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Serum osmolarity does not predict mortality in patients with respiratory failure

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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

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This study has not been published or presented anywhere before. I confirm that the manuscript has been submitted solely to this journal and is not published, in-press, or submitted elsewhere. I confirm that all the research meets the ethical guidelines, including adherence to the legal requirements of the study country. All authors declared that they participated in the design, conduct, and analysis of the article and approved the final version. In this study, national and international ethical rules are observed. Approval for this study was obtained from the Ankara Atatürk Chest Diseases and Chest Surgery Training and Research Hospital, Medical Specialization Education Board (Date: 04.03.2021, Decision number: 716). The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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evaluation. These scales and instruments are important tools for validating the therapeutic procedures used and keeping track of treatment quality and expenses. Simultaneously, they contribute to the adoption of more effective interventional and pharmacological therapy options.[2]

The "Acute Physiology and Chronic Health Evaluation II" (APACHE II) and the "Simplified Acute Physiology Score II" ("SAPS II") are 2 of the most well-known scales. These scales measure numerous physiologic parameters while taking age, chronic illnesses, and surgical history into consideration. The patients should be scored with both scales on the first day of admission to the "ICUs." Thus, we can assess the patient's condition and estimate the risk of mortality during hospitalization.[1]

Some factors are shared by all of the scales, but some variables are substituted by other variables that enhance the performance. The most significant distinctions were about concomitant chronic illnesses. The problem regarding the confusing effects of comorbidities on survival has been an accepted fact since the early 1970 s.[3] Many comorbidity scoring systems have been created and are now in use. One of the oldest and most commonly used systems is the modified "Charlson Comorbidity Index" ("mCCI").[4]

Another scale gaining popularity in "ICUs" is the "Sequential Organ Failure Assessment" ("SOFA") score. "SOFA" examines multiple organ dysfunction. "SOFA" is a daily evaluation score of a patient's status that is based on indicators that are frequently observed in "ICUs." It takes into consideration important systems characteristics but ignores chronic illnesses and aging.[5]

Multiple studies done in various "ICU" populations have established prognostic indicators that are documented in daily clinical practice or may be easily acquired.[6,7] Even though a single parameter is likely to give less information than complicated scores, single parameters can nevertheless be useful in ICUs practice. This research aims to identify the parameters that can be determined routinely, quickly, simply, and inexpensively, have prognostic significance and that can be routinely evaluated. Serum osmolarity may be measured with less cost and in less time than scoring methods.

The formula of serum osmolarity is (2 x Sodium) + (Glucose/18) + (Blood Urea Nitrogen/2.8). The normal limits are 275 to 295 mOsmol/L. Osmolarity refers to the number of solute particles per 1 L of solvent, whereas osmolality is the number of solute particles in 1 kg of solvent. For dilute solutions, such as blood, the difference between osmolarity and osmolality is insignificant.

"Serum osmolarity" has a significant impact on the extracellular and intracellular dispersal of water. Impairment in "serum osmolarity" is associated with intracellular dehydration or edema.

Some studies evaluated the prognostic significance of serum osmolarity. Öz et al[8] found that in patients with acute pulmonary embolism, the predictive value of plasma osmolarity showed significance for in-hospital mortality. Tsujimoto et al[9] evaluated predialysis patients in terms of plasma osmolarity and they found that plasma calculated osmolarity is associated with higher all-cause mortality. The same relationship was shown in patients with myocardial infarction, acute coronary syndrome, heart failure, and acute spontaneous intracerebral hemorrhage.[10–13] Our study will highlight whether this relationship is valid for patients with respiratory failure or not.

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.[5]

2.5. Statistical method

SPSS for Windows, version 22.0, was used to analyze the data (SPSS Inc., Chicago, IL). The Kolmogorov–Smirnov test was used to assess if the distribution of continuous variables was normal or not. The Levene test was performed to assess the homogeneity of variances. Continuous data were represented as mean SD for normal distributions and median (minimum-maximum value) for skewed distributions unless otherwise indicated. The number of cases was used to characterize categorical data (%). Analytical statistics differences in normally distributed variables between 2 independent groups were examined by Student *t* test. For comparisons of non-normally distributed data, the Mann–Whitney *U* test was used. Pearson's Chi-square test and Fisher's

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 osmolarity, "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. 5.1% (n = 23) died in the "PICU." All patients were followed up remotely until March 31, 3021, 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 ± 6.23. 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 osmolarity, "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 osmolarity 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 osmolarity	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 osmolarity*	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.

