Evaluating Stewart's Approach to Acid-Base Disorders in Predicting Patient Outcomes in Emergency and Intensive Care Units

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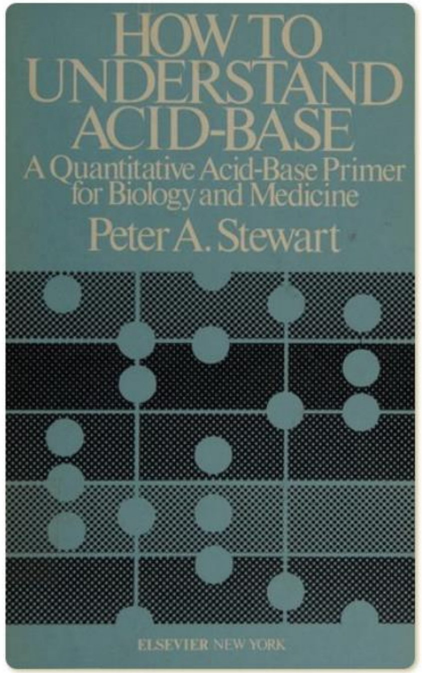
Acid-Base Disorders in Critically Ill Patients

- Acid-base disorders are common in critically ill patients and significantly affect clinical outcomes.
- Traditionally, the diagnosis of acid-base disorders has relied on the Henderson-Hasselbalch equation: $[H^+] = 24 \times PCO_2 / [HCO_3^-]$.
- While PCO_2 is typically regarded as a reliable indicator of the respiratory component, HCO_3^- may not always accurately reflect the metabolic component.

Limitations of the Conventional Acid-Base Approach

- The serum HCO_3^- concentration is influenced by changes in PCO_2, as both are part of the same buffer system.
- Acid-base assessments based on the Henderson-Hasselbalch equation may overlook the contributions of non-bicarbonate buffers and electrolytes in maintaining acid-base balance.
- While base excess (BE) and the anion gap are vital tools in the conventional approach to acid-base disorders, they often fall short in identifying the underlying causes.
- To overcome these limitations, the Stewart approach offers a more comprehensive perspective on the physiochemical mechanisms behind acid-base imbalances.

The Stewart Approach: Introducing an Alternative Approach to Acid-Base Disorders



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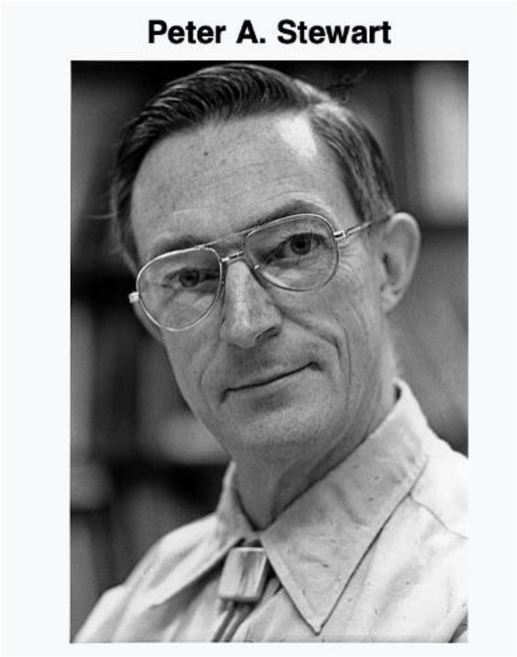


1921-1993

Stewart's original approach failed to gain popularity due to its complex equations, which made it difficult to apply in bedside settings. However, over the past three decades, researchers have introduced modifications that have simplified the approach, making it more practical for bedside application.

Alternative Definition of Acid and Base

Traditional definition of acid and base

Acids are H^+ donors ($AH \rightarrow H^+ + A^-$) and bases are H+ acceptors ($H^+ + A^- \rightarrow AH$).

Stewart's definition of acid and base

An acid solution is one in which concentration of [H+] exceed that of [OH-] whereas a basic solution is one in which [OH-] is higher than [H+].	$[H+] + [OH-] \leftrightarrow [H20]$ $K = \frac{[H+]\,[OH-]}{[H2O]}$ **K = [H+] [OH-]**

{[Na+]+[K+]+[Ca2+] + [Mg2+]} > {[Cl−]+[Lactate−]}

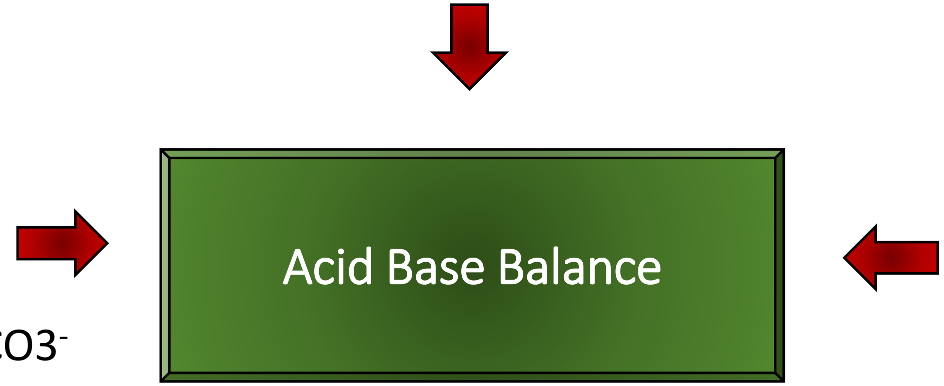
Strong Cations > Strong Anions

[H+] <[OH-]

