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Comparison of Base Excess Approach Versus Stewart's Physicochemical Method for the Evaluation of Metabolic Acid-Base Disturbances in Critically ill Patients Infected with SARS-CoV-2

SARS-CoV-2 ile Enfekte Kritik Hastaların Metabolik Asit Baz Bozukluklarının Değerlendirmesinde Baz Fazlalığı Yaklaşımı ile Stewart'ın Fizikokimyasal Yönteminin Karşılaştırması

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ABSTRACT

Objective: *Complex metabolic acid-base disturbances can be seen in critically ill patients infected with the SARS-CoV-2 virus. For arterial blood gas (ABG) analysis, base excess (BE) approach enables limited evaluation of the etiological factors. The Stewart's physicochemical approach, on the other hand, may not reveal etiological agents adequately. In this study, we aimed to compare BE approach versus physicochemical method for the evaluation of metabolic acid-base disturbances in critically ill patients infected with SARS-CoV-2.*
Method: *Between March 2020 and May 2020, ABG analysis results of a total of 113 patients (71 males, 42 females) infected with SARS-CoV-2 and hospitalized in the adult intensive care units were retrospectively analyzed. The patients were divided into groups according to the BE approach and evaluated for physicochemical components. The ABG and some electrolyte values were compared among groups.*
Results: *The most common acidotic components according to the Stewart's method were hyperphosphatemia (84.9%), but low strong ion difference (SID) acidosis (62.2%) in patients with metabolic acidosis according to the BE approach. Low SID acidosis (50%) and hyperphosphatemia (30.9%) in patients with normal BE and hyperphosphatemia (77.7%) in patients with metabolic alkalosis according to the BE approach were observed. In patients with metabolic acidosis according to BE approach, 71.6% of the patients had hypoalbuminemia and 24.5% of the cases had high SID alkalosis among the Stewart's alkalosis components. Strong ion gap (SIG) acidosis was seen in 11.1% and low SID acidosis was seen in 11.1% in patients with metabolic acidosis according to the BE approach.*
Conclusion: *Physiochemical approach seems to provide additional information regarding the etiological factors and unravel the invisible part of the iceberg for the evaluation of metabolic acid-base disturbances in critically ill patients infected with the SARS-CoV-2 virus.*

Keywords: *SARS-CoV-2, acid- base, base excess, Stewart, strong ion difference*

ÖZ

Amaç: *SARS-CoV-2 virüsü ile enfekte kritik hastalarda kompleks metabolik asit-baz bozuklukları görülebilir. Arteryel kan gazı (AKG) analizinde baz fazlalığı (BF) yaklaşımı ile, etiyolojik nedenler yeteri kadar ortaya konamayabilir. Stewart fizikokimyasal yaklaşımı ile AKG analizinde etiyolojik nedenler daha net ortaya konabilir. Bu çalışmanın amacı, SARS-CoV-2 ile enfekte kritik hastaların metabolik asit-baz bozukluklarının değerlendirmesinde BF yaklaşımı ile fizikokimyasal yaklaşımı karşılaştırmaktır.*
Yöntem: *Mart 2020-Mayıs 2020 tarihleri arasında SARS-CoV-2 ile enfekte olup erişkin yoğun bakım ünitelerinde yatan toplam 113 hastanın (71 erkek, 42 kadın) yoğun bakıma girişlerindeki AKG sonuçları retrospektif olarak incelendi. Hastalar BE yaklaşımına göre gruplara ayrıldı ve bu gruplar fizikokimyasal içeriklerine göre incelendi. AKG ve bazı elektrolit değerleri gruplar arasında karşılaştırıldı.*
Bulgular: *Stewart yöntemine göre en sık görülen asidotik komponentler, BF'ye göre metabolik asidozda olan hastalarda: hiperfosfatemi (%84.9) ve düşük güçlü iyon farkı (SID) asidozu (%62.2) idi. BE normal olan hastalarda: düşük SID asidoz (%50) ve hiperfosfatemi (%30.9); BF'ye göre metabolik alkalozu olan hastalarda hiperfosfatemi (%77.7) idi. BE değerine göre metabolik asidozda olan hastalarda, Stewart alkaloz komponentlerinden, %71.6'sında hipoalbuminemi, %24.5'de ise yüksek SID alkaloz olduğu görüldü. BE değerine göre metabolik alkalozda olan hastalarda, Stewart asidoz komponentlerinden: %11.1'inde güçlü iyon açığı (SIG) asidozu ve %11.1'inde düşük SID asidozu olduğu görüldü.*
Sonuç: *SARS-CoV-2 virüsü ile enfekte kritik hastaların metabolik asit baz bozukluklarının değerlendirmesinde fizikokimyasal yaklaşım, etiyolojik olarak daha ayrıntılı bilgi verebilir ve bu yaklaşım ile buzdağının görünmeyen kısmı görünür hale gelebilir.*

