Serum osmolarity does not predict mortality in patients with respiratory failure

Deniz Çelik, MD,⁎, Murat Yıldız, MD, Ayşe Çifci, MD

Abstract
We aimed to determine the parameters that affect mortality in pulmonary intensive care units that are faster and inexpensive to determine than existing scoring systems. The relationship between serum osmolarity and prognosis was demonstrated for predialysis patients, in acute pulmonary embolism, heart failure, acute coronary syndrome, myocardial infarction, and acute spontaneous intracerebral hemorrhage in the literature. We hypothesized that serum osmolarity, which is routinely evaluated, may have prognostic significance in patients with respiratory failure.

This study comprised 449 patients treated in the Pulmonary Intensive Care Clinic (PICU) of our hospital between January 1, 2020, and December 31, 2020. The modified Charlson Comorbidity Index (mCCI), Acute Physiology and Chronic Health Assessment (APACHE II), Sequential Organ Failure Evaluation Score (SOFA), Nutrition Risk Screening 2002 (NRS-2002), and hospitalization serum osmolarity levels were measured.

Of the 449 patients included in the study, 65% (n=292) were female and the mean age of all patients was 69.86±1.72 years. About 83.1% (n=373) of the patients included in the study were discharged with good recovery. About 4.9% (n=22) were transferred to the ward because their intensive care needs were over. About 6.9% (n=31) were transferred to the tertiary intensive care unit after their status deteriorated. About 5.1% (n=23) died in the PICU. In the mortality group, APACHE II (P=.005), mCCI (P<.001), NRS-2002 total score (P<.001), and SOFA score (P<.001) were significantly higher. There was no statistically significant difference between the groups in terms of serum osmolarity levels.

Although we could not determine serum osmolarity as a practical method to predict patient prognosis in this study, we assume that our results will guide future studies on this subject.

Abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II, APE = Acute Pulmonary Embolism, AUC = Area Under The Curve, BUN = Blood Urea Nitrogen, COPD = Chronic Obstructive Pulmonary Disease, GSC = Glasgow Coma Score, ICUs = Intensive Care Units, mCCI = Modified Charlson Comorbidity Index, NRS-2002 = Nutrition Risk Screening 2002, PICU = Pulmonary Intensive Care Unit, ROC = Receiver Operating Characteristic, SAPS II = Simplified Acute Physiology Score II, SOFA = Sequential Organ Failure Assessment.

Keywords: critically ill patients, pulmonary intensive care unit, serum osmolarity

1. Introduction
“Pulmonary Intensive Care Unit” (“PICU”) is a clinic where the management of patients who develop acute respiratory failure and have lung pathologies is performed. The early scales evaluating patient situations were used by physicians in the 1980s and are commonly used in “intensive care units” (“ICUs”).[1]

Several new scales were developed and the evolving of existing scales has been completed to ensure the most accurate patient...
2. Materials and methods

2.1. Selection of patients

This study included 449 patients treated in the “PICU” of our hospital between January 1, 2020, and December 31, 2020. The patients included in the study had severe respiratory failure and were transferred from the emergency unit, tertiary intensive care units, outpatient clinics, and other chest diseases wards. All patients whose data could be accessed and who gave consent at admission for clinical studies were included in the study. The study design is cross-sectional and does not require ethics committee approval due to its retrospective nature. Nevertheless, permission for this study was obtained from the Board of Education with the decision numbered 716 and dated March 4, 2021.

2.2. “Charlson Comorbidity Index” (CCI)

The original “Charlson Index” was developed by Mary Charlson in 1987. This index includes 19 comorbidities. These comorbidities are grouped into 4 main categories.[14] After the age of 40, a “modified Charlson Comorbidity Index” (“mCCI”) score is calculated by adding one point to the overall score for every 10 years.[15]

2.3. “Acute Physiology and Chronic Health Evaluation II” – “APACHE II”

“APACHE II,” one of the prognostic scoring systems, was developed and started to be used in 1985 (1). Physiologic variables and “Glasgow Coma Score” (“GCS”) were evaluated in “APACHE II.” Age was included in the scoring as a factor affecting mortality, regardless of disease severity, as it indicates a decrease in physiological reserve. The “APACHE II” highest value is 71. Mortality, which equals 25% when the total score is 25, increases to 80% at 35 points and above.[1]

2.4. “Sequential Organ Failure Assessment Score” (“SOFA”)

