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Stewart's Approach for Acid-base Disorders: Does the Strong Ion Difference and Effects Have an Impact on Intensive Care Unit Mortality?

Asit-baz Bozukluklarına Stewart Yaklaşımı: Güçlü İyon Farkı Yoğun Bakım Mortalitesini Etkiler mi?

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ABSTRACT *Objective:* The diagnosis and treatment of electrolyte and acid-base imbalances in intensive care unit (ICU) patients have critical importance. The value of Stewart's approach in revealing acid-base disorders is known. There are parameters defined according to this approach. This study investigates the impact of the chloride effect (Cl_{Effect}), sodium effect (Na_{Effect}), sodium-chloride effect ($Na\text{-}Cl_{Effect}$), strong ion difference (SID_{nl}) and Cl/Na ratio values calculated according to Stewart's approach on ICU mortality.

Materials and Methods: Two thousand patients whose Na, Cl, K, standard base excess (SBE), pH values were recorded and SID_{nl}, Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, Acute Physiology Assessment and Chronic Health Evaluation-II (APACHE-II) and Sequential Organ Failure Assessment (SOFA) scores calculated are included in this study. Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, SID_{nl}, Cl/Na ratio values were evaluated with a multivariable logistic regression model in terms of ICU mortality.

Results: Abnormal ranges of SID_{nl} (SID_{nl} <30 or SID_{nl} ≥43) were significantly increased in non-survivors than survivors (p=0.026). Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, Cl/Na ratio and their percentages of abnormal ranges were similar between survivor and non-survivor patients.In the multivariate logistic regression model, the likelihood of mortality was 3.5-fold (2.9-4.3), 1.7-fold (1.4-2.1) and 1.2-fold (1.0-1.5) increased by APACHE-II ≥26, SOFA >7, and SID_{nl} <30 or SID_{nl} ≥43 (p<0.001, p<0.001, p=0.041, respectively).

Conclusion: SID_{nl} is associated with ICU mortality, but pH, SBE, Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$ and Cl/Na ratio is not. SID_{nl} is one of the independent variables of Stewart's approach and is a valuable parameter in blood gas evaluations.

Keywords: Acid-base, strong ion difference, sodium, chloride, base excess, intensive care unit, mortality

ÖZ *Amaç:* Yoğun bakım ünitesi (YBÜ) hastalarında elektrolit ve asit-baz bozukluklarının tanı ve tedavisi kritik öneme sahiptir. Asit-baz bozukluklarını açıklamada Stewart yaklaşımının önemi bilinmektedir. Bu yaklaşıma göre tanımlanmış çeşitli parametreler vardır. Bu çalışmanın amacı, Stewart'ın yaklaşımına göre hesaplanan klorür etki (Cl_{Effect}), sodyum etki (Na_{Effect}), sodyum-klorür etki ($Na\text{-}Cl_{Effect}$) güçlü iyon farkı (SID_{nl}), Cl/Na oranı değerlerinin YBÜ mortalitesi üzerindeki etkilerini değerlendirmektir.

Gereç ve Yöntem: Bilgisayar destekli karar destek sistemine Na, Cl, K, standart baz fazlalığı (SBE), pH değerleri kaydedilen ve sisteme tanımlı formüller aracılığıyla SID, Na_{Effect}, Cl_{Effect}, $Na\text{-}Cl_{Effect}$, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) ve Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skorları hesaplanan 2.000 hasta bu çalışmaya dahil edilmiştir. Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, SID_{nl}, Cl/Na oranı değerleri multivariable lojistik regresyon modeli ile YBÜ mortalitesi açısından değerlendirildi.

Bulgular: Anormal SID_{nl} aralıkları (SID_{nl} <30 veya SID_{nl} ≥43), ölen hastalarda hayatta kalanlara göre anlamlı olarak yüksekti (p=0,026). Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, Cl/Na oranı ve bunların anormal aralıkları, hayatta kalan ve ölen hastalarda benzerdi. Multivariable lojistik regresyon modelinde, ölüm olasılığı APACHE-II ≥26, SOFA >7 ve SID_{nl} <30 veya SID_{nl} ≥43 olan hastalarda sırasıyla 3,5 kat (2,9-4,3), 1,7 kat (1,4-2,1) ve 1,2 kat (1,0-1,5) artmış olarak bulundu (p<0,001, p<0,001, p=0,041).