Anahtar kelimeler: *SARS-CoV-2, asit baz, baz fazlası, Stewart, güçlü iyon farkı*

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INTRODUCTION

Critically ill patients infected with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; novel coronavirus 2019 [COVID-19]) may undergo an evaluation for acid-base disturbances [1]. For arterial blood gas (ABG) analysis, three methods including physiological approach, base excess (BE) approach, and Stewart's physicochemical approach are being used. Currently, there is an ongoing debate on which one is superior, particularly for critically ill patients with metabolic disorders. The physiological approach (bicarbonate) is the earliest approach and relies on the Henderson-Hasselbalch equation [2]. The BE approach utilizes the BE/base deficit rather than bicarbonate [3].

Stewart introduced a quantitative, physicochemical approach to acid-base physiology in 1983 and provided a distinction between the independent variables affecting pH value, namely partial pressure of carbon dioxide (pCO_2), strong ion difference (SID), and non-volatile weak acid load (Atot) [4]. The most prominent superiority of the Stewart approach is that it provides information regarding the pathogenesis of acid-base disturbances. According to the Stewart approach, five main metabolic acid-base disturbances are defined. These include three types of acidosis (i.e., strong ion gap [SIG] acidosis, low SID acidosis, and high weak acid acidosis) and two types of alkalosis (i.e., low weak acid alkalosis and high SID alkalosis) [5]. The presence of weak acid phosphate causes acidosis with an increased concentration, while the presence of weak acid albumin causes alkalosis with a decreased concentration [6,7].

In the present study, we aimed to assess the acid-base status in critically ill patients infected with the SARS-CoV-2 virus, using BE based approach and Stewart approach and to compare their diagnostic sensitivity in detecting metabolic disturbances and to evaluate a possible relationship between classical and alternative parameters.

MATERIAL and METHODS

This single-center, cross-sectional, retrospective study was conducted in a tertiary hospital between 20.March.2020 and 20.May.2020. All patients aged ≥18 years who were infected with SARS-CoV-2 virus, underwent ABG analysis, and hospitalized in the adult intensive care units (ICUs) for a minimum of 24 hours were included in the study. Those who did not underwent ABG analysis or those with missing data in the hospital registry were excluded from the study. As this was a retrospective study, informed consent was not required. The study protocol was approved by the Ethics Committee for Non-Interventional Clinical Research (2020-200). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Medical data of the patients were retrieved from the digital medical records. Data related to age, sex, mechanical ventilation support or vasopressor support at the time of ICU admission, survival in the ICU, length of stay in the ICU (days), and Acute Physiology and Chronic Health Evaluation (APACHE II) scores were recorded. The first ABG specimens obtained at the time of ICU admission were analyzed. For the ABG analysis, ABL800 FLEX gasometer analyzer was used (Radiometer Medical, Copenhagen, Denmark). Among acid-base balance parameters, pH, pCO_2 (mmHg), standard BE (SBE) (mmol L^{-1}), actual bicarbonate content (HCO_3) (mmol L^{-1}), lactate (mmol L^{-1}), and sodium (mmol L^{-1}) were directly measured during ABG analysis. At the time of ICU admission, biochemical analysis was also performed and albumin (g L^{-1}), chloride (mmol L^{-1}), phosphate (mmol L^{-1}), magnesium (mg dL^{-1}), and calcium (mg dL^{-1}) were measured.

