, co-morbidities and 28 –d mortality between medical and surgical ICU patients. Mean APACHE II scores at ICU admission were 21.2 ± 8.3 and 20.9 ± 8.4 in medical and surgical patients, respectively (p = 0.75). The observed 28-d mortality was 44.6% among all patients; 44.9% in medical ICU patients and 44.4% in surgical ICU patients (p = 0.92). Concurrently, they also had a comparative degree of acid-base disturbance as determined by both the physicochemical (SIG, SIDeff) and the traditional approaches (AG, corrected AG) (Table 2).

Patients were grouped into survivors and non-survivors according to in-hospital survival truncated to 28 days (Table 3). Both non-survivors (n = 183) and survivors (n = 227) were similar with respect to age (62.0 ± 1.3 vs. 61.9 ± 1.1 years). Measured variables, namely albumin (2.4 ± 0.6 vs. 2.5 ± 0.7 gm/dL), pH (7.39 ± 0.04 vs. 7.41 ± 0.01), bicarbonate (16.0 ± 6.1 vs. 17.9 ± 7.5 mmol/l) and $PaCO_2$ (32.4 ± 13.5 vs. 29.5 ± 8.3 mmHg) were not different in non-survivor and survivor, respectively. Both variables derived from the physicochemical approach including SID_{app} (36.6 ± 5.4 vs. 38.5 ± 5.8 mEq/l), SID_{eff} (28.5 ± 7.1 vs. 32.3 ± 8.4 mEq/l) and SIG (9.8 ± 6.3 vs. 6.4 ± 5.3 mEq/l); and values obtained from the bicarbonate approach, namely, corrected AG (27.5 ± 8.9 vs. 20.4 ± 8.7 mmol/l) were all significantly different between non-survivors and survivors. As expected, the mean SIG in sepsis patients was significantly higher than that in non-sepsis patients (8.8 ± 6.4 vs. 5.7 ± 4.1 mEq/l, respectively: p = 0.01).

In order to compare predictive value between the traditional acid-base approach and the physicochemical approach, the authors found that both approaches showed different discrimination for the

Table 1. Demographic Data of the studied population

Data	Total (n = 410)	Medical ICU (n = 205)	Surgical ICU (n = 205)	p-value
Sex: Male, n (%)	116 (52.7)	115 (56.1)	101 (49.3)	0.16
Ages (Year)	61.9 ± 17.0	59.5 ± 17.6	64.2 ± 16.3	0.19
APACHE II	21.0 ± 8.4	21.2 ± 8.3	20.9 ± 8.4	0.75
Sepsis, n (%)	291 (71.0)	146 (71.2)	145 (70.7)	0.91
AKI, n (%)	257 (62.7)	132 (64.4)	125 (61.0)	0.12
DM, n (%)	121 (29.5)	61 (29.8)	60 (29.3)	0.16
CKD, n (%)	69 (16.8)	33 (16.1)	36 (17.6)	0.16
Hypoalbuminemia, n (%)	291 (71.0)	146 (71.2)	145 (70.7)	0.91
28-d Mortality, n (%)	183 (44.6)	92 (44.9)	91 (44.4)	0.92

Values are expressed as number (percentages) and mean ± standard deviation (SD)
ICU, intensive care unit; APACHE II, acute physiology and chronic health evaluation II; AKI, acute kidney injury; DM, Diabetes mellitus; CKD, Chronic Kidney Disease

Table 2. Different acid-base variables according to type of patients

Variable	Medical ICU (n = 205)	Surgical ICU (n = 205)	p-value
APACHE II	21.2 ± 8.4	20.9 ± 8.5	0.75
Bicarbonate (mmol/l)	18.8 ± 5.7	18.8 ± 5.5	0.87
Lactate (mmol/l)	4.2 (3.8, 4.8)	4.1 (3.6, 4.7)	0.86
AG (mmol/l)	20.6 ± 7.9	20.3 ± 7.8	0.69
Corrected AG (mmol/l)	23.9 ± 8.1	23.6 ± 8.1	0.70
SIG (mEq/l)	8.0 ± 6.1	7.8 ± 5.9	0.68
SIDe (mEq/l)	30.3 ± 7.3	30.3 ± 7.2	0.99

