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The Effectiveness of Scoring Systems and Various Biochemical Parameters in Predicting Survival in a Respiratory Intensive Care Unit

[Solunumsal Yoğun Bakım Ünitesi'nde Skorlama Sistemlerinin ve Çeşitli Biyokimyasal Verilerin Yaşam Beklentisine Etkisi]

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ABSTRACT

Aim: The aim of the present study was to compare various clinical and biochemical parameters, Acute Physiological and Chronic Health Evaluation II (APACHE II), and Sequential Organ Failure Assessment (SOFA) for their effectiveness in distinguishing surviving and non-surviving patients who had acute respiratory failure (ARF) while in the Respiratory Intensive Care Unit (RICU).

Materials and Methods: A prospective observational clinical study was carried out in the RICU of the Chest Disease Clinic. One hundred and sixteen patients were observed. Laboratory parameters and scoring points for the first 24 hours were recorded. Patients' demographic characteristics, biochemical parameters, length of stay at the RICU, and GCS, APACHE II and SOFA scores were also recorded. The primary outcome of the current study was the mortality rate in the RICU.

Results: Mortality rate was determined to be 39.6% (46 patients) of 116 patients, although the predicted mortality rate was 49.7 %. There was a statistically significant difference between surviving and non-surviving patients in terms of SOFA (p= 0.004, OR= 1.33, CI= 1.10-1.61), INR (p = 0.02, OR = 3.95, CI = 1.30-12.07), albumin (p= 0.02, OR= 2.58, CI= 1.17-5.64), and PCO2 levels (p= 0.005, OR= 1.04, CI= 1.01-1.06), respectively.

Conclusion: Our results suggest that the mortality rate may be higher when SOFA, INR, albumin and PCO2 abnormalities are seen. Co-morbidities such as non-pulmonary organ dysfunction and metabolic disorders other than respiratory failure may have contributed additionally to increased mortality risk for patients who were admitted to the RICU. These parameters should be taken into account when ARF patients are admitted to the RICU.

Key words: Respiratory ICU, mortality, outcome, biochemical parameters.

ÖZET

Amaç: Bu çalışma Solunumsal Yoğun Bakım Ünitesi (SYBÜ)'ne akut solunum yetmezliği nedeniyle (ASY) yatan hastaların çeşitli klinik ve biyokimyasal parametreleri ile Glasgow Koma Skalası (GKS), Acute Physiology Assessment and Chronic Health Evaluation II (APACHE II) ve Sequential Organ Failure Assessment (SOFA) skorlarını yaşayan ve ölen hastalar arasında karşılaştırarak etkinliklerini saptamak amacıyla yapıldı.

Gereç ve Yöntem: Bu ileriye dönük gözlemsel klinik çalışma, Göğüs Hastalıkları SYBÜ'nde yapıldı. Toplam 116 hasta değerlendirildi. hastaların ilk 24 saatteki laboratuar parametreleri ve skorlama sonuçları kaydedildi. Ayrıca hastaların demografik özellikleri, biyokimyasal parametreleri, SYBÜ'nde yatış süreleri, GKS, APACHE II ve SOFA skorları kaydedildi. Çalışmanın birincil sonlanım noktası SYBÜ mortalite oranlarıydı.

Bulgular: Hastaların beklenen mortalite oranı %49.7 iken, gerçekleşen mortalite oranı %39.6 (46 hasta) olarak bulundu. Hayatta kalan ve ölen hastalar arasında SOFA (p= 0.004, OR= 1.33, CI= 1.10-1.61), INR (p = 0.02, OR = 3.95, CI = 1.30-12.07), albumin (p= 0.02, OR= 2.58, CI= 1.17-5.64) ve PCO2 (p= 0.005, OR= 1.04, CI= 1.01-1.06) seviyeleri açısından istatistiksel olarak anlamlı farklılık mevcuttu.

Sonuç: Bulgularımız, SOFA, INR, albumin ve PCO2 anormalliklerinin varlığında mortalite oranlarının daha yüksek olabileceğini düşündürmektedir. SYBÜ'ne kabul edilen hastalarda ASY'ne ilave akciğer dışı organ fonksiyon bozukluğu, metabolik bozukluklar gibi ek organ disfonksiyonlarının olmasının mortalitenin yüksek seyretmesinde ek katkısı olabilir. Bu parametreler SYBÜ'ne ASY hastaları kabul edilirken dikkate alınmalıdır.

Anahtar Sözcükler: Solunumsal YBÜ, mortalite, prognoz, biyokimyasal parametreler.

Introduction

The mortality rates of intensive care units (ICU) vary between 16 and 67%, depending on the type of ICU and the variability of the diseases of the patients (1-3).