All patients were divided into three groups according to the BE approach as follows: Group A patients with metabolic acidosis (SBE <-2 mEq L^{-1}), Group B patients with normal SBE (-2 to 2 mEq L^{-1}), and Group C patients with metabolic alkalosis (SBE >2 mEq L^{-1}).

For quantitative acid-base analysis, the Stewart approach was used [4], while the effects of plasma proteins were assessed through the modified physicochemical approach described by Figge et al. [8]. The apparent SID (SIDa) was calculated as the difference between the strong cations and strong anions [9]. Effective SID was calculated based on the albumin, phosphate, and HCO_3 levels [3]. The strong ion gap (SIG) was calculated as the difference between the SIDa and SIDe [10]. Total concentration of weak acids

(Atot) was measured using the albumin and phosphate levels [11]. Figure 1 shows the formulas of SIDa, SIDe, SIG, and Atot.

The SIG >2 mEq L^{-1} indicated SIG acidosis [12]. The Cl/Na ratio was used to quantify the Stewart component of SID [13]. A Cl/Na ratio of >0.75 indicated low SID acidosis, while a Cl/Na ratio of <0.75 indicated high SID alkalosis. Hyperphosphatemia was defined as a serum phosphate concentration of >0.8 mmol L^{-1}, hypoalbuminemia as a serum albumin concentration of <35 g L^{-1}, and hyperlactatemia as a serum lactate concentration of >2 mmol L^{-1}. The corrected AG (AGcorr) was also calculated according to the anion gap (AG) [5] and abnormal albumin levels (Figure 1) [14].

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

SIDe = $[HCO3^-] + 0.28 \times [albumin\ (g\ L^{-1})] + 1.8 \times [phosphate\ (mmol\ L^{-1})]$

SIG = SIDa – SIDe

Atot = $2.7 \times [albumin\ (g\ L^{-1})] + 0.6 \times [phosphate\ (mg\ dL^{-1})]$

AG = $[Na^+] + [K^+] - [HCO3^-] - [Cl^-]$

$\mathbf{AG_{corrected}} = AG + 0.25 \times (40 - [albumin\ (g\ L^{-1})])$

Figure 1. Calculations regarding acid base disorders

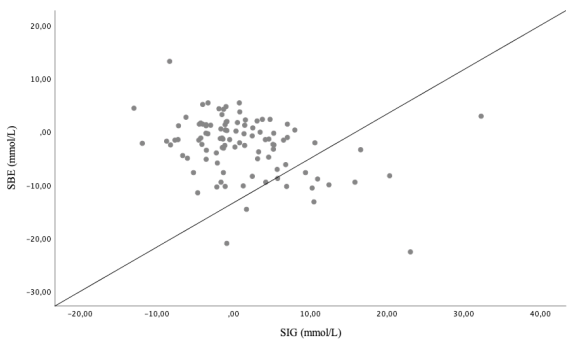

Figure 2. Correlation analysis between SBE and SIG.

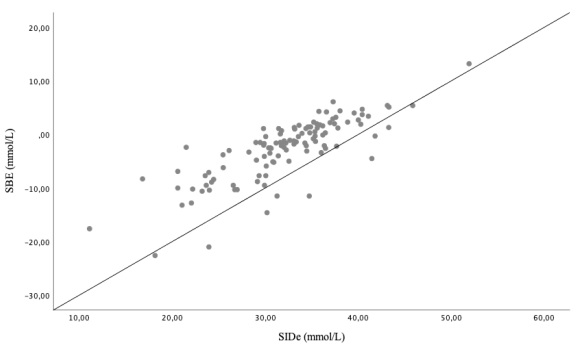

Figure 3. Correlation analysis between SBE and SIDe.

The ABG analysis was performed using the BE and Stewart approach. The number of patients with acid-base disturbances according to the Stewart method was calculated (Table II). The pH, $paCO_2$, HCO_3, AGcorr, SIDa, SIDe, SIG, Atot, and Cl/Na ratio were compared among the groups (Table III). Sodium, chloride, magnesium, calcium, albumin, and lactate s levels were also compared (Table IV). Correlations between SBE and SIG, SBE and SIDa, SBE and Atot, and SIG and AGcorr were investigated (Figures 2-5).