Normally distributed values are expressed as mean ± standard deviation (SD), and non-normally distributed values are expressed as median and interquartile range (IQR)
ICU, intensive care unit; APACHE II, acute physiology and chronic health evaluation II; AG, anion gap; SIG, strong ion gap; SIDe, effective strong ion difference

prediction of 28-d mortality as evaluated by the area under the ROC curves. Lactate had the best discriminative accuracy for mortality (aROC: 0.77, 95% CI 0.72 to 0.82), followed by corrected AG (aROC: 0.72, 95% CI 0.67 to 0.77) and AG (aROC: 0.68, 95% CI 0.63 to 0.74); while SIG had the worst discrimination value (aROC: 0.67, 95% CI 0.62 to 0.73) (Fig. 1, Table 4).

The authors found that there were only poor to fair correlations between the SIG, which derived from the physicochemical approach and values derived from the traditional approach (Table 5). Among them, the SIG and the cAG showed the best correlation (r = 0.72). There was no difference when comparing SIG between surgical and medical patients with the same severity of illness (APACHE II). In Sepsis patients the SIG were significantly higher than that of non-sepsis patients (8.8 ± 6.4 vs. 5.7 ± 4.1 mEq/l; p = 0.01).

Discussion

Bicarbonate center approach of acid-base disturbances in critically ill patients is commonly used in clinical practice. It is, however, recognized that this technique could not identify the complex metabolic disturbances seen in the critically ill patients[6-8]. The variable of bicarbonate-based approach, the anion gap (AG), is influenced by the abnormalities of plasma albumin, plasma sodium, and plasma chloride which are nearly ubiquitous in critically ill patients. Assessment of 'unmeasured anions', using the principles described by Stewart, may overcome these problems. Better identification of the metabolic derangement and improved understanding of the

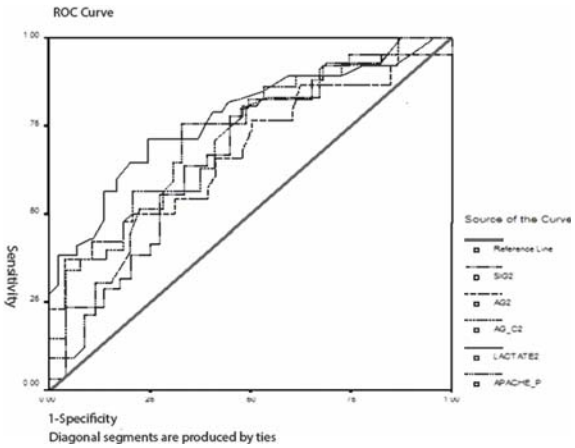

Fig. 1 Predictive ability of different approaches

Table 3. Measured and calculated admission parameters presented according to 28-d mortality

Parameters	Survivors (n = 227)	Non-survivors (n = 183)	p-value
APACHE II	18.4 ± 7.9	24.3 ± 7.8	0.01*
pH	7.41 ± 0.01	7.39 ± 0.04	0.42
Albumin (g/dl)	2.5 ± 0.7	2.4 ± 0.6	0.15
Bicarbonate (mmol/l)	17.9 ± 7.5	16.0 ± 6.1	0.92
Lactate (mmol/l)	3.9 ± 2.4	6.1 ± 3.9	0.02*
Corrected anion gap (mmol/l)	20.3 ± 8.6	27.5 ± 8.8	0.008*
Strong ion gap (mEq/l)	6.4 ± 5.2	9.7 ± 6.2	0.01*

Normally distributed values are expressed as mean ± standard deviation (SD), and non-normally distributed values are expressed as median and interquartile range (IQR)