Three Independent Variables of Acid-Base Balance based on Stewart's Approach

$\{[Na^{+}]+[K^{+}]+[Ca2^{+}]+[Mg2^{+}]\}-\{[Cl^{-}]+[Lactate^{-}]\}$

Strong Ion Difference: SID



PCO2

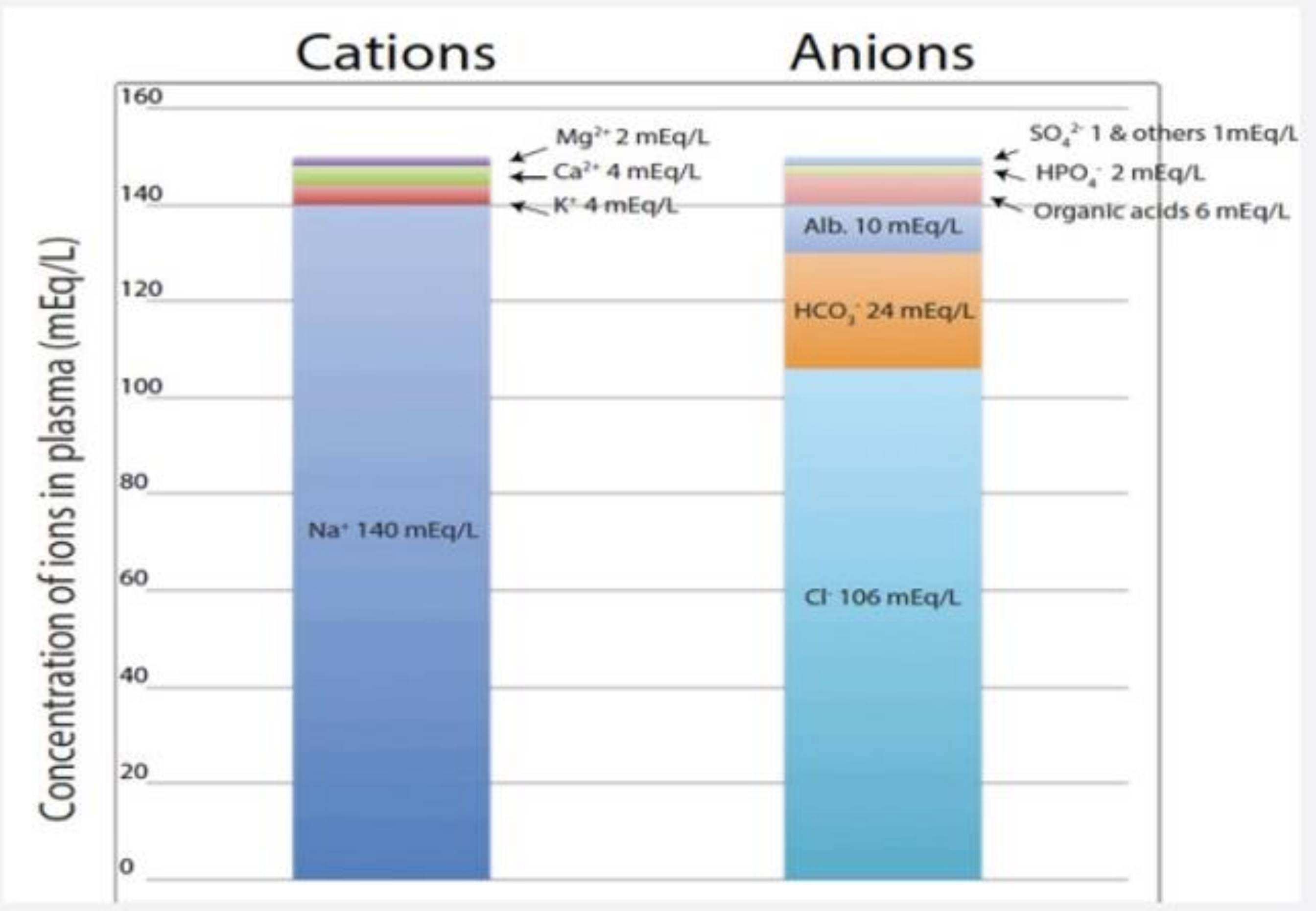
$H20 + CO2 \longleftrightarrow H^{+} + HCO3^{-}$

Atot: Total Anions

$AH \longleftrightarrow H^{+} + A^{-}$

(mostly phosphate and albumin)

Electroneutrality: The Equal Concentration of Anions and Cations



Berend K1, and Lundquist A L. J Anest & Inten Care Med 2017; 3(1):