Sonuç: SID_{nl}, YBÜ mortalitesi ile ilişkili iken, pH, SBE, Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$ ve Cl/Na oranı değildir. Stewart yaklaşımının bağımsız değişkenlerinden biri olan SID_{nl}, kan gazı değerlendirmelerinde önemli bir parametredir.

Anahtar Kelimeler: Asit-baz, güçlü iyon farkı, sodyum, klorür, baz açığı, yoğun bakım ünitesi, mortalite

Introduction

Acid-base disorders are commonly found in patients admitted to the intensive care unit (ICU) as a consequence of the underlying disease or inappropriate fluid resuscitation. They are associated with high mortality and morbidity, often accompanying critical diseases (1). Therefore, the assessment of acid-base disorders is critical for accurate diagnosis and effective treatment.

Debates on which approach is more logical and holistic in the analysis of acid-base balance have continued for many years (2). However, Stewart's approach is more comprehensive than the others, it can define subtle or combined acid-base disorders that cannot be detected using only the Henderson-Hasselbalch or base excess (BE) approaches (3,4). Traditional approaches are insufficient to reveal causal mechanisms (5). Gilfix et al. (6) devised an original Fencl concept showing the impact of changes in strong ion difference (SID) and the total amount of weak acids (A_{TOT}) on BE and designed simple formulas that do not require computers or calculators, aiming to make Stewart's approach accessible (7). With this approach, complex acid-base abnormalities can be detected at the bedside, and early treatment targeting underlying causes can be started (8,9).

This study aims to investigate the impact of the chloride effect (Cl_{Effect}), sodium effect (Na_{Effect}), sodium-chloride effect ($Na\text{-}Cl_{Effect}$), non-lactate strong ion difference (SID_{nl}), chloride/sodium ratio (Cl/Na ratio) values calculated according to Stewart's approach by a computer-based decision support system on ICU mortality.

Materials and Methods

The retrospective observational study was approved by the University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee with a protocol code. 2019/49 (decision no: 2019-02-25, date: 21.01.2019). During the admission of all patients to the ICU, information and consent forms were signed by the relatives of the patients, stating that the patient data would be used in retrospective scientific studies.

Definitions and Calculations of the Effects and SID

The physicochemical approach is based on four mechanisms (6):

1) Na_{Effect}: Changes in the amount of solvent (i.e. water) concentrate or dilute the solution, changing the SID (8). This diluting effect of water is called the "free water effect".

2) Cl_{Effect}: Indicates the amount of change from normal serum chloride (Cl_s) concentration. First of all, the correction should be made by considering the dilution effect on chloride. This correction ($Cl_{corrected}$) is obtained by multiplying the measured serum chloride concentration (Cl_s) by the ratio of standard sodium (140 mmol/L) to the measured sodium (Na_s).

3) Protein effect: It shows the change of dominant weak acids such as albumin.

4) Other effects: The effect of negative ions (lactate, ketoacids, formate, oxalate, salicylate, sulfate, and phosphate), most of which cannot be measured and cause strong ion gap metabolic acidosis.

In our study, SID was calculated from the differences of strong ions other than lactate, also known as SID_{nl} (10). (See Electronic Supplement for formulas used in effects and SID_{nl} calculations).

Study Population

Data of 9,038 patients hospitalized in University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Anesthesiology and Reanimation General ICU between 01.01.2013-31.12.2019 and registered with 'ImdSoft-Metavision/QlinICU Clinical Decision Support Software (Israel)' were obtained by Structured Query Language inquiries. Radiometer ABL 800 (Denmark) was used for blood gas analysis. Patients who stayed in the ICU for less than 48 hours (3,234) and patients whose Acute Physiology Assessment and Chronic Health Evaluation-II (APACHE-II) score was not calculated (2,101) were excluded from the study. Out of 3,703 patients, 2000 patients whose Na_s, Cl_s, K_s, standard base excess (SBE), pH values were recorded and SID_{nl}, Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, Cl/Na ratio, APACHE-II, and Sequential Organ Failure Assessment (SOFA) scores calculated are included in this study (Figure 1).