Table 4. Discriminative ability of different variables to predict 28-d mortality

Variable	aROC curve	95% CI	p-value
APACHE II	0.70	0.65-0.75	< 0.01
Bicarbonate	0.42	0.36-0.47	0.04
Lactate	0.77	0.72-0.82	< 0.01
Anion Gap	0.68	0.63-0.74	< 0.01
Corrected Anion Gap	0.72	0.67-0.77	< 0.01
Strong Ion Gap	0.67	0.62-0.73	< 0.01

aROC, area under the receiver operating characteristic; 95%CI, 95% confidence interval

Table 5. Correlation (r) between physicochemical and bicarbonate approaches

Variable	r
Anion gap & Strong Ion Gap	0.64
Corrected Anion Gap & Strong Ion Gap	0.72
Lactate &Strong Ion Gap	0.19

r, Spearman's correlation coefficient (0-0.25, little correla tion; 0.26-0.50, fair correlation; 0.51-0.75, moderate correla tion; 0.76-1.00, very good correlation)

underlying pathophysiology may lead to more appropriately directed therapy. However, the advantages of this physicochemical approach over the traditional bicarbonate approach remain controversial even after it has been applied in clinical practice[12,18]. In addition, recent studies have shown the inconsistent results regarding the discriminative ability to predict mortality in critically ill patients through use of the Stewart approach when compared to the traditional approach[19-23].

The authors results demonstrated that medical and surgical patients were comparable in acid-base status determined by the SIG, the unmeasured anion calculated by the Swart method, as well as by the AG, the unmeasured anion computed by the traditional method. The explanation may be that both groups had equivalent severity of illness as shown by similar APACHE II scores. This can be elucidated further by noting that, the sicker patients, such as patients with sepsis, and non-surviving patients also had higher SIG, corrected AG, and lactate levels than patients without sepsis, and so did survivors (Table 3). However, the other acid-base variables, such as bicarbonate and pH in both survivors and non-survivors were not statistically different.

Concerning whether SIG or other traditional values such as lactate, AG, and cAG should be utilized to predict clinical outcome, we found that plasma lactate concentration is the best choice to discriminate between survivors and non-survivors at 28 day in our studied population (aROC:0.77) followed by cAG, AG and SIG (aROC 0.72, 0.68, and 0.67, respectively). These are comparable with previous studies by Cusack et al[19] and Noritomi et al[20], where the predictive ability of bicarbonate approach derivatives such as anion gap, and corrected anion gap or lactate were better than SIG. Similar to ours, they enrolled mixed critically ill patients with a higher degree of disease severity (APACHE II 23-25) and a high number of multiple organ failures, especially acute kidney injury and sepsis. In contrast, the predictive ability of SIG was preferred in the studies which included only surgical or traumatic patients with lesser severity scores (APACHE II 19)[21] and a lower mortality rate[22]. This observation may be explained by the fundamental basis of this physicochemical approach. According to the Stewart formula, the SIG level is dynamic and can be modified by many treatment processes such as changes in ventilator setting leading to altered $PaCO_2$. Other input data of the formulation including pH, electrolytes, and albumin can be also varied by different types and amounts of intravenous fluid administration or by an organ supportive therapy such as renal replacement therapy. As a result, the greater complexity of the treatment offered the patient with higher severity of illness may lead to the greater inaccuracy of this complicated physicochemical approach to predict clinical outcome.

In fact, a variable with an aROC of 0.8 or more is needed for the favorable discriminative ability to predict clinical outcome. In the present study, the APACHE II score provided an aROC curve of 0.70. This is consistent with the previously published results[24], but suggests that even this complex score does not discriminate well between survivors and non-survivors in a different population from that of the original paper[14]. As demonstrated by a previous study[19], the corrected anion gap by the change of albumin (cAG) had more predictive ability than the standard AG calculation in our population. The authors would argue that plasma lactate is the feasible method and provides more accuracy to predict 28-d mortality in severely ill and complex patients than SIG. In case of unavailability of the lactate test, the cAG may be utilized instead. However, both lactate and cAG still had less discriminative ability than the accepted aROC value of 0.8, and should not be used solely as a prognostic marker.