Calculation of Strong Ion Difference and Strong Ion Gap

The Apparent Strong Ion Difference: SIDa

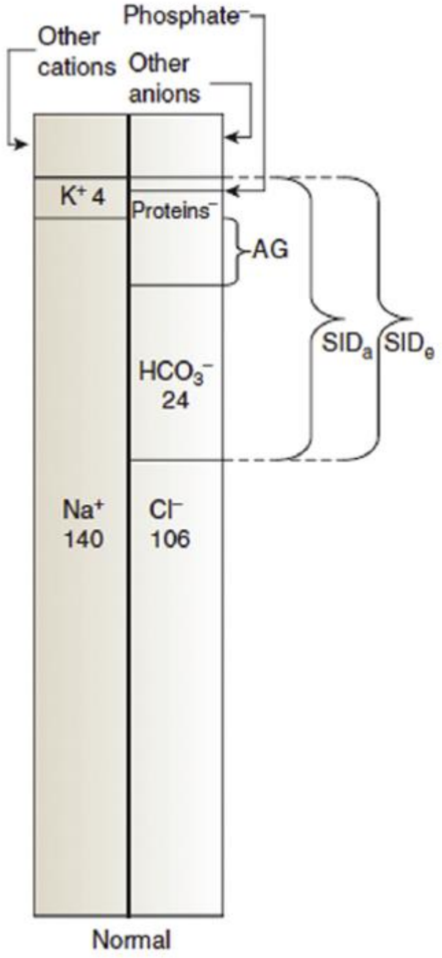
$$SIDa=[Na+]+[K+]+[Ca2+]+[Mg2+]-[Cl-]-[Lactate-]$$

The Effective Strong Ion Difference : SIDe

$$SIDe = 2.46\times10^{(pH-8)}\times PCO2+[Albumin\ (g/L)]\times(0.12\times pH-0.631)$$
$$+[Phosphate\ (mmol/L)]\times(0.309\times pH-0.469)$$

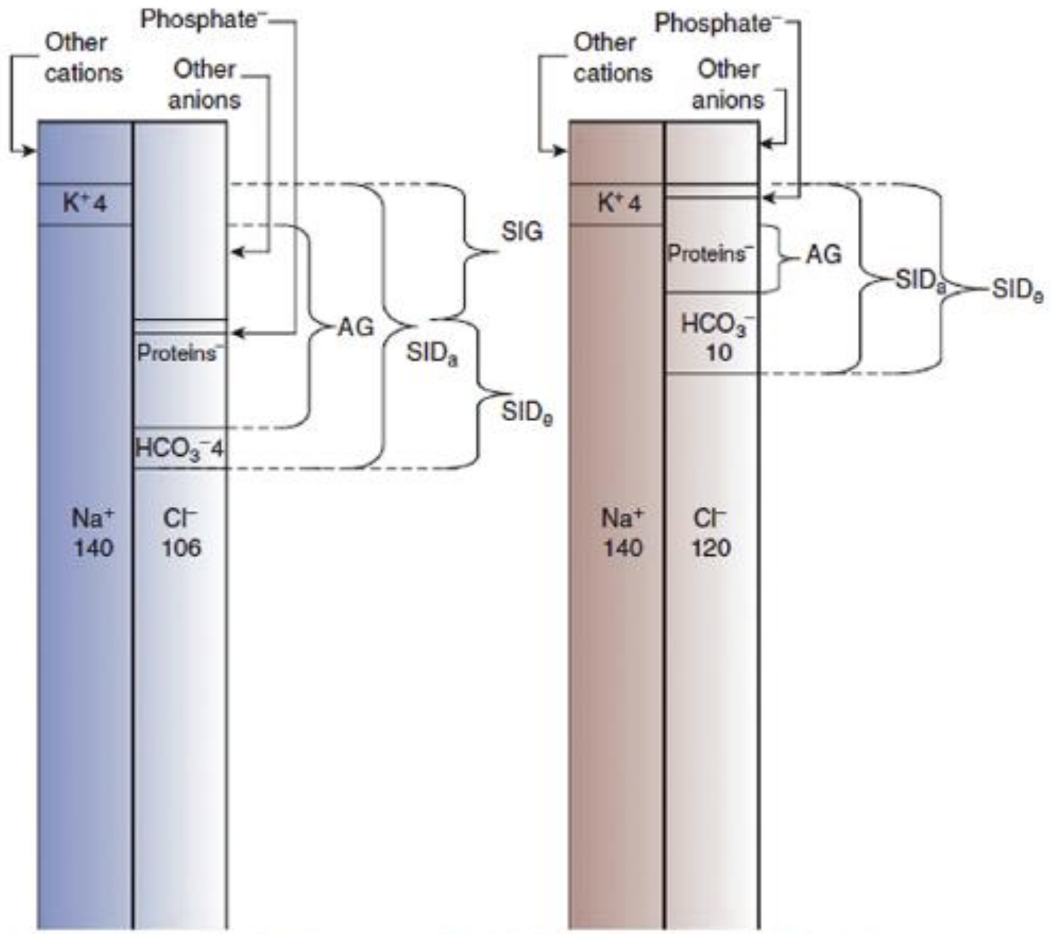
Strong Ion Gap: SIG

SIG= SIDa-SIDe (zero in normal condition)