“SOFA” was developed to evaluate organ failure in sepsis and then used for patients without sepsis as well. A total of 6 systems, including respiratory, cardiovascular, liver functions, coagulation, “GCS,” kidney functions were scored between 1 and 4, with the worst value being recorded daily. The total score varies between 6 and 24; a higher score indicates higher morbidity.[3]
exact test were used to compare categorical variables. The relationship between mortality and the risk variables results was assessed using both univariate and multivariate cox regression analysis. The long-term prognosis was determined using the Kaplan–Meier curve analysis. If serum osmolality, “APACHE II,” “mCCI,” “nutritional status scores,” “Nutrition Risk Screening 2002” (“NRS-2002”) total scores, and “SOFA” scores were related to the risk of death, receiver operating characteristic (ROC) curve analysis was performed to establish the threshold value. On all statistical analyses, a P value of .05 was regarded as a significant threshold.

3. Results

The study comprised 449 patients, 65% (n=292) were female, and the mean age of all patients was 69.86 ± 1.72 years. 3.1% (n=14) of the patients admitted to the “PICU” were referred from outpatient clinics, 4.7% (n=21) from the chest wards, 34.5% (n=155) from the emergency department, and 57.7% (n=259) from the tertiary “ICUs.” The majority of patients [83.1% (n=373)] were discharged with recovery. 4.9% (n=22) were transferred to the wards because their intensive care need was over. 6.9% (n=31) were transferred to the tertiary “ICUs” after their overall condition deteriorated. 51% (n=23) died in the “PICU.” All patients were followed up remotely until March 31, 2021, after the end of the study period. The patients who were discharged from the “PICU” to home or who were discharged to home following the transfer to the ward have died (38.1% (n=171)). The mean follow-up period of the patients was 157.56 ± 119.95 days. The mean number of hospitalization days in the “PICU” was 9.36 ± 2.23. It was observed that “diabetes mellitus,” “congestive heart failure,” and “coronary artery disease” were common comorbidities (37.6%, 35.4%, 26.1%, respectively). The serum osmolality, “APACHE II,” “mCCI,” “NRS-2002” total score, “SOFA” score, and laboratory parameters at admission are summarized in Table 1.

The clinical characteristics of 449 patients were divided into 2 groups based on their mortality conditions (Table 2). In the mortality group, patients were significantly older (P < .001), had shorter follow-up periods (P < .001), a higher presence of any tumor (P < .001), and a higher presence of metastatic solid tumor (P < .001). There are no notable distinctions between the 2 groups in terms of other variables.

The parameters that can be an indicator of mortality are compared in Table 3. In the mortality group, “APACHE II” (P = .005), “mCCI” (P < .001), “NRS-2002” total scores (P < .001), and “SOFA” scores (P < .001) were significantly higher. The number of patients with GCS ≤ 14 was significantly higher in the mortality group (P = .001). The number of patients with creatinine ≥ 1.2 mg/dL was significantly higher in the mortality group (P = .003). In terms of serum osmolality levels, there was no significant difference between the groups.

Comparisons according to mortality status are summarized in Table 4. Procalcitonin, leukocyte, neutrophil, red cell distribution width, creatinine, blood urea nitrogen, and C-reactive protein values at admission were higher in the mortality group. The hemoglobin, hematocrit, and albumin were lower. There were no significant differences in terms of other factors.

Univariate Cox regression analysis was used to analyze the factors predicting survival. As we had a follow-up period, we used Cox regression analysis instead of logistic regression. Variables found to be significant in the univariate Cox regression analysis were included in the multivariate cox regression analysis. The backward LR method was used. The most meaningful model

### Table 1

Results of evaluation scores and laboratory parameters.