Inclusion criteria: All patients older than 17 years were admitted to the medical or surgical ICU.

Exclusion criteria: Patients hospitalized for less than 48 hours and whose Na_s, Cl_s, K_s, SBE, pH values were not recorded or effects, SID_{nl}, scores not calculated.

Statistical Analysis

Data were analyzed using SPSS 22 for Windows (IBM Corp., Armonk, NY, USA). Mean ± standard deviation, median (interquartile range), frequencies and percentages were used for descriptive data. The conformity of the quantitative data to the normal distribution was tested with the Kolmogorov-Smirnov test and graphical examinations.

Student's t-test and Mann-Whitney U test were used for comparisons between two groups (survivors and nonsurvivors) of quantitative variables. Pearson chi-square test was used to compare qualitative data. The optimal cut-off level for APACHE-II score, SOFA score, SBE and pH to affect mortality was evaluated with receiver operating characteristic analysis using the Youden index. Multivariate logistic regression analysis was used for the likelihood of mortality. APACHE-II score, SOFA score, SID_{nl}, SBE and pH were added to the multivariate model. A p-value of <0.05 was used to determine the significance.

Results

The study was conducted with 2,000 patients, 40.1% (n=803) female and 59.9% (n=1197) male (Table 1). The median age of the patients was 67 years. The median values

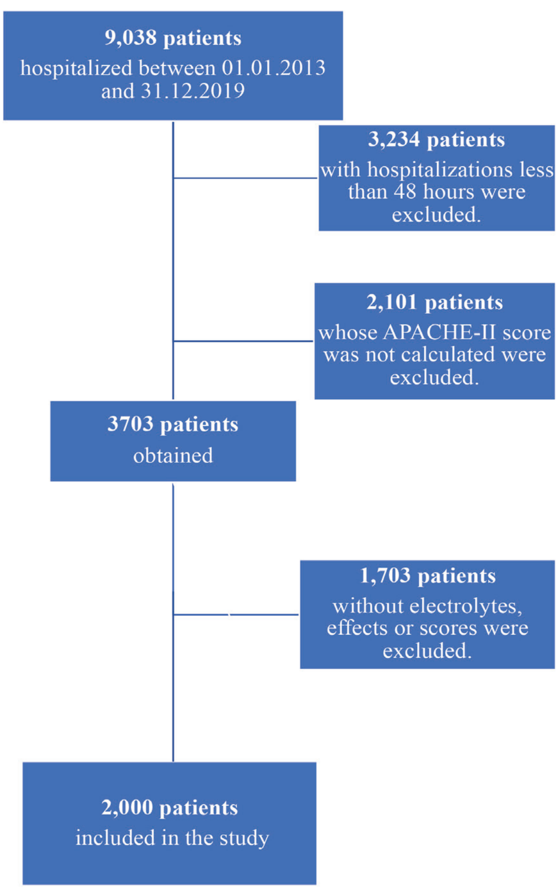

Figure 1. Flow chart of study participants
APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II