Table 2

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

Parameters	Mortality group (n = 171)		Survivors (n = 278)		P
	n	%	n	%	
Gender					
Male	116	67.8%	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	0.4%	0.999	
Mild liver disease	5	2.9%	6	2.2%	.755
Diabetes mellitus	60	35.1%	109	39.2%	.381
Hemiplegia	-	2	0.7%	0.527	
Moderate kidney disease	13	7.6%	15	5.4%	.348
Presence of any malignancy	29	17.0%	16	5.8%	<.001
Lymphoma	1	0.6%	–		.381
Moderate liver disease	1	0.6%	–		.381
Presence of metastatic solid malignity	13	7.6%	2	0.7%	<.001

"Continuous variables were expressed as either the mean ± standard deviation SD or median minimum-maximum value and categorical variables Continuous variables were expressed as either the mean ± standard deviation SD and median minimum-maximum value expressed as either frequency percentage. Continuous variables were compared with the Student *t* test or Mann–Whitney *U* test and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant *P*-values are in bold."

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

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 5).

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 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%)	.003
	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 (262.38–320.93)	294.10 (235.25–345.33)	.098
"APACHE II " median (min-max)		18 (3–47)	16 (0–34)	.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 either the mean ± standard deviation (SD) or median (minimum-maximum value). Continuous variables were compared with the Student *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.

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	(560–80,900)	**.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	±8.66	**<.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	(2.82–486)	.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 osmolarity*	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 *t* test or Mann–Whitney *U* test. Statistically significant *P* values are in bold."

* At admission.

prediction is important in "ICU" administration.[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.[19]

The "APACHE II" is the most widely applied scoring system in "ICUs" across the world.[20] Vasilevskis et al[21] conducted a study and concluded that only the "APACHE II" indicated a good distinction in predicting "ICU" mortality. Godinjak et al[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 5

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

		Wald	P	HR	95.0% CI for HR	
Step 1	Age	4.554	.033	1.028	1.002	1.055
	Serum osmolarity	0.066	.797	0.998	0.984	1.012
	"APACHE II"	2.970	.085	0.978	0.953	1.003
	"mCCI"	7.868	.005	1.119	1.034	1.211
	"NRS-2002 total score"	0.327	.567	0.860	0.513	1.442
	"SOFA score*"	14.033	<.001	1.232	1.105	1.375
	Leukocyte*	7.796	.005	1.010	1.000	1.020
	Hemoglobin*	0.032	.858	0.981	0.799	1.206
	Hematocrit*	0.060	.806	0.992	0.931	1.057
	Calcium*	0.501	.479	1.091	0.857	1.388
	Blood urea nitrogen*	4.182	.041	1.013	1.001	1.025
	Albumin*	0.392	.531	0.978	0.911	1.049
Step 7	Age	7.579	**.006**	1.025	1.007	1.044
	"APACHE II"	3.006	**.083**	0.978	0.954	1.003
	"mCCI"	9.748	**.002**	1.128	1.046	1.217
	"SOFA score*"	14.389	**<.001**	1.231	1.106	1.370
	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.

specificity 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."[23] Ceriani et al[24] reported that the "SOFA" score on the first day was reliable for the anticipation of in "ICUs" 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.[25] The concomitant diseases may affect patient morbidity and mortality. Charlson et al[14] invented a scoring system for the anticipation of 1-year mortality in hospitalized patients and validate it. Murray et al[26] 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[27] 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.[27] 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.[28] 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 osmolarity in clinical settings. The studies were conducted on certain populations and diseases. Öz et al[8] 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.[8]

Tsujimoto et al[9] 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.[9]

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.[10–13]

There was no study on the predictive importance of serum or plasma osmolarity in respiratory failure patients that were identified in an English literature search. Although 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. This constitutes the main contribution of the study to the literature.

"Serum osmolarity" has a significant impact on the extracellular and intracellular dispersal of water. Impairment in "serum osmolarity" associated with intracellular dehydration or edema. These conditions are very frequent in patients admitted to the "ICUs," with potentially undesirable consequences.[29]

Holtfreter et al[30] revealed that "serum osmolarity" anticipates mortality in "ICUs" (AUC = 0.732) and they revealed an "S-shaped" relation between them. Shen et al[31] concluded that hyperosmolarity has a "U"-shaped association with mortality. Nicholson et al[32] state that both the calculated hypo-osmolarity and hyperosmolarity at admission were related to higher mortality.

However, in this study, we found no significant difference in terms of mean "serum osmolarity." 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 osmolarity 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.[33,34] Clinical studies have shown that there is no correlation between hypernatremia, which reflects the effect of serum osmolarity to a certain extent, and ICU mortality in patients with respiratory disease.[35]

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, 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

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