Prognostic effect of serum sodium, glucose, creatinine in patients with acute pulmonary thromboembolism

Akut pulmoner tromboembolide serum sodyum, kreatinin ve glukoz değerlerinin prognoza etkisi

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ABSTRACT

Aim: Pulmonary thromboembolism is a disease with high mortality and morbidity. In this study, the impacts of serum sodium, glucose and creatinine levels on prognosis were investigated.
Patients and Methods: The data of the patients with PTE who received treatment between January 2010 and December 2012 were analyzed retrospectively. Routine laboratory values, arterial blood gas and transthoracic echocardiography results at the time of admission and 30-day mortality rates were recorded.
Results: The mean serum sodium level and eGFR in the group with high mortality were significantly lower compared to the other group, while the serum glucose level was higher. When the compatibility of these markers with PESI was examined, it was found that serum sodium level and eGFR were lower and serum glucose level was higher in PESI class V compared to the other classes, and this difference was statistically significant.
Conclusion: In this study, it was found that serum sodium, glucose and eGFR levels, which have the advantage of availability in every center, were compatible with RVD, troponin and PESI parameters that were previously proven prognostic factors in determining the mortality risk in acute PTE.

Key words: Acute pulmonary thromboembolism, hyponatremia, hyperglycemia, creatinine clearance.

ÖZ

Amaç: Pulmoner tromboemboli, mortalitesi ve morbiditesi yüksek olan bir hastalıktır. Bu çalışmada serum sodyum, glukoz ve kreatinin değerlerinin prognoz üzerine olan etkileri araştırılmıştır.
Hastalar ve Yöntemler: Ocak 2010 ile Aralık 2012 tarihleri arasında PTE tanısı ile yatırılarak tedavi edilen hastaların verileri retrospektif olarak incelendi. Başvuru anındaki rutin laboratuvar değerleri, arteriyel kan gazı ve transtorasik ekokardiyografi sonuçları ile 30 günlük mortalite oranları kaydedildi.
Bulgular: Her iki grup karşılaştırıldığında mortalitesi yüksek olan grubun ortalama serum sodyum düzeyi ve eGFR, diğer gruba göre anlamlı olarak daha düşükken, serum glukoz düzeyi daha yüksek saptandı. Bu belirteçlerin PESI ile uyumluluğu incelendiğinde ise PESI sınıf V'de diğer sınıflara göre serum sodyum düzeyinin ve eGFR'nin daha düşük, serum glukoz düzeyinin daha yüksek olduğu saptandı ve bu fark istatistiksel olarak anlamlı bulundu.
Sonuç: Çalışmamızda, her merkezde kolaylıkla uygulanabilme avantajına sahip parametreler olan serum sodyum, glukoz ve eGFR düzeylerinin, akut PTE'de mortalite riskini belirlemede, daha önce etkinliği kanıtlanmış prognostik faktörler olan RVD, troponin ve PESI parametreleri ile uyumluluk gösterdikleri saptandı.

Anahtar kelimeler: Akut pulmoner tromboemboli, hiponatremi, hiperglisemi, kreatinin klirensi.

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INTRODUCTION

Pulmonary thromboembolism (PTE) is frequently caused by the obstruction of the pulmonary artery or its branches with the fragments plucked from the thrombus located in the deep leg veins. Tumor cells, fat particles and amniotic fluid in addition to thrombus, can also rarely cause PTE [1]. Its incidence varies between 0.1 and 0.3%, and it has high mortality and morbidity. Mortality is reported as 25-30% in untreated cases and 2-8% in those who receive treatment [2,3]. Today, some clinical parameters such as elevated troponin-T levels, echocardiography, right ventricular dilatation (RVD) and shock or hypotension are used to predict mortality in PTE patients [1]. Among these, assessment of RVD requires echocardiography equipment with a clinician specialized in the field, and troponin levels cannot be studied in every laboratory. These difficulties necessitate new markers which are simpler, faster, inexpensive and easily accessible. In some recent studies, increased serum glucose, hyponatremia and renal dysfunction are thought to have an effect on prognosis in some cardiopulmonary diseases [4,5,6].