Table 1. Patients' chracteristics and outcomes	
Patients, n	**2,000**
Age, years	67 (55-78)
Male, n (%)	1,197 (59.9)
BMI, (kg/m^2)	26.1 (24.2-29.4)
SOFA score	8 (6-11)
APACHE-II	26 (21-31)
Diagnosis, n (%)	
Medical	1,862 (93.1)
Surgery	138 (6.9)
pH	7.33 (7.23-7.40)
$PaCO_2$, (mmHg)	40.2 (33.4-49.0)
SBE, (mmol/L)	-4.5 (-9.2; -0.2)
Cl_s, (mmol/L)	107 (103-112)
Na_s, (mmol/L)	139 (136-144)
K, (mmol/L)	4.0 (3.6-4.4)
Cl_{Effect}, (mmol/L)	-5.1±9.0
$-14.1 \leq Cl_{Effect} \leq 4.9$	1,465 (73.2)
Cl_{Effect} <-14.1 or Cl_{Effect} >4.9	535 (26.8)
Na_{Effect}, (mmol/L)	0.0 (-1.2-1.2)
$-1.2 \leq Na_{Effect} \leq 1.2$	1,127 (56.3)
Na_{Effect} <-1.2 or Na_{Effect} >1.2	873 (43.7)
$Na\text{-}Cl_{Effect}$, (mmol/L)	-4.9±10.5
$-15.5 \leq Na\text{-}Cl_{Effect} \leq 4.6$	1,384 (69.2)
$Na\text{-}Cl_{Effect}$ <-15.5 or $Na\text{-}Cl_{Effect}$ >4.6	616 (30.8)
SID_{nl}, (mmol/L)	37 (30-43)
$30 \leq SID_{nl} \leq 43$	1,092 (54.6)
SID_{nl} <30 or $SID_{nl} \geq 43$	908 (45.4)
Cl/Na ratio	0.77 (0.72-0.81)
0.72≤ Cl/Na ratio ≤0.81	1,161 (58.1)
Cl/Na ratio <0.72 or Cl/Na ratio >0.81	839 (41.9)
Lactate, (mmol/L)	1.4 (1.0-2.0)
Urea, (mg/dL)	44 (27-70)
Creatine, (mg/dL)	0.7 (0.5-1.13)
Duration of IMV, (h)	88 (20-272)
Length of ICU stay, (h)	124 (48-306)
AKI, n (%)	796 (39.8)
Mortality, n (%)	1,069 (53.5)

AKI: Acute kidney injury, APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II, BMI: body mass index, ICU: intensive care unit, IMV: invasive mechanical ventilation, $PaCO_2$: partial carbon dioxide pressure, $_s$: serum, SBE: standard base excess, SID_{nl}: non-lactate strong ion difference, SOFA: Sequential Organ Failure Assessment, Cl_{Effect}: chloride effect, Na_{Effect}: sodium effect, Cl/Na ratio: chloride/sodium ratio of SOFA and APACHE-II scores were 8 (6-11) and 26 (21-31), respectively (Table 1). The mortality rate was 53.5% (n=1,069). The percentages of abnormal ranges of Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, SID_{nl} and Cl/Na ratio were differently found (Table 1).

In non-survivors, SBE, pH, duration of invasive mechanical ventilation and length of ICU stay (LOS-ICU) were significantly decreased whereas SOFA and APACHE-II scores were significantly increased than survivors (p<0.001, p<0.001, p=0.034, p<0.001, p<0.001 and p<0.001 respectively) (Table 2).

Although median values of SID_{nl} were similar between the two groups, the percentage of abnormal ranges of SID_{nl} (SID_{nl} <30 or SID_{nl} ≥43) were significantly increased in non-survivors than survivors (p=0.390, p=0.026) (Table 2).

On the other hand, Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$, Cl/Na ratio and their percentages of abnormal ranges were also similar between survivor and non-survivor patients (p=0.846, p=0.309; p=0.072, p=0.612; p=0.981, p=0.903; p=0.706, p=0.218) (Table 2).

Cut-off and area under curve values of SOFA score, APACHE-II, SBE and pH were >7 [0.66 (0.64-0.69)], ≥26 [0.74 (0.72-0.76)], ≤-4.4 mmol/L [0.59 (0.56-0.61)] and <7.33 [0.57 (0.54-0.59)], respectively (p<0.001 for all) (Table 3).

In the multivariate logistic regression model, the likelihood of mortality were 3.5-fold (2.9-4.3), 1.7-fold (1.4-2.1) and 1.2-fold (1.0-1.5) increased by APACHE-II ≥26, SOFA >7, and SID_{nl} <30 or SID_{nl} ≥43, respectively (p<0.001, p<0.001, p=0.041) (Table 4).

Discussion

In the present study, it was shown that SOFA score, APACHE-II and abnormal SID_{nl} values (<30 or ≥43) at the ICU admission were associated with mortality. This highlights the importance of the Stewart approach and its metabolic component, SID. Unlike some studies, we didn't find any relationship between SBE, pH and mortality (11-14). SBE and pH are known as dependent variables, hence, we think that it can be the reason for this result. Discussions on the superiority of approaches to the diagnosis and treatment of acid-base disorders continue today (15-18). However, the physicochemical approach is thought to provide a broader perspective. In patients with normal pH and SBE values, it was shown that low SID, which can only be detected by Stewart's approach, is associated with prolonged hospitalization even at neutral pH (19). Furthermore, it is also known that SID and SID_{nl} were associated with increased ICU mortality and length of stay in ICU (10,20,21). For this reason, SID, especially SID_{nl}, is a more important blood-gas parameter which affects outcomes in the ICU.