Adrogue HJ., et al´ Am J Kidney Dis. 2016;68(5):793-802

SIG Acidosis/High Anion gap Acidosis vs. High SID Acidosis



High AG (normochloremic) metabolic acidosis
or
SIG acidosis

Normal AG (hyperchloremic) metabolic acidosis
or
SID acidosis

Adrogue HJ., et al´ Am J Kidney Dis. 2016;68(5):793-802

Five Types of Acid-Base Disorders Based on the Stewart Approach

- **Low SID Acidosis:** An increase in chloride levels or, less commonly, significant sodium loss
- **High SID Alkalosis:** A decrease in chloride or an increase in sodium
- **Acidosis from Increased Weak Acids:** Accumulation of weak acids, such as phosphates
- **Alkalosis from Decreased Weak Acids:** Conditions such as hypoalbuminemia
- **Acidosis from SIG:** Unmeasured anions, such as lactate, ketoacids, fumarate, oxalate, or other ions produced during hypoxia or reduced tissue perfusion

Background

- Despite the potential advantages of the Stewart approach, clinical practice continues to rely heavily on the traditional method.
- Studies investigating the prognostic value of Stewart's (physicochemical) approach for patient outcomes are limited and have produced inconsistent results.
- This prospective cohort study aims to evaluate acid-base disorders in critically ill patients using Stewart's approach and to explore its relevance in predicting mortality in ICU patients.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- All patients admitted to the two emergency departments and five intensive care units of Masih Daneshvari University Hospital in Iran during a three-month period from June 21 to September 22, 2024.

Exclusion Criteria:

- Age under 18 years
- Initial serum creatinine level greater than 2 mg/dL at hospital admission
- History of Kidney replacement therapy during the current hospitalization

Methods

- The clinical data of participants included demographics, reasons for admission, vital signs, clinical findings, lab parameters, final outcomes, date of death or discharge, and length of stay. APACHE II scores were determined at hospital admission.

- Laboratory tests measured pH, HCO_3^-, PCO_2, sodium, potassium, calcium, magnesium, chloride, lactate, albumin, phosphate, and base excess. These values were recorded upon ICU or emergency department admission and tracked weekly until discharge, death, or 28 days in the ICU.

- Following this, the study assessed the effect of Stewart's acid-base parameters on outcomes like mortality, hospital length of stay, and mechanical ventilation duration.

Formulas for Calculating Stewart's Acid-Base Parameters

SIDa$=[Na^+]+[K^+]+[Ca^{2+}]+[Mg^{2+}]-[Cl^-]-[Lactate^-]$

SIDe$=2.46\times10^{(pH-8)}\times PCO_2+[Albumin\ (g/L)]\times(0.123\times pH-0.631)+[Phosphate\ (mmol/L)]\times(0.309\times pH-0.469)$