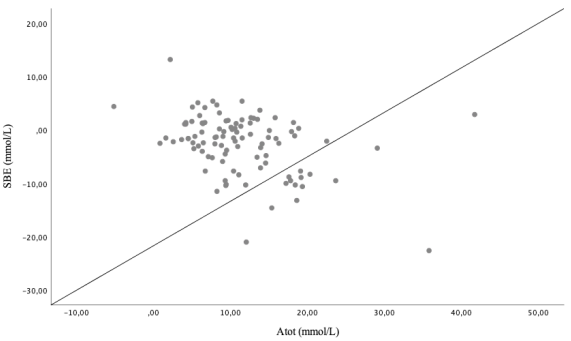

Figure 4. Correlation analysis between SBE and Atot

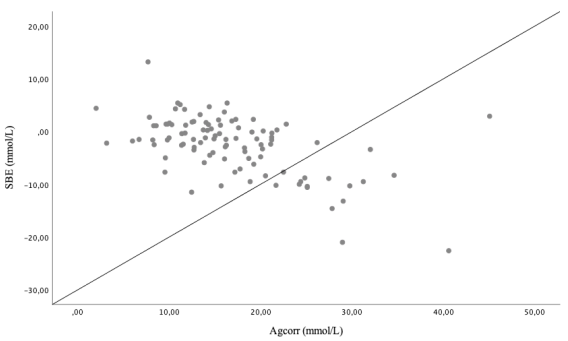

Figure 5. Correlation analysis between SBE and AGcorr

Statistical Analysis

Statistical analysis was performed using the IBM SPSS for MAC version 25.0 software (IBM Corp. Released 2017. IBM SPSS Statistics for MAC, Version 25.0. Armonk, NY: IBM Corp). Shapiro-Wilk test was used to consider normal distribution of continuous variables. Categorical variables were expressed in frequency and percentage, while continuous variables were expressed in mean ± standard deviation (SD), or median (interquartile range [IQR] 25^{th}-75^{th}). One-way analysis of variance (ANOVA) was used to compare normally distributed continuous variables. In the presence of statistically significant difference ($p<0.05$), the Tukey test was used for pairwise com-

parisons. The Kruskal-Wallis test was carried out to compare non-normally distributed continuous variables. Bonferroni correction was used for pairwise comparisons. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 127 critically ill patients with COVID-19 were enrolled in the study. Fourteen patients were excluded due to missing data and finally a total of 113 patients were evaluated. Demographic and clinical characteristics of the patients are shown in Table I. The median length of stay in the ICU was 7.3 days and the median survival rate was 53 percent.

According to the BE approach, the most common metabolic disorder was metabolic acidosis in 46.9% of the patients in Group A and the least common one was metabolic alkalosis in 15.9% of the cases in Group C (Table II). The most common acidotic components with the Stewart method were hyperphosphatemia (84.9%) and low SID acidosis (62.2%) in Group A. The most common acidotic components with the Stewart method were low SID acidosis (50%) and hyperphosphatemia (30.9%) in Group B. The most common acidotic component with the Stewart method was hyperphosphatemia (77.7%) in Group C.

Among the BE values, hypoalbuminemia was seen in 71.6% and high SID in 24.5% among the Stewart

Table I. Descriptive statistics of demographic and clinical data

	Results
Age (years)	69.3 (61.5-82)
Males	71 (62.8)
Mechanical ventilation at admission	39 (34.5)
Vasopressors at admission	25 (22.1)
Survivors	60 (53)
Days in the ICU	7.3 (2-9)
APACHE II	24.2 (18-28)

Descriptive statistics are presented as medians (interquartile range 25th-75th) or n (%).
ICU: Intensive Care Unit; APACHE II: Acute Physiology and Chronic Health Evaluation II