Actually, SID_{nl} is a parameter which is used to detect electrolyte effect on acid-base status. And, a few electrolyte evaluation approaches are defined in the literature such as Fencl's corrections, base excess chloride (BE_{Cl}) and Cl/Na ratio (6,7,22,23). In our study, we didn't observe any relationship among all serum levels of electrolytes (Cl_s, Na_s, K_s), effect values of them (Cl_{Effect}, Na_{Effect}, $Na\text{-}Cl_{Effect}$), Cl/Na ratio and ICU mortality except for SID_{nl}. Effect values (Cl_{Effect}, $Na\text{-}Cl_{Effect}$), which are suitable for the Fencl concept that we used in our study, take into account the $Cl_{corrected}$ instead of the Cl_s in chloride measurements (6,7). The lack of mention of any correction in Stewart's approach has caused the Fencl concept to be criticized in this respect (23,24). Gucyetmez et al. (23) claimed that the best chloride evaluation approach was the BE_{Cl}. Indeed, SID_{nl} and BE_{Cl} mainly refer to the difference between Na and Cl in accordance with their formulas (23). Our results obviously show that approaches based on the difference between Na and Cl such as SID_{nl} and BE_{Cl} are also more valuable parameters to lead electrolyte effects on mortality in the ICU. For this reason, we can argue that the serum values of electrolytes should be evaluated without any correction.

Surprisingly, the median lactate value (1.4 mmol/L) was higher in survivor patients than in non-survivor patients (1.3 mmol/L) in our study. Therefore, no relationship was found between lactate and mortality. However, it is known that high lactate levels are associated with high mortality (25-28).

In this study, it was also found that APACHE-II ≥26 and SOFA score >7 were associated with higher mortality. This result is consistent with previous studies (29-31). In addition, as expected, the duration of mechanical ventilation and the LOS-ICU were found to be longer in non-survivor patients.

Although all parameters of the quantitative method have been previously defined in the software, it is not known how effectively these data are used by intensive care physicians and how they affect the treatment of patients. Also, due to the retrospective nature of our study, we could not test the adequacy of the sample size.