SIG$=SIDa-SIDe$

Sodium effect $= 0.3 \times ([Na^+] - 140)$

Chloride effect $= 102 - ([Cl^-] \times 140/[Na^+])$

Albumin effect $= 0.25 \times [42 - Albumin\ (g/L)]$

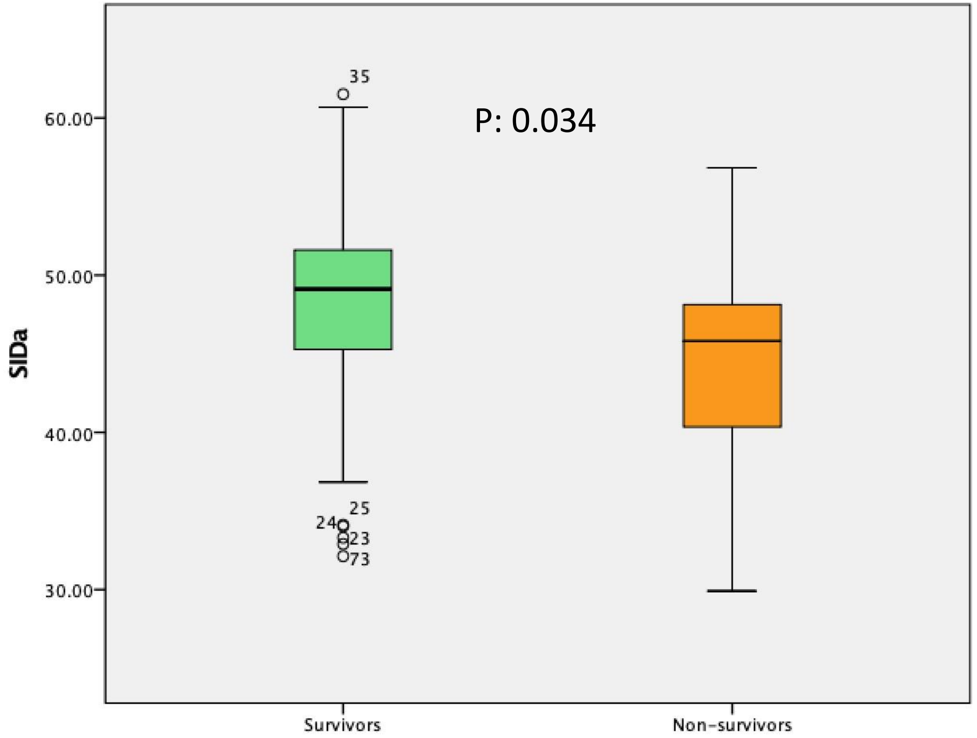
Basic Characteristics of Participants

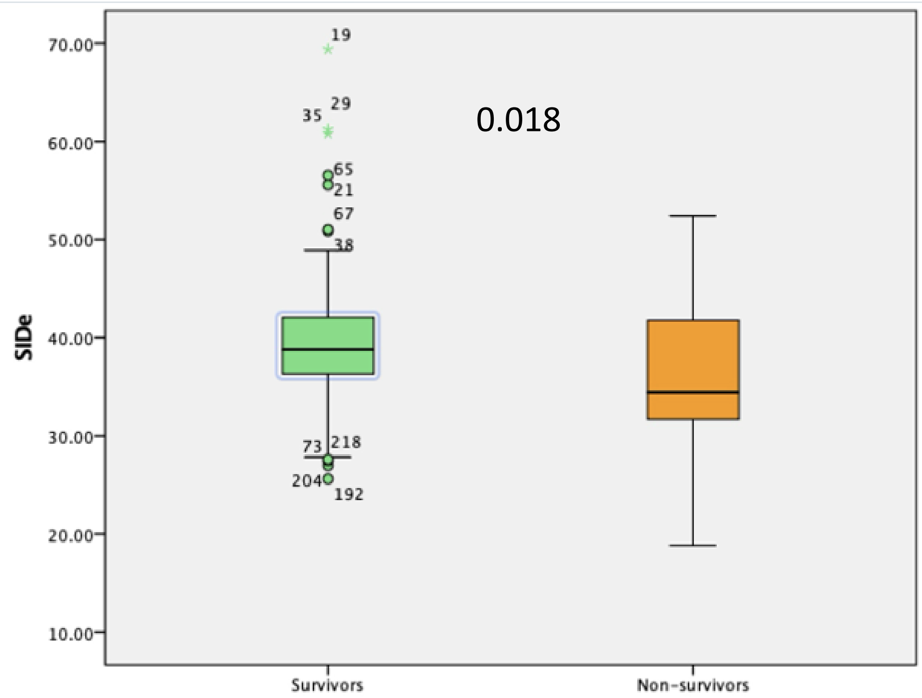
Characteristic	Values in survivors	Values in Non-survivors
Number of patients (Total:219)	178 (81.3%)	21 (9.6%)
Mean age (years)	59.0 ± 15.4	62.6± 14.8
Sex, male	117 (66.1%)	15 (71%)
ICU admissions	32(17.9%)	16 (76.1%)
Hospital admission period (days)	9.5 ± 6.7	9.8 ± 7.2
Most common presenting symptoms		
• Dyspnea	132 (74.1%)	15 (71.4%)
• Cough	56 (31.5%)	7 (33.3%)
• Hemoptysis	26 (14.8%)	1 (4.7%)
• Fever	18 (10.2%)	4 (19%)
• Loss of consciousness	9 (8.2%)	7 (33.3%)
Comorbidities		
• DM	28 (16%)	3(14.3%)
• HTN	61 (34.8%)	7 (33.3%)
• IHD	34 (19.5%)	3 (14.3%)
• Airway disease	50 (28.6%)	4 (19%)