| Parameters                      | Mean       | SD        | Median    | Minimum | Maximum  |
|---------------------------------|------------|-----------|-----------|---------|----------|
| Serum osmolality                | 294.68     | 11.41     | 294.81    | 235.25  | 345.33   |
| “APACHE II”                     | 16.66      | 7.66      | 16        | 0       | 47       |
| “mCCI”                          | 5.06       | 2.28      | 5         | 0       | 15       |
| “NRS-2002” total score          | 4.53       | 1.10      | 4         | 3       | 7        |
| “SOFA” score                    | 3.73       | 1.72      | 3         | 0       | 13       |
| Procalcitonin                   | 1.09       | 4.21      | 0.10      | 0.01    | 35.20    |
| Leukocyte                       | 11,329.87  | 5525.02   | 10,110    | 1030    | 60,100   |
| Lymphocyte                      | 1220.45    | 999.5     | 1030      | 110     | 9300     |
| Neutrophil                      | 9747.78    | 8096.2    | 8270      | 560     | 100,010  |
| Hemoglobin                      | 13.10      | 2.67      | 13        | 6.3     | 19.2     |
| Red cell distribution width     | 16.17      | 2.75      | 15.5      | 11.8    | 28.7     |
| Hematocrit                      | 42.24      | 8.92      | 41.3      | 10.4    | 64.3     |
| Platelet                        | 244.08     | 106.92    | 225       | 14      | 1087     |
| Sodium                          | 138.42     | 5.03      | 139       | 110     | 159      |
| Potassium                       | 5.63       | 22.74     | 4.5       | 2.7     | 486      |
| Calcium                         | 8.74       | 0.75      | 8.8       | 4.4     | 11.9     |
| Creatinine                      | 1.68       | 8.49      | 0.93      | 0.39    | 141      |
| Glucose                         | 151.69     | 69.67     | 133       | 28      | 524      |
| Blood urea nitrogen             | 26.37      | 13.89     | 23        | 5       | 98       |
| Albumin                         | 33.16      | 9.17      | 33.6      | 10.4    | 187      |
| C-reactive protein              | 62.55      | 77.13     | 31        | 0       | 527      |
| Urine density                   | 1010.68    | 66.47     | 1014      | 0       | 1055     |
| Serum osmolality                | 295.88     | 13.21     | 295.3     | 262.3   | 345.3    |

Continuous variables were expressed as either the mean ± standard deviation (SD) or median (minimum–maximum value).

* At admission.

APACHE II = Acute Physiology and Chronic Health Evaluation II, mCCI = modified Charlson Comorbidity Index, NRS-2002 = Nutrition Risk Screening 2002, SOFA = Sequential Organ Failure Assessment.
that can explain mortality is the seventh step model. According to the seventh step results, age, “APACHE II” score, “mCCI” score, “SOFa” score, leukocyte level, blood urea nitrogen levels, and albumin levels at admission were the parameters that predicted mortality (Table 3).

The patients were classified into 2 groups according to the median value of osmolarity and the differences in survival were analyzed. The serum osmolarity value did not differ statistically in terms of survival between the groups ($P > .05$). Furthermore, no statistical significance was detected in the ROC analysis for serum osmolarity.

4. Discussion

Identifying the risk of mortality and clinical risk factors for resource use for critically ill patients in ICUs has great importance.[16] There are several ICU score systems available, and new scoring systems are being developed. The main aim is to acquire a quantitative and accurate evaluation of organ dysfunction and assessment of morbidity in ICUs. “APACHE II, III and IV,” “SAPS,” “SOFa,” “Mortality Prediction Model,” “Multiple Organ Dysfunction Score,” and “Logistics Organ Dysfunction Score” are essential tools to characterize the patients of “ICUs” and explain mortality variations.[17] Outcome

| Table 2 |
| --- |
| The clinical characteristics of the 2 groups were compared based on clinical outcome. |

| Parameters | Mortality group (n = 171) | Survivors (n = 278) | P |
| --- | --- | --- | --- |
| Gender | | | |
| Male | 116 | 67.9% | 176 | 63.3% | .329 |
| Female | 55 | 32.2% | 102 | 36.7% | |
| Follow-up period (day) (min-max) | 58 | 0-390 | 207.5 | 0-364 | <.001 |
| Admission days | 8 | 1-35 | 8 | 1.38 | .260 |
| Coronary artery disease | 50 | 29.2% | 67 | 24.1% | .228 |
| Congestive heart failure | 69 | 40.4% | 90 | 32.4% | .086 |
| Peripheral vascular disease | 2 | 1.2% | 6 | 2.2% | .716 |
| History of a cerebrovascular disease | 8 | 4.7% | 6 | 2.2% | .136 |
| Dementia | 5 | 2.9% | 4 | 1.4% | .311 |
| Chronic lung disease | 161 | 94.2% | 248 | 89.2% | .074 |
| Connective tissue disease | 1 | 0.6% | 1 | 0.4% | .999 |
| Peptic ulcer disease | 1 | 0.6% | 6 | 2.2% | .381 |
| Diabetes mellitus | 60 | 35.1% | 109 | 39.2% | .381 |
| Mild liver disease | 5 | 2.9% | 6 | 2.2% | .381 |
| Moderate liver disease | 13 | 7.6% | 15 | 5.4% | .348 |
| Moderate kidney disease | 13 | 7.6% | 15 | 5.4% | .348 |
| Seizure disorder | 1 | 0.6% | 1 | 0.4% | .999 |
| Presence of metastatic solid malignity | 13 | 7.6% | 2 | 0.7% | <.001 |