Table 2. Comparison between survivors and non-survivors			
	Survivors (n=931)	Non-survivors (n=1069)	p-value
Age, years	67 (54-77)	68 (56-78)	0.100
Male, n (%)	564 (60.6)	633 (59.2)	0.534
BMI, (kg/m^2)	26.1 (24.5-29.4)	26.1 (24.2-29.4)	0.329
SOFA score	7 (5-9)	9 (7-12)	<0.001
APACHE-II	23 (18-27)	29 (24-33)	<0.001
Diagnosis, n (%)			
Medical	860 (92.4)	1,002 (93.7)	0.232
Surgery	71 (7.6)	67 (6.3)	
pH	7.34 (7.26-7.41)	7.31 (7.21-7.40)	<0.001
$PaCO_2$, (mmHg)	40.4 (33.8-48.4)	40.1 (33.0-49.6)	0.827
SBE, (mmol/L)	-3.6 (-7.3; 0.0)	-5.6 (-10.8; -0.7)	<0.001
Na_s, (mmol/L)	139 (137-143)	139 (136-144)	0.682
Cl_s, (mmol/L)	108 (103-112)	107 (102-112)	0.152
K_s, (mmol/L)	4.0 (3.6-4.5)	3.9 (3.5-4.4)	0.144
Cl_{Effect}, (mmol/L)	-5.2±8.8	-5.1±9.2	0.846
$-14.1 \leq Cl_{Effect} \leq 4.9$	692 (74.3)	773 (72.3)	0.309
Cl_{Effect} <-14.1 or Cl_{Effect} >4.9	239 (25.7)	296 (27.7)	
Na_{Effect}, (mmol/L)	0.0 (-0.9; 1.2)	-0.3 (-1.2; 1.2)	0.072
$-1.2 \leq Na_{Effect} \leq 1.2$	519 (55.7)	608 (56.9)	0.612
Na_{Effect} <-1.2 or Na_{Effect} >1.2	412 (44.3)	461 (43.1)	
$Na\text{-}Cl_{Effect}$, (mmol/L)	-5.0 (-11.6; 1.3)	-5.1 (-11.7; 2.0)	0.981
$-15.5 \leq Na\text{-}Cl_{Effect} \leq 4.6$	643 (69.1)	741 (69.3)	0.903
$Na\text{-}Cl_{Effect}$ <-15.5 or $Na\text{-}Cl_{Effect}$ >4.6	288 (30.9)	328 (30.7)	
SID_{nl}, (mmol/L)	36 (31-43)	37 (30-44)	0.390
$30 \leq SID_{nl} \leq 43$	533 (57.3)	559 (52.3)	0.026
SID_{nl} <30 or $SID_{nl} \geq 43$	398 (42.7)	510 (47.7)	
Cl/Na ratio	0.76 (0.73-0.81)	0.77 (0.72-0.81)	0.706
0.72≤ Cl/Na ratio ≤0.81	554 (59.5)	607 (56.8)	0.218
Cl/Na ratio <0.72 or Cl/Na ratio >0.81	377 (40.5)	462 (43.2)	
Lactate, (mmol/L)	1.4 (1.1-2.1)	1.3 (1.0-1.9)	0.068
Urea, (mg/dL)	44 (27-70)	44 (28-71)	0.587
Creatinine, (mg/dL)	0.71 (0.47-1.15)	0.72 (0.46-1.11)	0.979
AKI, n (%)	540 (58.0)	664 (62.1)	0.085
Duration of IMV, (h)	89 (0-272)	88 (26-272)	0.034
Length of ICU stay, (h)	139 (52-328)	111 (48-286)	<0.001

AKI: Acute kidney injury, APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II, BMI: body mass index, ICU: intensive care unit, IMV: invasive mechanical ventilation, $PaCO_2$: partial carbon dioxide pressure, $_s$: serum, SBE: standard base excess, SID_{nl}: non-lactate strong ion difference, SOFA: Sequential Organ Failure Assessment, Cl_{Effect}: chloride effect, Na_{Effect}: sodium effect, Cl/Na ratio: chloride/sodium ratio

Table 3. Cut-off and area under curve values of significantly difference variables in non-survivors

	Cut-off values	AUC (95% CI)	p-value
APACHE-II	≥26	0.74 (0.72-0.76)	<0.001
SOFA score	>7	0.66 (0.64-0.69)	<0.001
SBE, (mmol/L)	≤-4.4	0.59 (0.56-0.61)	<0.001
pH	<7.33	0.57 (0.54-0.59)	<0.001

APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II, AUC: area under curve, CI: confidence interval, SBE: standard base excess, SOFA: Sequential Organ Failure Assessment

Table 4. Multivariate logistic regression model for likelihood of mortality

	OR (95% CI)	p-value
APACHE-II≥26	3.5 (2.9-4.3)	<0.001
SOFA score >7	1.7 (1.4-2.1)	<0.001
SID_{nl} <30 or SID_{nl} ≥43, (mmol/L)	1.2 (1.0-1.5)	0.041
SBE ≤-4.4, (mmol/L)	1.2 (0.9-1.5)	0.102
pH<7.33	0.9 (0.8-1.2)	0.872

APACHE-II: Acute Physiology Assessment and Chronic Health Evaluation-II, CI: confidence interval, OR: odds ratio, SBE: standard base excess, SID_{nl}: non-lactate strong ion difference, SOFA: Sequential Organ Failure Assessment

Conclusion

The importance of Stewart's approach, especially in defining complex acid-base disorders, is known. The results of our study show that SID_{nl} is associated with ICU mortality, but pH, SBE and $Na\text{-}Cl_{Effect}$ are not. Therefore, SID_{nl} is a valuable parameter in blood gas evaluations.

Ethics

Ethics Committee Approval: The retrospective observational study was approved by the University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee with a protocol code. 2019/49 (decision no: 2019-02-25, date: 21.01.2019).