Mortality and Admission Parameters of Stewart’s Approach to Acid-Base Disorders

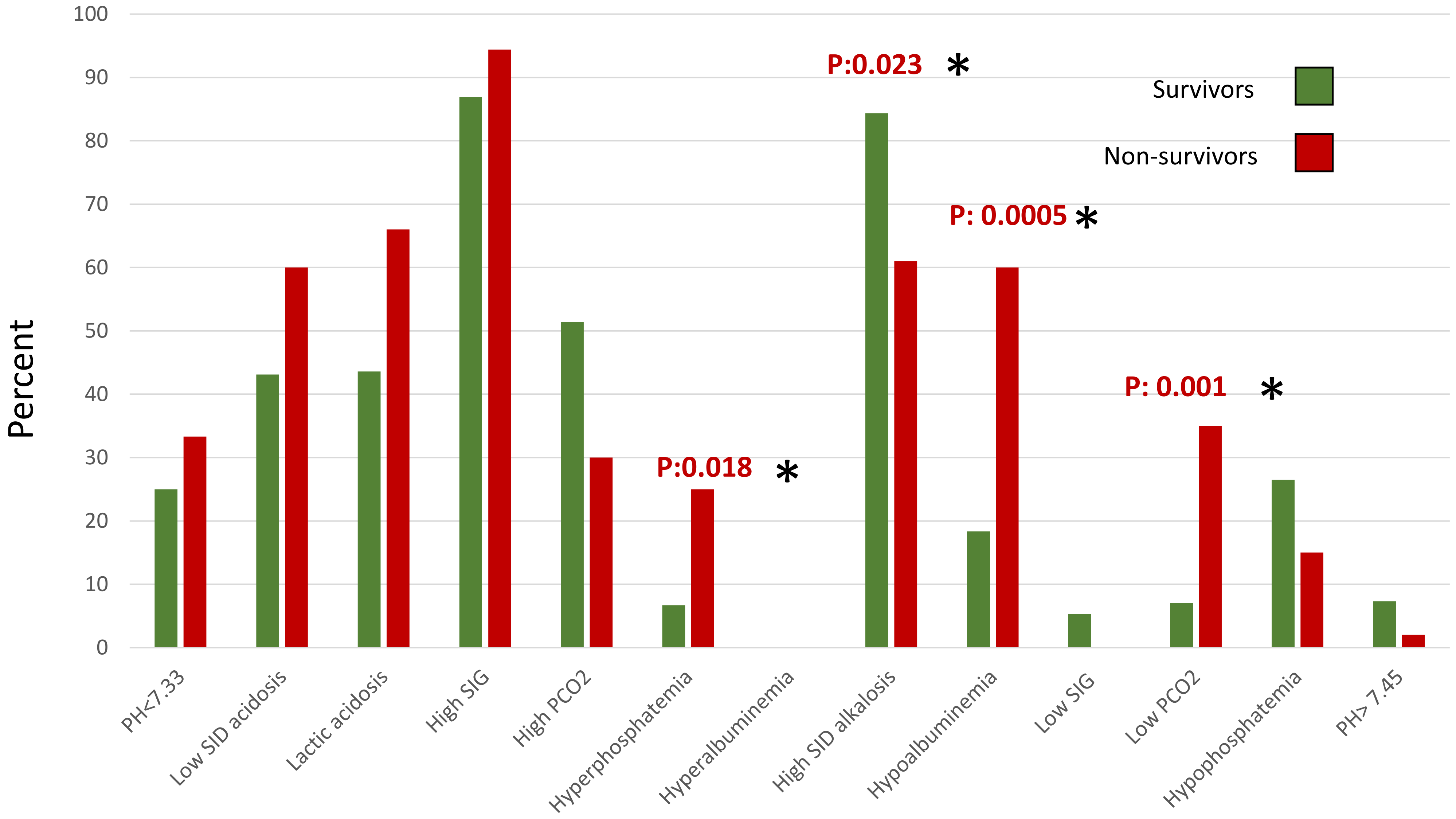
	Survivors N=166	Non- survivors N=20	Mean difference (95% CI)	P value
SIDa (mEq/L)	48.2 ± 5.6	45.1 ± 6.4	3.02 (0.23,5.8)	**0.034**
SIDe (mEq/L)	39.4 ± 5.7	36.0 ± 8.4	3.4 (0.6,6.22)	**0.018**
SIG (mEq/L)	8.7 ± 6.2	9.1 ± 5.9	-0.4 (-3.4,2.6)	0.79
Lactate (mmol/L)	2.2 ± 1.3	3.0 ± 2.2	-0.8 (-2,0.3)	0.13
Phosphate (mmol/L)	1.1 ± 0.3	1.3± 0.5	-0.2 (-0.4, -0.03)	**0.018**
Albumin (g/dL)	3.9 ± 0.6	3.2 ± 0.4	0.6 (0.3, 0.9)	**0.000**
Cl (mEq/L)	100.8 ± 5.8	101.6 ± 6.4	-0.73(-3.52.05)	0.604
Na (mEq/L)	140.4 ± 2.9	139.3 ± 4.8	1.0 (-4.2,2.4)	0.604
Sodium effect (mEq/L)	0.1 ± 0.9	-0.2 ± 1.4	0.3 (-0.4, 1)	0.387
Chloride effect (mEq/L)	1.3 ±5.7	0.5 ± 6.4	0.7 (-2.1, 3.5)	0.613
PH	7.4 ± 0.1	7.4 ± 0.1	-0.01 (-0.06, 0.03)	0.533
PCO2 (mmHg)	48.3 ± 13.2	42.4 ± 16.5	5.9 (-2, 13.9)	0.066
HCO3 (mEq/L)	26.8 ± 5.4	24.8 ± 8.7	2.0 (-2, 6.2)	0.310