Many studies have found that lactate is a good early predictor of morbidity and mortality in both traumatic patients[25,26] and patients with septic shock[27,28]. However, the predictive ability has been questioned in patients without shock. The response of circulating lactate to resuscitation may improve the discrimination between survivors and non-survivors. The use of sequential measurements of lactate with both peak measurements and ability to clear lactate in response to treatment are more reasonable both for predicting patients' prognosis and for guiding shock resuscitation[29].It is possible that sequential SIG measurements may be more informative than individual measurements.

There are a number of potential reasons for the poor discriminative ability of SIG in this study. Firstly, by compensating for abnormalities in electrolytes and albumin and taking lactate out of the equation (if lactate is less than 2 meq/L), the abnormalities associated with an adverse outcome may be being removed leading to reducing the predictive power of the SIG. Second, the type of fluids used for resuscitation may have an iatrogenic effect on the SIG as previously described in both healthy volunteers and surgical patients[30]. The acidosis seen in our patients was accounted partly by hyperchloremia secondary to infusions of chloride-rich solution. It became apparent during the course of the present study that fluid regimes at our institution-that is, the use of isotonic saline or modified gelatin with its high anion content-may be influencing the SIG. In addition, hetastarch infusion in healthy volunteers results in the change consistent with metabolic acidosis[31]. If part of the acidosis seen in our patients was iatrogenic due to chloride-rich solutions or starch, the effect would be increase in SIG and therefore erroneously indicate a pathological acid-base disturbance with assumed associated adverse effect on outcome. As such, less ill patients are labeled as more severely ill due in part to changes from resuscitation fluids given and hence the prognostic value of these indices is lost.

There are a number of limitations in the present study. The population was relatively small and reflective of a single tertiary care medical center. Importantly, since the authors did not collect the details of fluid administration, the authors were unable to make adjustments according to the quantity and type of intravenous fluid that our patients received. A larger study which includes the accurate records of type and quantity of intravenous fluids administered to patients prior to ICU admission, as well as the sequential measurements of SIG, is needed to determine the usefulness of assessing unmeasured anions using Stewart's principles.

Conclusion

Compared to the traditional approach, an alternative Stewart approach would not provide greater advantage in the ability to predict mortality in the studied population. Because of required complex calculations, the usefulness of such approach in bedside clinical practice may be limited.

Potential conflicts of interest

None.

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การใช้ค่า Strong ion gap เพื่อทำนายอัตราตายในผู้ป่วยวิกฤตที่เข้ารับการรักษาในหออภิบาล

รณิษฐา รัตนะรัต , ชัยอนันต์ โสดาภักดิ์, เอกรินทร์ ภูมิพิเชฐ, ปฏิภาณ ตุ่มทอง

ภูมิหลัง: *เนื่องจากยังมีข้อขัดแย้งในการประยุกต์ใช้การประเมินสภาพกรดด่างในผู้ป่วยวิกฤตโดยใช้หลักการของ Stewart ในการทำนายผลลัพธ์ทางคลินิกในกลุ่มผู้ป่วยวิกฤตกลุ่มต่างๆ*