Informed Consent: During the admission of all patients to the ICU, information and consent forms were signed by the relatives of the patients, stating that the patient data would be used in retrospective scientific studies.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.T., S.A., K.A.T., Concept: F.T., S.A., Z.Ç., Design: F.T., S.A., Data Collection and Process: F.T., S.A., B.Ö.B., K.A.T., Z.Ç., Analysis or Interpretation: F.T., S.A., B.Ö.B., G.Ö.Y., K.A.T., Z.Ç., Literature Search: F.T., Z.Ç., Writing: F.T., S.A., G.Ö.Y., K.A.T., Z.Ç.

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References

1. Gunnerson KJ, Kellum JA. Acid-base and electrolyte analysis in critically ill patients: are we ready for the new millennium? Curr Opin Crit Care 2003;9:468-73.
2. Zanella A, Langer T, Caironi P, Gattinoni L, Pesenti A. Reply by Zanella et al. to Swenson. Am J Respir Crit Care Med 2020;202:908-9.
3. Moviat M, van den Boogaard M, Intven F, van der Voort P, van der Hoeven H, Pickkers P. Stewart analysis of apparently normal acid-base state in the critically ill. J Crit Care 2013;28:1048-54.
4. Dubin A, Menises MM, Masevicius FD, Moseinco MC, Kutscherauer DO, Ventrice E, et al. Comparison of three different methods of evaluation of metabolic acid-base disorders. Crit Care Med 2007;35:1264-70.
5. Cove M, Kellum JA. The end of the bicarbonate era? A therapeutic application of the Stewart approach. Am J Respir Crit Care Med 2020;201:757-8.
6. Gilfix BM, Bique M, Magder S. A physical chemical approach to the analysis of acid-base balance in the clinical setting. J Crit Care 1993;8:187-97.
7. Fencl V, Jabor A, Kazda A, Figge J. Diagnosis of metabolic acid–base disturbances in critically ill patients. Am J Respir Crit Care Med 2000;162:2246-51.
8. Magder S, Emami A. Practical approach to physical-chemical acid-base management. Stewart at the bedside. Ann Am Thorac Soc 2015;12:111-7.
9. Story DA. Stewart acid-base: a simplified bedside approach. Anesth Analg 2016;123:511-5.
10. Gucyetmez B, Atalan HK. Non-lactate strong ion difference: a clearer picture. J Anesth 2016;30:391-6.
11. Schork A, Moll K, Haap M, Riessen R, Wagner R. Course of lactate, pH and base excess for prediction of mortality in medical intensive care patients. PLoS One 2021;16:e0261564.
12. de Meneses FA, Bezerra I, Ribeiro E, Furtado AH Junior, Peixoto AA Junior. Base excess and early mortality in patients admitted to the general intensive care unit at a university hospital in Fortaleza. Crit Care 2007;11(Suppl 3):P13.
13. Azevedo L, Park M, Sanga R, Ferreira G, Palma L, Brauer L, et al. Base excess and lactate as predictors of mortality in medical ICU patients. Crit Care 2004;8(Suppl 1):P328.
14. Palma L, Ferreira G, Amaral A, Brauer L, Azevedo LCP, Park M. Acidosis and mortality in severe sepsis and septic shock evaluated by base excess variation. Crit Care 2003;7(Suppl 3):P39.
15. Alevrakis E, Gialelis N, Vasileiadis I. Strong ion difference in urine: A measure of proton excretion or of the net plasma charge alteration? Acta Physiol (Oxf) 2020;230:e13559.
16. Bie P. Strong ion difference: Inconsistencies lining up. Acta Physiol (Oxf) 2021;232:e13616.
17. Vasileiadis I, Alevrakis E, Gialelis N. Stewart's approach: just a heresy or another lens into acid-base physiology? Acta Physiol (Oxf) 2021;232:e13622.
18. Bie P. Strong ion difference: questionable stewardship. Acta Physiol (Oxf) 2021;233:e13667.
19. Janssen JW, van Fessem JMK, Ris T, Stolker RJ, Klimek M. The hidden secrets of a neutral pH-blood gas analysis of postoperative patients according to the Stewart approach. Perioper Med (Lond) 2021;10:15.
20. Berndtson AE, Palmieri TL, Greenhalgh DG, Sen S. Strong ion difference and gap predict outcomes after adult burn injury. J Trauma and Acute Care Surg 2013;75:555-60; discussion 560-1.
21. Kaplan LJ, Kellum JA. Initial pH, base deficit, lactate, anion gap, strong ion difference, and strong ion gap predict outcome from major vascular injury. Crit Care Med 2004;32:1120-4.
22. Atalan HK, Güçyetmez B. The effects of the chloride:sodium ratio on acid-base statusand mortality in septic patients. Turk J Med Sci 2017;47:435-42.
23. Gucyetmez B, Tuzuner F, Atalan HK, Sezerman U, Gucyetmez K, Telci L. Base-excess chloride; the best approach to evaluate the effect of chloride on the acid-base status: A retrospective study. PLoS One 2021;16:e0250274.
24. Stewart PA. Modern quantitative acid-base chemistry. Can J Physiol Pharmacol 1983;61:1444-61.
25. Gharipour A, Razavi R, Gharipour M, Modarres R, Nezafati P, Mirkheshti N. The incidence and outcome of severe hyperlactatemia in critically ill patients. Intern Emerg Med 2021;16:115-23.
26. Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, et al. Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. Intensive Care Med 2016;42:202-10.
27. Ferreruela M, Raurich JM, Ayestarán I, Llompart-Pou JA. Hyperlactatemia in ICU patients: Incidence, causes and associated mortality. J Crit Care 2017;42:200-5.
28. Rishu AH, Khan R, Al-Dorzi HM, Tamim HM, Al-Qahtani S, Al-Ghamdi G, et al. Even mild hyperlactatemia is associated with increased mortality in critically ill patients. Critic Care 2013;17:R197.
29. Naved SA, Siddiqui S, Khan FH. APACHE-II score correlation with mortality and length of stay in an intensive care unit. J Coll Physicians Surg Pak 2011;21:4-8.
30. Ho KM. Combining sequential organ failure assessment (SOFA) score with acute physiology and chronic health evaluation (APACHE) II score to predict hospital mortality of critically Ill patients. Anaesth Intensive Care 2007;35:515-21.
31. Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, et al. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit. JAMA 2017;317:290-300.