Comparison of SID (SIDa and SIDe) Between Survivors and Non-Survivors

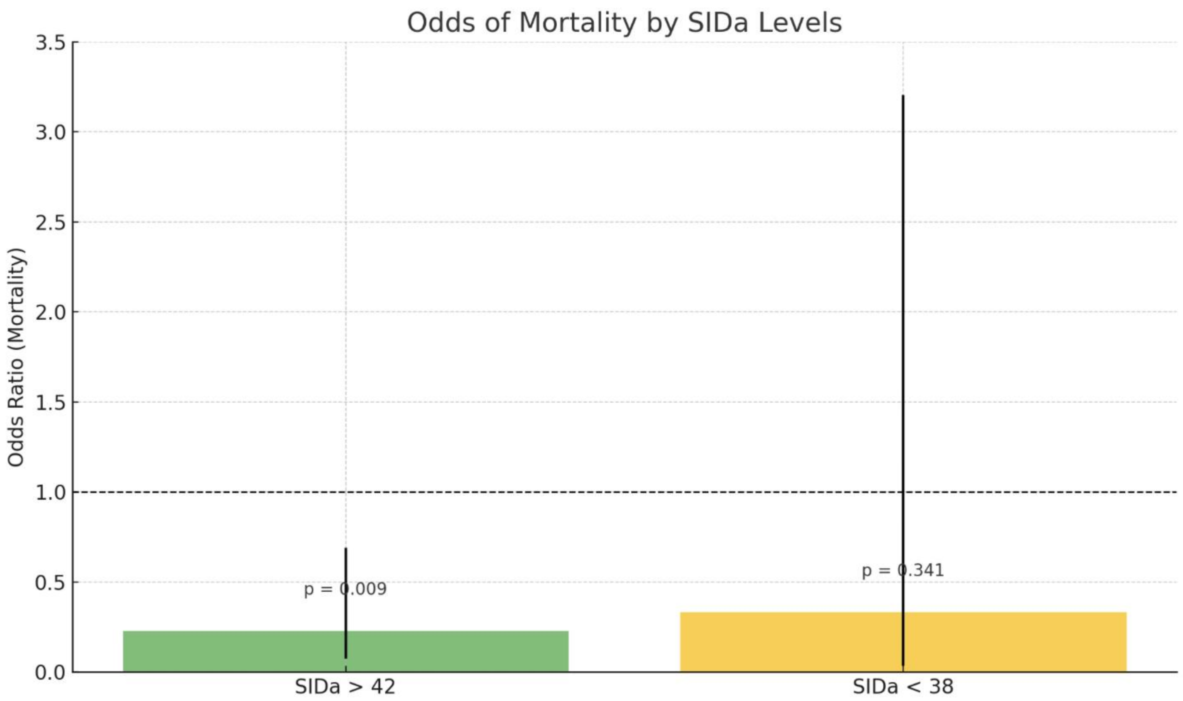




The Incidence of Acid Base Disorders Based on Stewart's Approach



Logistic Regression Analysis of Mortality in Subgroups Based on SIDa Values



Odds of Mortality by SIDa Levels with 95% Confidence Intervals

Group	B	Odd Ratio	95% CI	P value	Interpretation
SIDa >42	-1.099	0.228	-0.075 to 0.690	0.009	71.2% lower odds of mortality (significant)
SIDa(38-42)		1.000			Reference group
SIDa<38	-1.009	0.333	0.035 to 3.205	0.341	No significant effect

Logistic Regression Analysis of Mortality in Subgroups Based on SIDe Values

Group	B	Odd Ratio	95% CI	P value	Interpretation
SIDe <38	-1.099	2.933	0.790 to10.895	0.108	No significant effect
SIDe(38-42)	6.581	1.000			Reference group
SIDe>42	-1.48	2.083	0.472 to 9.200	0.333	No significant effect

Other Findings

We were not able to find any significant correlation between parameters of Stewart's approach and the duration of admission to the hospital or mechanical ventilation period.

Impact of chloride and strong ion difference on ICU and hospital mortality in a mixed intensive care population