Continuous variables were expressed as the mean ± standard deviation or median (minimum-maximum value) of categorical variables. Continuous variables were compared using Student's t-test or Mann-Whitney U-test. Statistically significant P-values are in bold.

There were no patients with diabetes mellitus, leukemia, and AIDS diagnosis causing end-organ damage.

| Table 3 |
| --- |
| Comparison of 2 groups’ potential mortality predictors based on clinical outcome. |

| Parameters | Mortality group (n = 171) | Survivors (n = 278) | P |
| --- | --- | --- | --- |
| Glasgow Coma Score, n (%) | | | |
| 15 | 100 (58.5%) | 206 (74.1%) | .001 |
| 13-14 | 43 (25.1%) | 51 (18.3%) | |
| 10-12 | 15 (8.8%) | 16 (5.8%) | |
| 6-9 | 4 (2.3%) | 3 (1.1%) | |
| <6 | 9 (5.3%) | 2 (0.7%) | |
| Serum creatinine level (mg/dL) n (%) | | | |
| <1.2 | 119 (69.6%) | 226 (81.3%) | .03 |
| 1.2-1.9 | 47 (27.5%) | 45 (16.2%) | |
| 2-3.4 | 2 (1.2%) | 7 (2.5%) | |
| 3.5-4.9 | 2 (1.2%) | – | |
| >5 | 1 (0.6%) | – | |
| Serum osmolarity median (min-max) | 295.85 (224.28–320.93) | 294.10 (235.25–345.33) | .003 |
| “APACHE II” median (min-max) | 18 (6-47) | 16 (6-34) | .005 |
| “mCCI” median (min-max) | 6 (1-15) | 4 (0-12) | <.001 |
| “NRS-2002” total score median (min-max) | 5 (3-7) | 4 (3-7) | <.001 |
| “SOFA” score median (min-max) at admission | 4 (0-13) | 3 (1-8) | <.001 |

Continuous variables were expressed as the mean ± standard deviation or median (minimum-maximum value). Continuous variables were compared using Student’s t-test or Mann–Whitney U-test. Statistically significant P-values are in bold.

APACHE II = Acute Physiology and Chronic Health Evaluation II, mCCI = modified Charlson Comorbidity Index, NRS-2002 = Nutrition Risk Screening 2002, SOFA = Sequential Organ Failure Assessment.
prediction is important in “ICU” administration.\cite{18} Outcome prediction is one of the parameters of “ICU” performance, and it is important for monitoring “ICU” performance and comparing it to different “ICUs.” Outcome prediction can be beneficial in informing families of critically ill patients about possible complications. The prediction may guide therapeutic decision-making and resource allocation.\cite{19}

The “APACHE II” is the most widely applied scoring system in “ICUs” across the world.\cite{20} Vasilievskis et al.\cite{21} conducted a study and concluded that only the “APACHE II” indicated a good distinction in predicting “ICU” mortality. Godinjak et al.\cite{22} stated that an “APACHE II” score of more than 27.5 could anticipate the worst outcome of intensive care patients with a specificity of 93.4% and a sensitivity of 74.5%. We use the “APACHE II” in the admission to the “PICU” as well. In line with the literature, in this study, the “APACHE II” scores were higher in the mortality group. If the “APACHE II” cut-off value is set at 16.5, the sensitivity is calculated to be 57.9% and the

Table 4

The laboratory parameters of 2 groups were compared based on clinical outcome.