Electronic Supplement

Supplementer Data

SID (strong ion difference), Sodium Effect, Chloride Effect, Sodium Chloride Effect were calculated using the formulas defined in ImdSoft-Metavision/QlinICU Clinical Decision Support Software over the laboratory parameters of the patients with the software language as shown below (1-4):

Chloride Effect

```
If Parameters.Uvalue("Cl")>0 then
cl=Parameters.Uvalue("Cl")
Else
cl=0
End If
If Parameters.Uvalue("Na+")>0 then
na=Parameters.Uvalue("Na+")
Else
na=0
End If
If na>0 and cl>0 then
Return_Value=Round(((140/na)*cl),2)
Else
Return_Value="--"
End If
If Parameters.Uvalue("Cl")>0 then
cl=Parameters.Uvalue("Cl")
Else
cl=0
End If
If Parameters.Uvalue("Na+")>0 then
na=Parameters.Uvalue("Na+")
Else
na=0
End If
If cl>0 and na>0 then
Return_Value=102-(Round(((140/na)*cl),2))
Else
Return_Value="--"
End If
```

Sodium Effect

```
If Parameters.Uvalue("Na+")>0 then
Na=Parameters.Uvalue("Na+")
Else
Na=0
End If
If na>0 then
Return_Value=Round((0.3*(Na-140)),2)
Else
Return_Value="--"
End If
```

Sodium Chloride effect

```
Value"Sodium Effect"+ Value" Chloride Effect"
```

Chloride /Sodium Ratio

```
a=("Klor")
b= ("Sodyum")
if  a>0 and  b>0 then
result=Round((a/b),2)
else
result=" "
end if
Return_Value =result
```

SID_{nl}

```
if ("Na+")>0 then
s=("Sodyum")
k=("Klor")
p=("Potasyum")
Return Value=Round(((s+p)-k),0)
```