วัตถุประสงค์: *เพื่อเปรียบเทียบความสามารถในการจำแนกผู้ป่วยวิกฤตที่รอดชีวิตที่ 28 วันหลังผู้ป่วยรักษาในหออภิบาล โดยใช้ตัวแปรที่ได้จากการวิเคราะห์สภาพกรดด่างในร่างกายของผู้ป่วยแบบ Physicochemical approach เปรียบเทียบกับ Bicarbonate approach และเพื่อประเมินความแตกต่างของค่า strong ion gap (SIG) ในกลุ่มผู้ป่วยหนักอายุรกรรมเปรียบเทียบกับผู้ป่วยหนักศัลยกรรม รวมถึงในกลุ่มผู้ป่วยที่มีหรือไม่มีภาวะsepsis*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังในผู้ป่วย 410 รายจากหออภิบาลผู้ป่วยหนักทั้งอายุรกรรมและศัลยกรรมในโรงพยาบาลระดับตติยภูมิ ประเมินสภาพกรดด่างของผู้ป่วยเมื่อแรกรับทั้ง Bicarbonate approach ซึ่งใช้ค่าตัวแปรคือ anion gap (AG),corrected anion gap (cAG) และ lactate และประเมินสภาพกรดด่างแบบ Physicochemical approach โดยใช้ strong ion gap (SIG) จากนั้นนำค่าตัวแปรจากการประเมินทั้งสองวิธีดังกล่าวมาเปรียบเทียบความสามารถในการทำนายอัตราตายที่ 28 วันโดยเปรียบเทียบจากพื้นที่ใต้กราฟ receiver operating characteristic (aROC)*

ผลการศึกษา: *จากผู้ป่วยจำนวน 410 รายที่ทำการศึกษา เป็นผู้ป่วยหนักอายุรกรรม 205 ราย (50%) เป็นผู้ชาย 226 ราย (55%) อัตราตาย 44.6% พบว่าผู้ป่วยหนักอายุรกรรมและศัลยกรรมไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติใน อายุเฉลี่ย (59 ± 18 ปี และ 64 ±16 ปี ตามลำดับ), APACHE II score (21.2 ± 8.3 และ 20.9 ± 8.4 ตามลำดับ), การมีภาวะsepsis (70 vs. 71%) รวมถึงอัตราตาย (45%vs44%) เปรียบเทียบสภาวะกรดด่างในผู้ป่วยที่เสียชีวิตและผู้ป่วยที่รอดชีวิต แสดงโดย pH (7.39±0.04 vs. 7.41±0.01), serum bicarbonate (16.0 ± 6.1 vs. 17.9 ±7.4), และ $PaCO_2$ (32.4 ± 13.4 vs. 29.4 ± 8.2) พบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ผู้ป่วยที่เสียชีวิตจะมี SIG และ cAG สูงกว่าผู้ป่วยที่รอดชีวิตอย่างมีนัยสำคัญทางสถิติ (SIG: 9. 7 ± 6.2 vs. 6.4 ± 5.2, cAG 27.5 ± 8.8 vs. 20.3 ± 8.6 ตามลำดับ) พื้นที่ใต้กราฟ aROC curve ของ lactate, cAG, AG และ SIG มีค่า 0.77, 0.72, 0.68 และ 0.67 ตามลำดับ ความสัมพันธ์ (correlation) ระหว่างค่า SIG และค่าตัวแปรกลุ่ม cAG มีความสัมพันธ์กันปานกลาง ในผู้ป่วยอายุรกรรมหรือศัลยกรรมที่มี APACHE II score เท่ากันไม่พบความแตกต่างกันของค่า SIG สำหรับผู้ป่วยที่มีภาวะ sepsis จะมีค่า SIG ที่สูงกว่าผู้ป่วยที่ไม่มีภาวะ sepsis อย่างมีนัยสำคัญทางสถิติ (8.81 ± 6.38 vs. 5.74 ± 4.14; p = 0.01)*

สรุป: *ตัวแปรที่ได้จากการประเมินสภาพกรดด่างโดยอาศัยหลักการของ Stewart ไม่สามารถทำนายอัตราตายในผู้ป่วยที่ทำการศึกษาได้ดีกว่าการประเมินสภาพกรดด่างแบบเดิม และเนื่องจากความซับซ้อนในการคำนวณค่าดังกล่าว การนำมาใช้ในเวชปฏิบัติยังมีข้อจำกัด*