| Parameters                  | Mortality group (n = 171) | Survivors (n = 278) | P  |
|-----------------------------|---------------------------|---------------------|----|
|                            | Median (min-max) ± SD     | Median (min-max) ± SD |    |
| Procalcitonin*              | 0.12 (0.01–27.4)         | 0.08 (0.01–35.2)    | .005 |
| Leukocyte*                  | 10.670 (1180–36,650)     | 10.850 (1030–60,100) | .001 |
| Lymphocyte*                | 960 (130–8970)           | 1085 (110–9300)     | .052 |
| Neutrophil*                | 8650 (911–100,010)       | 7810 (560–90,000)   | .006 |
| Hemoglobin*                | 12.29 ±2.67              | 13.59 ±2.55         | <.001 |
| Red cell distribution width*| 16 (12.1–23.7)           | 15.3 (11.8–28.7)    | .013 |
| Hematocrit*                | 39.57 ±8.72              | 43.88 ±6.66         | <.001 |
| Platelet*                  | 233 (52–715)             | 219.5 (14–1087)     | .286 |
| Sodium*                    | 138.18 ±5.16             | 138.56 ±4.94        | .437 |
| Potassium*                 | 4.5 (2.7–7.5)            | 4.5 (2.8–486)       | .440 |
| Calcium*                   | 8.70 ±0.77               | 8.76 ±0.74          | .375 |
| Creatinine*                | 1 (0.39–57)              | 0.9 (0.4–141)       | .003 |
| Glucose*                   | 140 (47–408)             | 129.5 (28–524)      | .164 |
| Blood urea nitrogen*       | 27 (9–98)                | 21 (5–78)           | <.001 |
| Albumin*                   | 31.74 ±5.45              | 34.04 ±10.76        | .010 |
| C-reactive protein*        | 45 (1–352)               | 25 (0–527)          | <.001 |
| Urine density*             | 1009.96 ±79.75           | 1011.14 ±56.74      | .858 |
| Serum osmolality*          | 296.38 ±14.11            | 295.55 ±12.72       | .797 |

*Continuous variables were expressed as either the mean ± standard deviation (SD) or median (minimum-maximum value). Continuous variables were compared with the Student test or Mann–Whitney U test. Statistically significant P values are in bold.*

*At admission.

Table 5

Multivariate cox regression analysis was applied to identify variables that predict survival in patients admitted to the “PICU.”

| Step 1 | Wald | P       | HR (95.0% CI for HR) |
|--------|------|---------|---------------------|
| Age    | 4.554 | .033    | 1.028 (1.002–1.055) |
| Serum osmolality | 0.066 | .797    | 0.998 (0.984–1.012) |
| “APACHE II” | 2.970 | .085    | 0.978 (0.953–1.003) |
| “mCCCI” | 7.868 | .005    | 1.119 (1.034–1.211) |
| “NRS-2002 total score” | 0.327 | .567    | 0.960 (0.931–1.057) |
| “SOFA score*” | 14.033 | <.001   | 1.000 (1.000–1.000) |
| Leukocyte* | 7.796 | .005    | 1.010 (1.000–1.020) |
| Hemoglobin* | 0.032 | .858    | 0.981 (0.799–1.206) |
| Hematocrit* | 0.060 | .806    | 1.000 (0.986–1.013) |
| Calcium* | 0.501 | .479    | 0.960 (0.911–1.019) |
| Blood urea nitrogen* | 4.182 | .041    | 1.013 (1.001–1.025) |
| Albumin* | 0.392 | .531    | 0.978 (0.952–1.000) |

Step 7

| Step 7 | Wald | P       | HR (95.0% CI for HR) |
|--------|------|---------|---------------------|
| Age    | 7.579 | .006    | 1.025 (1.007–1.044) |
| “APACHE II” | 3.006 | .083    | 0.978 (0.954–1.003) |
| “mCCCI” | 9.748 | .002    | 1.128 (1.046–1.217) |
| “SOFA score*” | 14.389 | <.001   | 1.010 (1.000–1.020) |
| Leukocyte* | 8.425 | .004    | 1.010 (1.000–1.020) |
| Blood urea nitrogen* | 4.764 | .029    | 1.012 (1.001–1.023) |
| Albumin* | 4.094 | .043    | 0.972 (0.946–0.999) |

*At admission.*

*Statistically significant P values are in bold.*

APACHE II = Acute Physiology and Chronic Health Evaluation II, CI = Confidence interval, HR = hazard ratio, mCCI = modified Charlson Comorbidity Index, NRS-2002 = Nutrition Risk Screening 2002, SOFA = Sequential Organ Failure Assessment, Wald = test statistic. SOFA: Sequential Organ Failure Assessment Score.
specify to be 56.1%. In addition, in the ROC analysis of this study, the AUC of “APACHE II” was calculated as 0.578, and we found this result as statistically significant. This result shows that in this study, the “APACHE II” can anticipate mortality in line with the literature.