Table II. Stewart approach components in each of the subgroups

	SBE <–2 mEq L^{-1} Group A n=53	–2 mEq L^{-1}< SBE <2 mEq L^{-1} Group B n=42	SBE > 2 mEq L^{-1} Group C n=18
Number of patients (n=113)	53 (46.9)	42 (37.1)	18 (15.9)
Patients with SIG acidosis	22 (42)	11 (26)	2 (11.1)
Patients with low SID acidosis	33 (62.2)	21 (50)	2 (11.1)
Patients with hyperphosphatemia	45 (84.9)	13 (30.9)	14 (77.7)
Patients with hypoalbuminemia	38 (71.6)	31 (73.8)	16 (88.8)
Patients with high SID alkalosis	13 (24.5)	14 (33.3)	11 (61.1)
Patients with hyperlactatemia	38 (71.7)	18 (42.8)	3 (16.6)

Descriptive statistics are presented as n (%)
SBE: standard base excess; SIG: strong ion gap; SID: strong ion difference

Table III. Acid-base and electrolyte data

	SBE < –2 mEq L^{-1} Group A n=53	–2 mEq L^{-1} < SBE < 2 mEq L^{-1} Group B n=42	SBE > 2 mEq L^{-1} Group C n=18	p
pH	(7.30±0.11)^{a}	(7.42±0.06)^{b}	(7.37±0.07)^{b}	<0.001
$paCO_2$ (mmHg)	38.5 (29.6-43.3)^{a}	38.4 (30.8-43.1)^{a}	53.5 (41.6-65.3)^{b}	<0.001
HCO_3 (mmol L^{-1})	(18.1±4)^{a}	(23.9±2.4)^{b}	(29.8±3.9)^{c}	<0.001
AGcorr (mmol L^{-1})	19.9 (14.2-25.1)^{a}	14.1 (10.03-17.3)^{b}	14.6 (9.9-16.5)^{b}	<0.001
SIDa (mmol L^{-1})	31.2 (26.7-33.9)	33.6 (30.2-37.9)^{a}	40.3 (34.8-43.5)^{b}	<0.001
SIDe (mmol L^{-1})	^{a}(28±5.72)^{a}	(34±3)^{b}	(39.6±4.2)^{c}	<0.001
SIG (mmol L^{-1})	2.8 (-2.1-6.7)	-0.63 (-3.6-2.4)	0.27 (-4,6 -2.06)	0.058
Atot (mmol L^{-1})	12 (6.8-16.8)^{a}	9.4 (6.2-12)^{b}	9 (5.9-13.8)^{ab}	0.043
Cl/Na ratio	(0.77±0.03)^{a}	(0.75±0.33)^{a}	(0.72±0.04)^{b}	<0.001

Descriptive statistics are presented as means ± SD or medians (interquartile range 25th-75th).
SBE: standard base excess; Agcorr: anion gap corrected for albumins; SIDa: apparent strong ion difference; SIDe: effective strong ion difference; SIG: strong ion gap; Atot: weak acid concentration; Cl/Na: chloride/sodium

Table IV. Acid-base and electrolyte data

	SBE < −2 mEq L^{-1} Group A n=53	−2 mEq L^{-1} < SBE < 2 mEq L^{-1} Group B n=42	SBE > 2 mEq L^{-1} Group C n=18	p
Sodium (mmol L^{-1})	134.3±5.8	133±7.1	137.2±8.0	0.089
Chloride (mmol L^{-1})	(103.8±5.8)[a]	(100.4±5.7)[b]	(98.8±4)[b]	0.003
Phosphate (mmol L^{-1})	1.14 (0.0-1.53)[a]	0.84 (0.0-1.14)[b]	0.96 (0.00-1.28)[ab]	0.041
Magnesium (mg dL^{-1})	2±0.4	2.1±0.48	1.95±0.31	0.376
Calcium (mg dL^{-1})	8.28±1	8.44±0.75	8.32±0.66	0.729
Albumin (g L^{-1})	29±6	32±4	30±3	0.086
Lactate (mmol L^{-1})	4.06 (1.8-5.2)[a]	2 (1-2.7)[b]	1.5 (1.1-1.9)[b]	<0.001

Descriptive statistics are presented as means ± SD or medians (interquartile range 25th-75th)
SBE: standard base excess

alkalosis components in Group A. In Group C, SIG acidosis was seen in 11.1% and low SID acidosis in 11.1% in patients with metabolic alkalosis according to the BE approach. Hyperlactatemia was most commonly seen in Group A (71.1%) among all groups. According to the SBE approach, 42.8% of the patients with normal acid-base status had hyperlactatemia (Table II).