There are several scoring systems which have been developed for predicting ICU mortality, such as the Acute Physiology Assessment and Chronic Health Evaluation (APACHE) II, Simplified Acute Physiology Score (SAPS) II and Mortality Probability Models (MPM), as well the Sepsis related Organ Failure Score (SOFA), for predicting the degree of organ failure and the number of organs failing (4, 5).

Various factors have been identified as predictors of ICU mortality: respiratory failure requiring mechanical ventilation, severity of underlying disease, renal failure, sepsis, presence of malignancy, age, various biochemical and physiological parameters, cardiac failure-arrhythmia, body mass index, and APACHE II scores (2, 3, 6-9).

Many investigators have shown that the outcome of patients with acute respiratory failure (ARF) is affected by various non-pulmonary organ dysfunctions (8, 10-17).

Determination of the factors predicting mortality is of interest to intensivists during management of patients in the ICU.

For these reasons, we carried out this study in a respiratory intensive care unit (RICU) to determine the factors influencing mortality rates. We compared the results of several clinical and biochemical parameters, APACHE II, SOFA and GCS of patients who did or did not survive during their stay in the RICU.

Materials and Methods:

This prospective observational clinical study was carried out between August 2007 and August 2008. We are actively involved in managing patients with ARF at our specialized RICU in Dicle University Medical Faculty Hospital.

Patients with known malignant diseases were excluded. The co-morbidities of the patients were ischemic heart diseases, cerebrovascular diseases, diabetes mellitus, arrhythmias, renal insuffiency, gastrointestinal hemorrhages, neuromuscular diseases, rheumatological diseases, and hepatic cirrhosis. The time between admittance and the end of stay in the RICU was recorded as length of stay.

The diagnostic criteria of ARF were accepted as (room air), PaO_2 <55 mm Hg (hypoxemic RF), or $PaCO_2$ > 45 mm Hg (hypercapnic RF) in arterial blood gas analyses. All patients received standard treatment procedures in relation with their diseases. This study was carried out in accordance with the principles of the Helsinki Declaration.

Demographic data were recorded for a total of 116 patients (83 males, 33 females) who were admitted to the RICU. Also, APACHE II and SOFA scores, Glasgow Coma Scale, white blood cells (WBC), red blood cells (RBC) and platelet (Plt) counts, hemoglobin (Hgb), hematocrit (Hct), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), sodium, potassium, chlorine, glucose, urea and creatinin levels, prothrombin time (PTT), INR (International Normalized Ratio), alanin aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), total (T) bilirubin, direct (D) bilirubin, total protein, and albumin levels were recorded for the first 24 hours after RICU admission. Arterial blood gas (ABG) parameters such as pH, pO_2, pCO_2, lactate, HCO_3, osmolality, and base excess (BE) were also recorded. In addition, vital signs such as body temperature, respiratory rate (RR), heart rate (HT), systolic and diastolic blood pressure (SBP and DBP) were recorded for the first 24 hours after RICU admission. APACHE II and SOFA scores were calculated from the worst values during the first 24 hours after RICU admission.

Hematological parameters were obtained with Cell_DYN 3700, Abbott, USA, CRP; Immage Immunochemistry S/N 2528, Beckman Coulter, USA, ESR; Sed Rate-Screener, Greiner Bio-One, Austria; biochemical parameters with Architect c 16000^{TM}, Abbott, USA, and ABG parameters with ABL 700, Radiometer, Denmark.

Statistical Analysis

Continuous variables were analyzed using student's t-test, and chi square test was used to compare ordinal variables. Baseline parameters significant on univariate analysis at $p < 0.20$ were identified as potential predictor variables. These parameters were evaluated using multivariate logistic regression analysis (backward stepwise method) to determine independent predictors of mortality. Significance was considered at $p \leq 0.05$ (only two tailed) for the present study. Analyses were performed using SPSS version 15.0 (SPSS, Inc., Chicago, USA).

Results

Mean age of patients was 64 ± 17 years, with a range from 19 to 100 years. Twenty-eight percent of the patients were female (33 patients), and 72% were male (83 patients). The age of 83 of the 116 patients (71.55%) was 60 years or higher. There was no statistical difference between surviving and non-surviving patients in terms of age and sex distribution ($p= 0.27$, $p= 0.70$ respectively). The most common cause of admission to RICU was ARF due to COPD exacerbation. The other causes of the admission to RICU of patients were shown in Table 1. There was at least one co-morbidity in 63 (53.4%) of the patients (34 non-surviving, 29 surviving), at least two co-morbidities in 23.3% of the patients, and at least three in 4.3% of the patients. These were diabetes mellitus (12), neurological (11), renal (10), hepatic (5), thyroid (2) and other diseases (4).