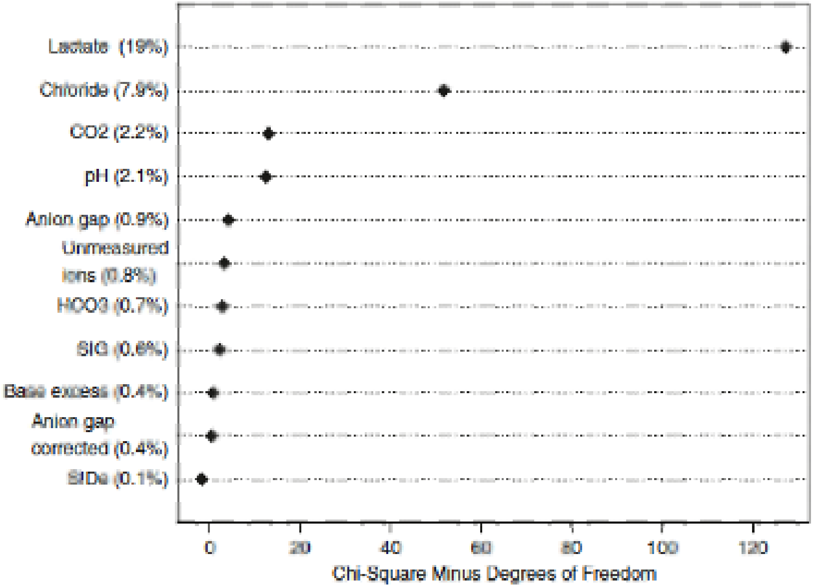
	Outcome: 30-day mortality[a] ($n = 2350$)				Outcome: hospital mortality[b] ($n = 2156$)			
	n	% outcome (%)	Odds ratio (95 % CI) versus normochloremia	*p* value	*n*	% outcome (%)	Odds ratio (95 % CI) versus normochloremia	*p* value
Chloride category								
Normochloremia	287	5.6			246	13.4		
Hypochloremia	21	23.8	3.49 (0.62–19.62)	0.16	15	40.0	1.45 (0.30–7.18)	0.64
Moderate hyperchloremia	596	3.0	0.63 (0.26–1.54)	0.31	550	5.1	0.43 (0.22–0.83)	0.01
Severe hyperchloremia	1446	2.7	0.57 (0.22–1.44)	0.23	1345	4.5	0.37 (0.18–0.73)	0.004
	n	% outcome (%)	Odds ratio (95 % CI) versus mean SID	*p* value	*n*	% outcome (%)	Odds ratio (95 % CI) versus mean SID	*p* value
SIDa category								
Intermediate SIDa	941	2.6			873	5.2		
Low SIDa	1110	2.0	1.46 (0.68–3.11)	0.34	1015	4.1	1.13 (0.63–2.03)	0.68
High SIDa	229	10.7	0.85 (0.39–1.83)	0.67	268	14.9	0.71 (0.38–1.31)	0.27
			Area under ROC 88.3 %				Area under ROC 83.9 %	
			Maximal VIF 3.53				Maximal VIF 3.58	
			Tolerance 0.66				Tolerance 0.66	

In this study, hyperchloremia at the time of admission was linked to poorer outcomes. However, a reduced strong ion difference (SID) did not significantly affect mortality.

Regenmortel NV., Ann. Intensive Care 2016; 6:91

A comparison of Prognostic Significance of Acid-Base Markers in Critically Ill Patients: A Cohort Study

Acid-base markers	Survivors (*n* = 5954)	Non-survivors (*n* = 924)	*p* value[a]
1. Arterial pH	7.35 (7.29–7.39)	7.28 (7.17–7.37)	0.001
2. Arterial CO_2 tension, mmHg	40 (35–45)	40 (34–48.8)	0.022
3. Actual bicarbonate conc., mmol/L	21 (19–23)	18 (14–21.8)	0.001
4. Chloride conc., mmol/L	110 (107–113)	109 (105–114)	0.891
5. Lactate conc., mmol/L	1.5 (1.0–2.4)	2.7 (1.4–5.6)	0.001
6. Actual base excess, mmol/L	−3 (−6 to −1)	−7 (−12 to −3)	0.001
7. Anion gap, mmol/L	12.5 (10.1–15.0)	15.0 (11.9–19.5)	0.001
8. Anion gap albumin-corrected, mmol/L	15.5 (12.8–18.5)	18.7 (14.8–23.6)	0.001
9. SIG with lactate, mmol/L	4.2 (1.5–7.1)	6.5 (3.0–10.8)	0.001
10. SIG without lactate, mmol/L	2.2 (−0.3 to 5.0)	2.5 (−0.4 to 5.8)	0.028
11. SID-effective, mmol/L	33.5 (30.5–36.2)	30.7 (26.7–34.7)	0.001
12. Other unmeasured ions, mmol/L	2.1 (−1.0 to 4.9)	−1.5 (−7.3 to 2.5)	0.001



Many acid-base markers showed significant differences between survivors and non-survivors in critically ill patients. The prognostic value of the Strong Ion Gap (SIG) was modest and inferior to arterial lactate levels. Among all acid-base markers evaluated in this large cohort, arterial lactate concentration provided the best discrimination in predicting outcomes.

Ho et al. Journal of Intensive Care 2016; 4:43

Beyond pH, Bicarbonate, and PCO_2 in Acid-Base Disorders

HCO3
PH
PCO2

Cl
Lactate
Na
Phosphate
Albumin
Other unmeasured anions
Mg
Ca
K

Conclusion

- The traditional approach to acid-base disorders, though useful for interpreting most cases, has limitations and does not fully explain the mechanisms underlying metabolic changes.
- A low strong ion difference (SID) may be a valuable predictor of mortality, indicationg that the use of chloride-rich solutions in critically ill patients may contribute to worse outcomes and thus requires careful consideration.
- However, whether decreased SID plays a causal role in increasing mortality or is simply a marker of disease severity remains a critical question for future research.
- The role of hypoalbuminemia, a common finding in critically ill patients that often contributes to metabolic alkalosis, is frequently overlooked in these cases.
- Hyperphosphatemia, identified in this study as a cause of metabolic acidosis due to increased total anions, was significantly more frequent in non-survivors.
- Finally, the complexity of the Stewart approach highlights the need for further investigation to optimize its clinical use and enhance patient outcomes.