The “SOFA” score is a validated tool to anticipate morbidity and mortality in ICUs. Ceriani et al. reported that the “SOFA” score on the first day was reliable for the anticipation of in ICU’s mortality. In our study, the first-day “SOFA” score was significantly higher for the mortality group. “SOFA” score, which is simpler than “APACHE II,” may be preferred in predicting mortality.

It is often not possible to predict what a patient’s health status will be after an acute injury or serious illness. The concomitant hospital mortality in APE patients. The concomitant levels of plasma osmolality may have a predictive value for in-hospital mortality. In our study, the first-day “SOFA” score was significantly higher for the mortality group. “SOFA” score, which is simpler than “APACHE II,” may be preferred in predicting mortality.

It is often not possible to predict what a patient’s health status will be after an acute injury or serious illness. The concomitant diseases may affect patient morbidity and mortality. Charlson et al. invented a scoring system for the anticipation of 1-year mortality in hospitalized patients and validate it. Murray et al. state that the “Charlson Index” was anticipated 1-year mortality for the emergency unit patient population. Although the patients included in our study mostly had respiratory failure due to lung pathologies, we found a strong association between the “mCCI” score and mortality. In conclusion, the sum of the index score is an indicator of disease burden and anticipated mortality.

Chen et al. found that “NRS-2002” scores anticipate 1-year mortality in chronic obstructive pulmonary disease (COPD) patients with respiratory failure. They revealed that the cut-off value that could predict long-term mortality was 3 points and above for “NRS-2002.” “NRS-2002” score being ≥3 at the time of admission was interpreted as an indicator of increased risk of mortality. In this study, we found the “NRS-2002” total scores were significantly higher in the mortality group.

In addition, we observed that the increase in “blood urea nitrogen (BUN)” and the decrease in albumin, which can be directly or indirectly related to nutrition, are associated with mortality. “BUN” reflects prognosis in different diseases. Its role in tubular reabsorption and physiological fluid balance is known. We assume that integrating the “NRS-2002” score with other objective nutritional evaluation modalities and some laboratory values (such as “BUN,” albumin) can predict the patient’s prognosis more precisely.

Some studies evaluated the prognostic significance of serum osmolality in clinical settings. The studies were conducted on certain populations and diseases. Oz et al. found that in patients with acute pulmonary embolism (APE), the predictive value of plasma osmolality showed significance for in-hospital mortality. They enrolled 245 consecutive intermediate or high-risk APE patients. The study population was divided into three groups based on the increased plasma osmolality. The in-hospital mortality was the primary endpoint. After adjusting for all risk factors, in-hospital mortality was significantly higher in the highest plasma osmolality group. They concluded that elevated levels of plasma osmolality may have a predictive value for in-hospital mortality in APE patients.

Tsujimoto et al. evaluated predialysis patients in terms of plasma osmolality. They planned a prospective cohort study of 1240 patients undergoing hemodialysis (HD). As a conclusion, they found that low predialysis calculated osmolality was an independent risk factor of all-cause mortality.

The relationship between serum osmolality and mortality was shown in patients with myocardial infarction, acute coronary syndrome, heart failure, and acute spontaneous intracerebral hemorrhage in different studies. There was no study on the predictive importance of serum or plasma osmolality in respiratory failure patients that were identified in an English literature search. Although our main hypothesis, serum osmolality, and other biochemical laboratory parameters were not successful in predicting the risk of mortality independently, our study was conducted with a large number of patients in a specific disease group. This constitutes the main contribution of the study to the literature.

“Serum osmolality” has a significant impact on the extracellular and intracellular dispersal of water. Impairment in “serum osmolality” associated with intracellular dehydration or edema. These conditions are very frequent in patients admitted to the ICUs, with potentially undesirable consequences. Holtfreter et al. revealed that “serum osmolality” anticipates mortality in “ICUs” (AUC=0.732) and they revealed an “S-shaped” relation between them. Shen et al. concluded that hyperosmolality has a “U”-shaped association with mortality. Nicholson et al. state that both the calculated hypo-osmolality and hyperosmolality at admission were related to higher mortality.