The demographic characteristics (age, gender etc.) of surviving and non-surviving patients were similar. The logistic regression analysis of the influence of clinical

scores, and biochemical and demographic parameters on the RICU outcome of the patients, are shown in Table 2.

Although the mean APACHE II scores were 21.0±7.1 for surviving patients and 29.8±7.6 for non-surviving patients, no difference was observed between the two groups by logistic regression analysis (p= 0.23, OR= 0.94, CI= 0.84-1.04). And although the mean APACHE II score was 24 and the predicted death rate was 49.7%, the actual death rate was determined as 39.6%. The mean SOFA score for surviving patients was 3.83 ± 2.21, and for non-surviving patients it was 6.17 ± 3.27. There was a statistically significant difference between surviving and non-surviving patients in terms of SOFA (p= 0.004, OR= 1.33, CI= 1.10-1.61).

INR levels of surviving patients were 1.23 ± 0.36 and 1.50 ± 0.52 for non-surviving patients. There was a statistically significant difference between surviving and non-surviving patients in terms of INR levels (p = 0.02, OR = 3.95, CI = 1.30-12.07).

Mean albumin levels were found to be 2.75 ± 0.62 g/dl in surviving patients, and 2.34 ± 0.67 g/dl in non-surviving patients. There was a statistically significant difference between surviving and non-surviving patients in terms of albumin levels (p= 0.02, OR= 2.58, CI= 1.17-5.64).

Hypercapnia was found in 47 out of a total of 62 COPD patients. Twenty-seven of them were non-surviving (23.27%). There was a statistically significant difference between surviving and non-surviving patients in terms of PCO2 levels (p= 0.005, OR= 1.04, CI= 1.01-1.06).

There was no statistically significant difference between non-surviving and surviving patients in the cases of clinical and biochemical parameters of age, gender, lactate, CRP, AST, ALT and osmolality.

The median length of stay in the RICU was 10 days (range 1 to 139 days), which was 5 days (range 1 to 72 days), for non-surviving patients, and 11.5 days (range 3 to 139 days), for surviving patients. The difference was statisti-

Table 1. The causes of the acute respiratory failure for admission of patients to the respiratory intensive care

	Total (n=116, 100%)	Survived (n=70, 60%)	Non-survived (n=46 40%)
COPD*	67 (58%)	43 (37%)	24 (21%)
Pneumonia	40 (34%)	21 (18%)	19 (16%)
Massive PTE	15 (13%)	8 (7%)	7 (6%)
Severe Sepsis/Septic shock	8 (7%)	2 (2%)	6 (5%)
Other causes**	13 (11%)	7 (6%)	6 (5%)

*Chronic obstructive pulmonary disease

**Acute Respiratory Distress Syndrome, Criptogenic Organizing Pneumonitis, Pulmo-renal Syndrome, Interstitial lung disease, Obesity hypoventilation syndrome, Obstructive sleep apnoea, severe Bronchial Asthma exacerbation

Table 2. The multivariate analysis of the influence of clinical scores, and biochemical and demographic parameters on the RICU outcome of the patients.

	p	OR	95.0% CI
Age	0.50	1.01	(0.98-1.04)
Lactate	0.43	1.01	(0.98-1.05)
Gender	0.20	0.50	(0.17-1.46)
CRP	0.10	1.00	(0.99-1.01)
pCO2	0.005	1.04	(1.01-1.06)
Osmolality	0.70	1.01	(0.97-1.05)
AST	0.92	1.00	(0.99-1.01)
ALT	0.70	1.00	(0.99-1.01)
Albumin	0.02	2.58	(1.17-5.64)
INR	0.02	3.95	(1.30-12.07)
SOFA	0.004	1.33	(1.10-1.61)
APACHE II	0.23	0.94	(0.84-1.04)

OR, odd's ratio; CI, confidence interval; CRP, C reactive protein; PaCO2, partial arterial carbon dioxide pressure; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; INR, International normalized ratio; SOFA, Sequential organ failure assessment; APACHE, acute physiology and chronic health evaluation.

cal significant between surviving and non-surviving patients in terms of length of stay ($p < 0.01$).

Discussion

Risk prediction is an important issue in intensive care. The APACHE II score is commonly used as a severity score during the first 24 hours in the ICU, while the SOFA score was developed to estimate morbidity during ICU stay.