There was a statistically significant intergroup difference in the pH, $paCO_2$, HCO_3, AGcorr, SIDa, SIDe, Atot, and Cl/Na ratio (p<0.05) (Table III). The pH value of Group A was statistically significantly lower than the other groups, and the $paCO_2$ value of Group C was statistically significantly higher than the other groups. The HCO_3 values of all three groups were different from each other being the lowest for Group A and highest for Group C.

Group A had higher AGcorr than other groups . Grup C had higher SIDa values than other groups, and the SIDe values of all three groups were different from each other being the lowest for Group A and the highest for Group C. While Group C had lower Cl/Na values than other groups (p<0.05). Although there was a statistically significant difference in the Atot values among the three groups (p<0.05), according to the pairwise group comparisons, only the comparison between Groups A and Group B was statistically significant (p<0.05).

There was also a statistically significant difference as for chloride, phosphate, and lactate levels among the groups (p<0.05) (Table IV). The chloride levels of Group C were lower than the other groups, phosphate levels in Group B were lower than Group A, lactate levels of Group A were higher than other groups (p<0.05).

Correlation analysis revealed a weakly positive relationship between the SBE and SIG (r=0.348; p<0.001) (Figure 2). In addition, there was a strongly positive relationship between the SBE and SIDe (r=0.805; p<0.001) (Figure 3), a weakly positive relationship between SBE and Atot (r=0.381; p<0.001) (Figure 4), and a moderately positive relationship between SBE and AGcorr (r=0.557; p<0.001) (Figure 5).

DISCUSSION

In the present study, we compared BE versus Stewart's method for the evaluation of metabolic acid-base disturbances in critically ill patients with COVID-19. Our study results showed that in this patient population Stewart approach was more useful in diagnosing metabolic acid-base disturbances than BE approach. In patients with normal acid-base status according to the BE, 50% of the patients had low SID acidosis, while 73.8% of the patients had hypoalbuminemic alkalosis when the Stewart method was used.

From the classical point of view, the most common metabolic disorder is metabolic acidosis in critically ill patients [5,13,15,16]. In our study, similarly, the most frequent metabolic disorder was metabolic acidosis in patients with COVID-19 disease. Previous studies showed that the Stewart method was superior to other approaches in the diagnosis of metabolic disorders in the ICU patients [13,15-17]. The most common causes of metabolic acidosis are pneumonia, sepsis, septic shock, myocarditis, cardiogenic shock,

and acute renal failure in critically ill patients with COVID-19 [18].

In our study, Group A patients had the majority of Stewart acidosis components. This finding indicates that Stewart approach is valuable in the evaluation of etiopathogenesis of metabolic acidosis in patients with COVID-19 disease. However, the frequency (%) of the Stewart acidosis components does not provide information about the extent of the metabolic acidosis. Therefore, etiopathogenesis should be individually evaluated in each patient. In our study, the higher rate of hyperphosphatemic acidosis component in Group C rather than Group B (77.7% vs. 30.9%, respectively) can be considered as a specific criterion for COVID-19 disease.

Albumin is a negative acute phase reactant which has antioxidant properties. Component of hypoalbuminemic alkalosis was most commonly seen in all groups in our study, consistent with previous studies [13,19]. In addition, albumin has been shown to downregulate the expression of angiotensin-converting enzyme 2 (ACE2) receptors, which are the entry gates into the cell, and increased serum albumin levels have been associated with an increased mortality risk [20]. One of the major findings of the current study is that components of alkalosis and acidosis were more frequently seen in Group A and Group C, respectively. This finding is also consistent with previous studies involving critically ill patients [5,21,22]. Hypoalbuminemia in Groups A and B and hyperphosphatemia in Group C may have an equilibrating effect on the acidosis-alkalosis balance.

A lactate level of >2 mmol L^{-1} indicates inadequate tissue perfusion, which is one of the diagnostic criteria of sepsis and critically ill COVID-19 patients. As expectedly, the majority of the patients (71.7%) with acidosis have hyperlactatemia [23]. In our study, 42.8% of the patients in Group B had also hyperlactatemia, which is one of the main findings of the study. This finding indicates that inadequate tissue perfusion has already started and the tissue buffer capacity has been already exceeded in critically ill COVID-19 patients with normal acid-base status.