However, in this study, we found no significant difference in terms of mean “serum osmolality.” For explaining this result, we assumed that our study comprised only COPD patients with respiratory failure patients, unlike other studies. So, it should be considered that our patient group was more homogeneous and therefore no difference in serum osmolality could be observed. On the contrary, the findings for patients with pulmonary disease are conflicting.

Experimental data revealed that the hyperosmolar environment (400 mmoL/L, in vitro) can suppress lung injury by upregulating the translation of cytokine-encoding messenger RNAs and reducing the adhesion of neutrophils to pulmonary microvascular endothelial cells. Clinical studies have shown that there is no correlation between hypernatremia, which reflects the effect of serum osmolality to a certain extent, and ICU mortality in patients with respiratory disease.

4.1. Limitations

This study was a single-centered study with a homogenous population. However, such large-scale studies conducted in specific intensive care units such as “PICU” are very few in the literature. The analysis of the entire 1-year data was carried out to avoid bias in terms of acute respiratory failure developing over seasonal shifting exacerbations of respiratory diseases. The strongest aspect of our study is that it presents real-life data.

5. Conclusion

The diagnosis, treatment, and management capabilities of critical patients are increasing. Moreover, there is a strong consensus that critically ill cases should be hospitalized in intensive care units, and those patients who are not critical and at a low risk of mortality place an excessive financial burden on the system. Many studies are carried out to reduce intensive care costs, measure ICU performance, and enhance the standard of patient care. For using the “ICUs” system efficiently, cases should be categorized according to disease severity and mortality risks. However, for critically ill patients, a heterogeneous patient population complicates risk stratification.

We found that the scoring systems (“APACHE II, SOFA, mCCI, NRS-2002 scores”), which are frequently used in
intensive care units, we were successful in predicting the risk of mortality in our patient group, in line with the literature. In addition, we observed that advanced age, higher leukocyte, higher BUN, and low albumin levels at hospitalization predicted mortality risk in line with the literature. However, we have also concluded that our main hypothesis, serum osmolarity, and other biochemical laboratory parameters were not successful in predicting the risk of mortality independently. Our study was conducted with a large number of patients in a specific disease group. Although we could not identify a practical method in our study, we think that our results will guide future studies on this subject. This study addressed a knowledge gap concerning the association between serum osmolarity and mortality risk, and this is the study’s key addition to the literature.

Author contributions

Conceptualization: Deniz Çelik, Murat Yildz.
Data curation: Deniz Çelik, Murat Yildz, Ayşe Cifçi.
Formal analysis: Deniz Çelik, Murat Yildz, Ayşe Cifçi.
Investigation: Deniz Çelik, Murat Yildz, Ayşe Cifçi.
Methodology: Deniz Çelik, Murat Yildz, Ayşe Cifçi.
Project administration: Deniz Çelik, Murat Yildz.
Resources: Deniz Çelik, Murat Yildz.
Supervision: Deniz Çelik, Murat Yildz.
Validation: Deniz Çelik, Murat Yildz.
Visualization: Deniz Çelik, Murat Yildz.
Writing – original draft: Deniz Çelik, Murat Yildz, Ayşe Cifçi.
Writing – review & editing: Deniz Çelik, Murat Yildz, Ayşe Cifçi.