The aim of this study was to evaluate the correlation between the pulmonary embolism severity index (PESI) and initial serum sodium, glucose and creatinine levels, used alone and in combination, in the patients who had PTE diagnosis only and received treatment as well as their impact on the prognosis.

PATIENTS AND METHODS

The study was carried out at the Akdeniz University Faculty of Medicine Chest Diseases Clinic. The medical data of the patients who were hospitalized with the diagnosis of PTE between January 2010 and December 2012 were analyzed retrospectively. Patients with a high probability of PTE according to ventilation-perfusion (V/Q) scintigraphy and patients diagnosed with acute PTE by CT scan angiography were included in the study. Patients with a low probability according to V/Q scintigraphy and those with suboptimal CT angiography were not included in the study. In addition, patients with comorbidities such as chronic renal failure, acute coronary artery disease, and diabetes mellitus were excluded from the study.

Demographic characteristics, vital signs, state of consciousness, routine laboratory values at the time of admission, arterial blood gas and transthoracic echocardiography results along with 30-day mortality rates were recorded.

According to the results of echocardiography, right ventricular dysfunction was interpreted to be positive in the presence of at least one of the following findings:

1. Right ventricular dilatation (right ventricular end-diastolic diameter ≥30 mm or end-diastolic diameter ratio of RV/LV ≥1)

2. Paradoxical septal motion (PSM)

3. Right ventricular hypokinesis

4. Tricuspid regurgitation (jet velocity ≥2.5 m/min)

5. Pulmonary artery pressure (PAP)> 30 mmHg

The patients were divided into three groups according to the right ventricular dysfunction seen in the echocardiography as massive, submassive and non-massive PTE according to their hemodynamic stability. In massive PTE, pulmonary arterial obstruction is 60-75%. In submassive embolism, this rate is less than 60%. In non-massive emboli, small distal vessels are obstructed.

PESI [7] variables (Table 1. Pulmonary embolism severity index variables) were used for each patient to determine the patients with high 30-days short-term mortality risk in acute PTE and who needed hospitalization (Class 1: Point <65; Class 2: Point 65-85; Class 3: Point 86-10; Class 4: Point 106-125; Class 5: Point:>125).

Table 1. Pulmonary embolism severity index variables

Variable	Point
Age	1 point - for any ages
Male gender	10
Cancer	30
Heart failure	10
Chronic obstructive pulmonary disease	10
Pulse > 110/min	20
Systolic Blood Pressure <100 mmHg	30
Number of breaths ≥ 30/min	20
Body temperature < 36ºC	20
Disorientation, stupor, lethargy, coma	60
Oxygen saturation < %90	20

Glomerular filtration rates (eGFR) were calculated using the MDRD formula using the serum creatinine levels at the time of admission. According to this formula;

$$GFR = 141 \times \min(Scr/\kappa, 1)\alpha \times \max(Scr/\kappa, 1)-1.209 \times 0.993Age \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

Ethical Approval: This study was approved by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee.

Statistic: Data were analyzed by using SPSS package program. Mann Whitney U test was used for double comparisons, Fischer analysis test was performed for categorical comparisons and Pearson correlation analysis was used to determine the link between parameters. Chi-square test was used to calculate the difference between the two groups and Student's t-test was used to evaluate the different parameters. The p value <0.05 was considered statistically significant.

RESULTS

Medical data of 145 patients with PTE who received treatment were analyzed. Eleven patients with diabetes mellitus, 4 patients with coronary artery disease and 17 patients with chronic renal failure were excluded. A total of 112 patients were included in the study because medical records of one patient could not be obtained. Of these patients, 59 (52.7%) were women and 53 (47.3%) were men, and the mean age was 60.8±1.6 years. Demographic data of the patients are shown in Table 2.

In our study, there was no significant difference between the prognoses in male and female cases (p: 0.755). Mortality was not observed in 86(76.8%) patients (Group I) during the first 30 days, whereas it was seen in 26(23.2%) patients (Group II).