The pH indicates the presence of acidemia or alkalemia, while BE provides information about the metabolic component. Group C patients had concomitant respiratory acidosis and metabolic alkalosis based on the overall evaluation of pH, $paCO_2$, and HCO_3 values. As critical COVID-19 disease is a respiratory condition, the presence of respiratory acidosis in Group C patients is an expected result. However, it is of utmost importance to be able to distinguish between acute and chronic states of respiratory acidosis. Based on the coefficients of compensation mechanisms [24], it can be speculated that chronic respiratory illness was seen in Group C. Additionally, COVID-19 disease is associated with hypoxemic respiratory failure in the acute phase; however, underlying chronic obstructive pulmonary disease increases the likelihood of chronic respiratory acidosis in these patients.

In our study, the discrepancy in the AGcorr values between Group A and the other groups suggests the diagnostic compliance between the SBE and AG. The SBE value provides an information about the extent of metabolic acidosis, while AGcorr value provides an insight into the etiology of metabolic acidosis. Of note, AGcorr and SIG represent the unmeasured anions. In the light of these data, etiological factors playing a role in high AG metabolic acidosis should be primarily evaluated, as in Group A in our study.

Furthermore, discrepancy in the SIDe values among the groups suggests the presence of an inference to the content of the SIDe. Etiological factors which reduce SIDe include excessive retention of water (hyponatremia), hyperchloremia, and low SIG (lactic or ketoacidosis) [25]. In our study, there was no statistically significant difference in the SIG and sodium levels among the three groups, although there was a significant difference as for chloride levels. These findings indicate that hyperchloremia is the most common metabolic component of SIDe in critically ill patients with COVID-19. Normal SIG value ranges between 0 and 2 mEq L^{-1}. In our study, the median SIG was 2.8 mmol L^{-1} and the median lactate value was 4.06 mmol L^{-1} in Group A, supporting lactic acidosis as the more frequently seen etiology in the high SIG acidosis group.

Albumin is 2.7-, and phosphate is 0.6- fold effective in the calculation of Atot and Atot is primarily affected by albumin alterations. In our study, there was

no significant difference in the albumin levels among the groups. However, we observed a significant difference in the phosphate levels, indicating that the discrepancy in the Atot values during the early stages of the disease may have resulted mainly from phosphate levels in critically ill COVID-19 patients.

In our study, the discrepancy in the Cl/Na ratios among the groups suggests the presence of a diagnostic compliance between BE and Cl/Na approaches. The main reason for discrepancy in the Cl/Na ratio is the difference in chloride levels. Excessive chloride levels can be explained by the utilization of isotonic fluids and resuscitation before ICU admission. Previous studies also showed that hyperchloremia was associated with the use of iatrogenic isotonic 0.9% NaCl and resuscitation [17,26].

Among the Stewart metabolic components using SBE, there was a strong correlation between SIDe and SBE, weak correlation between Atot and SBE, and also between SIG and SBE in our study. These findings suggest that the effect of sodium and chloride is greater than the effect of lactate and volatile weak acids in BE approach in the early stage of COVID-19 in critically ill patients. In addition, a strong correlation existed between SBE and AGcorr, consistent with previous studies [22,27].

Although the present study is valuable in providing additional information to the body of knowledge on critically ill COVID-19 patients obtained using ABG analysis, its retrospective design and small sample size are its main limitations. In addition, we were unable to classify patients according to the organ diseases and results of ABG analysis could be evaluated only at the time of ICU admission.

In conclusion, our study results suggest that critically ill patients infected with the SARS-CoV-2 virus may suffer from severe metabolic acidosis at the time of ICU admission. The Stewart approach is superior to BE approach in the evaluation of metabolic acid-base disturbances. ABG analysis using Stewart approach has a greater diagnostic accuracy to evaluate electrolytes and albumin levels simultaneously. Although Stewart approach seems to be more complex, it can be calculated using web-based applications.

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