References

[1] Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818–29.
[2] Weingarten S, Bolus R, Riedinger MS, et al. The principle of parsimony: Glasgow Coma Scale score predicts mortality as well as the APACHE II score for stroke patients. Stroke 1990;21:1280–2.
[3] Feinstein AR. The pre-therapeutic classification of co-morbidity in chronic disease. J Chronic Dis 1970;23:455–68.
[4] Sarfati D. Review of methods used to measure comorbidity in cancer populations: no gold standard exists. J Clin Epidemiol 2012;65: 924–33.
[5] Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707–10.
[6] Strauss R, Wehler M, Mehler K, et al. Thrombocytopenia in patients in the medical intensive care unit: bleeding prevalence, transfusion requirements, and outcome. Crit Care Med 2002;30:1765–71.
[7] Bhatla A, Sankaralingam S, Dundas R, et al. Influence of raised plasma osmolality on clinical outcome after acute stroke. Stroke 2000;31: 2043–8.
[8] Oz A, Canlar T, Hayiroglu MI, et al. The predictive value of plasma osmolality in in-hospital mortality in patients with acute pulmonary embolism. Clin Respir J 2019;13:174–83.
[9] Tsujiyama Y, Tsutsui M, Ohnishi T, et al. Low predialysis plasma calculated osmolality is associated with higher all-cause mortality: the Japanese Dialysis Outcomes and Practice Patterns Study (J-DOPPS). Nephron 2020;144:138–46.
[10] Tatli MA, Kaya A, Keskın M, et al. Can we use plasma hyperosmolality as a predictor of mortality for ST-segment elevation myocardial infarction? Coron Artery Dis 2017;28:70–6.
[11] Rohla M, Freyhofer MK, Tenterzis I, et al. Plasma osmolality predicts clinical outcome in patients with acute coronary syndrome undergoing percutaneous coronary intervention. Eur Heart J Acute Cardiovasc Care 2014;3:84–92.
[12] Kaya H, Yucel O, Ege MR, et al. Plasma osmolality predicts mortality in patients with heart failure with reduced ejection fraction. Kardiol Pol 2017;75:316–22.
[13] Nag C, Das K, Ghosh M, Khandakar MR. Plasma osmolality in acute spontaneous intra-cerebral hemorrhage: does it influence hematoma volume and clinical outcome? J Res Med Sci 2012;17:548–51.
[14] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
[15] Beddu S, Bruns FJ, Saul M, et al. A simple comorbidity scale predicts clinical outcomes and costs in dialysis patients. Am J Med 2000;108:609–13.
[16] Mendez-Tellez PA, Dorman T. Predicting patient outcomes, futility, and resource utilization in the intensive care unit: the role of severity scoring systems and general outcome prediction models. Mayo Clin Proc 2005;80:161–3.
[17] Rapsang AG, Shyam DC. Scoring systems in the intensive care unit: a compendium. Indian J Crit Care Med 2014;18:220–8.
[18] Shortell SM, Zimmerman JE, Rousseau DM, et al. The performance of intensive care units: does good management make a difference? Med Care 1994;32:508–25.
[19] Cullen DJ, Chernow B. Predicting outcome in critically ill patients. Crit Care Med 1994;22:1345–8.
[20] Salihu HJ, Soares M. ICU severity of illness scores: APACHE SAPS and MPM. Curr Opin Crit Care 2014;20:557–65.
[21] Vasilevskis EE, Kuzniewicz MW, Cason BA, et al. Mortality probability model III and simplified acute physiology score II: assessing their value in predicting length of stay and comparison to APACHE IV. Chest 2009;136:89–101.
[22] Godinjak A, Iglc A, Rama A, et al. Predictive value of SAPS II and APACHE II scoring systems for patient outcome in a medical intensive care unit. Acta Med Acad 2016;45:97–103.
[23] Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: a systematic review. Crit Care 2008;12:R161.
[24] Ceriani R, Mazzoni M, Bortone F, et al. Application of the sequential organ failure assessment score to cardiac surgical patients. Chest 2003;123:1229–39.
[25] Jencks SF, Dobsin A. Refining case-mix adjustment. The research evidence. N Engl J Med 1987;317:679–86.
[26] Murray SB, Bates DW, Ngo L, et al. Charlson Index is associated with resource utilization in the intensive care unit: the role of severity scoring systems and general outcome prediction models. Mayo Clin Proc 2014;89:217–29.
[27] Aronson D, Mittleman MA, Burger AJ. Elevated blood urea nitrogen level as a predictor of mortality in patients admitted for uncomplicated heart failure. Am J Med 2004;116:466–73.
[28] Bulat M, Klarica M. Fluid filtration and reabsorption across microvascular walls: control by oncotic or osmotic pressure? (secondary classification). Croat Med J 2014;55:291–8.
[29] Holtfreter B, Bandt C, Kuhn SO, et al. Serum osmolality and outcome in intensive care unit patients. Acta Anaesthesiol Scand 2006;50:970–7.
[30] Shem Y, Cheng X, Ying M, et al. Association between serum osmolality and mortality in patients who are critically ill: a retrospective cohort study. BMJ Open 2017;7:e015729.
[31] Nicholson T, Bennett K, Silke B. Serum osmolality as an outcome predictor in hospital emergency medical admissions. Eur J Intern Med 2018;57:70–5.
[32] Aronson D, Mittleman MA, Burger AJ. Elevated blood urea nitrogen level as a predictor of mortality in patients admitted for uncomplicated heart failure. Am J Med 2004;116:466–73.