We found statistically significant differences between surviving and non-surviving patients according to INR levels. To our knowledge, no data is available about RICU mortality and INR levels. Therefore, our data can be useful on this subject. In hospital-based and centralized anti-coagulation clinics in Sweden, the records of 42 451 patients (42% women) who attended 46 clinics were analyzed. A marked decrease was reported in mortality from all causes with increasing INR in the range of 1-1.8, but also a substantial increase in mortality for INR values >2.5 (18). Our results suggest that the high values of INR may be used for mortality prediction in the RICU.

In our study, we found by using the SOFA scores that multiple organ failure was related to high mortality rates. Flaatten et al. reported that mortality increased with the additional number of organs in failure (19). Also, Vasilyev et al. maintained that ARF patients with multi-organ failure had lower survival rates (10%) than those with pulmonary dysfunction alone (45%) (20). Timsit et al. reported that daily LOD and SOFA scores showed good accuracy and internal consistency, and they could be used to adjust severity for events occurring in the intensive care unit (21). Acute kidney failure as a symptom of the multiple organ dysfunction syndrome results in a mortality of up to 60% (22). ICU mortality was 3 times higher in ARF with respect to other patients (42.8% vs 14.0%, $p < 0.01$) (23). Holtfreter et al. reported a significant correlation between urea level and ICU mortality by using univariate analysis (24). Our findings indicate that the high SOFA scores related with the multiple organ failure and realized high mortality level.

Laupland et al. showed that patients with prolonged critical illness had high mortality rates in the acute phase (25). In intubated patients, the cause of the acute attack of COPD, presence of co-morbidity, sepsis, diastolic blood pressure (DBP), length of hospital stay and RICU stay, APACHE II score on admission, complications of MV, serum hemoglobin, C-reactive protein (CRP) levels, arterial blood $PaCO_2$, HCO_3 levels, and inadequate metabolic compensation for respiratory acidosis were found to show a statistically significant difference between survivors and non-survivors (26). We detected that the PCO_2 level of non-surviving patients was significantly higher than that of surviving patients. According to our findings, the mortality rates have been high in the patients who have high PCO2 levels in the first 24 hours.

We found statistically significant differences between the two groups in serum albumin levels. It has been well documented by other researchers that hypoalbuminemic patients have a higher morbidity and mortality rate when compared with patients with normal serum albumin (27, 28). We found relationship between low serum albumin levels and RICU mortality.

Elevated initial and 24-hour lactate levels were significantly correlated with mortality and appeared to be superior to corresponding base deficit levels in 137 surgical ICU patients who had serial lactate and blood gas measurements (29). The lactate level was determined to be higher than 7.2 in 93 patients (80.1%). Thirty-six of these were non-surviving (38.7%). We did not observe significant difference in lactate levels between the two groups.

Interestingly, Holtfreter et al. reported elevated serum osmolality at ICU admission, associated with an increased mortality risk in critically ill patients (24). However, we did not observe any difference in serum osmolality between surviving and non-surviving patients.

Also, we did not determine any statistically significant differences between surviving and non-surviving patients in terms of the levels of CRP, AST, and ALT. Many studies have shown various non-pulmonary organ dysfunctions in patients with ARF (8, 10-17).

Holtfreter et al. indicated that pH level was correlated with ICU mortality by using univariate analysis (24). Our results were not consistent with the results of this study.

Although the mean APACHE II score was 24 and the predicted death rate was 49.7%, the actual death rate was calculated as 39.6%, which is similar to that reported earlier (29, 30). When the blood gas analysis, age and APACHE II scores were evaluated as determinants of survival, APACHE scores seemed to predict survival more significantly ($p<0.05$) (31). We found no statistical difference between surviving and non-surviving patients in terms of APACHE II scores.

Vasilyev et al. suggested that the most important predictors of hospital survival rates of patients in ARF supported by mechanical ventilation were as follows: (1) severity of lung dysfunction; (2) etiology of the ARF; (3) intensity of mechanical ventilation required to achieve acceptable blood gas values; (4) existence and severity of hypoxemia when the patient is receiving maximum safe ventilator support; (5) duration of mechanical ventilation before the patient shows significant improvement in natural lung function; and (6) existence of multi-organ dysfunction in patients with ARF (20).

One of the main points of our study results is that 83 out of the 116 patients were over 60 years old (71.55%). In the elderly, the increased co-morbidity may contribute considerably to mortality. It is expected that the population of those aged 65 and over will reach 58% in the 2050s and that these individuals will constitute about 50% of ICU patients (32).

Conclusion

Co-morbidities such as non-pulmonary organ dysfunction and metabolic disorders other than respiratory failure may make an additional contribution to increased mortality risk for patients who are admitted to the RICU.

Our results suggest that the mortality rate may be higher when a number of biochemical abnormalities are seen in addition to ARF.

These biochemical parameters should be taken into account when ARF patients are admitted to the RICU.

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