Age, sex, heart rate, systolic blood pressure, respiratory rate, body temperature, PaO2, PaCO2, alveolo-arterial O2 gradient (AaDO2), D-dimer, troponin, glucose, sodium and eGFR variables between the two groups are compared. In group I PaO2, sodium and eGFR, in group II respiratory rate, heart rate, troponin, glucose were significantly higher. There was a significant difference in terms of high-sensitivity troponin at the time of

admission, but no difference was found in D-dimer levels. In addition, 58 (51.8%) of the patients with PTE had RVD. The mortality rate in the first 30 days was 3.8% in cases without RVD while it was 38.4% in cases with RVD.

Table 2. Demographic characteristics of patients

Gender	
Female	59 (%52,7)
Male	53 (%47,3)
Age (mean)	60,8 ± 1,6 (years)
Pulse (mean)	87,23 (±1,75) (/min)
Number of breaths (mean)	23,22 (±0,45) (/min)
Systolic Blood Pressure (mean)	119,78 (±1,70) (mmHg)
PESI	
I	27 (24,1%)
II	28 (25%)
III	22 (19,6%)
IV	22 (19,6%)
V	13 (11,6%)
Diagnosis Method	
V/Q	36 (32,1%)
CTPA	76 (67,9%)
Service	
Intensive Care Service	21 (18,8%)
Clinic Service	91 (81,3%)

Of the 112 patients included in the study, 20 had massive, 38 had submassive and 54 had non-massive PTE. When the patients with massive and non-massive patients were compared, the mortality rate was found to be significantly higher in the massive group (p<0.001); when the submassive and non-massive embolism cases were compared, mortality rate was significantly higher in the submassive group (p <0.001). There was no significant difference between the submassive and the massive group (p: 0.059). Thrombolytic therapy was given to 16 of 20 patients with massive PTE, and thrombolytic therapy was not given to the other 4 patients due to presence of contraindication for thrombolytic therapy. There was no statistically significant difference in mortality between patients with and without thrombolytic therapy (p: 0.649).

PTE severity index was calculated for each patient. The mortality rates in PESI II-III-IV were similar when the relation between PTE severity index groups and mortality rates were examined. The mortality rate was significantly lower when

PESI I was compared with the other classes (p <0.001). However, it was significantly higher in PESI V cases compared to the other groups (p <0.001).

The mean sodium levels of patients at the time of admission are evaluated. A statistically significant relationship was found between the mortality rate and the serum sodium level below 135 mol/l (p:0.001). (In group I 29.1% of patients and in group II 70.9% of patients).

The mean eGFR of 112 patients who were included in the study was calculated as 87.59 mL/min, while the mean eGFR was 45.5 mL/min in the patients who died and 100.3 mL/min in the other patients. The prognoses of 2 groups with eGFR <60 ml/min and ≥60 ml/min were compared. Mortality in patients with eGFR <60 ml/min was 41.67 times higher compared to the other group (p<0.001).

The serum glucose levels of the patients at the time of admission were found to be above 140 mg/dl in the group with mortality, which was significantly higher than the group without mortality (p <0.001).

When the two groups were compared, the mean serum sodium level and eGFR of the group with high mortality were significantly lower and the serum glucose level was higher than the other group.

DISCUSSION

Pulmonary thromboembolism is a disease with high mortality and morbidity. Some clinical parameters such as elevated serum troponin-T and RVD in echocardiography are used to predict mortality in patients with PTE [1]. In our study, troponin positivity and RVD were found to be significant in the diagnosis and monitoring the prognosis of PTE (p<0.001). However, there is a need for new indicators that can predict the prognosis of PTE and which can be an alternative to these indicators that require technical infrastructure and specialist. Therefore, it is claimed that these parameters can be used in some studies investigating the effects of renal dysfunction along with changes in serum glucose and sodium levels on prognosis in cardiopulmonary diseases. In our study, we investigated the effects of these parameters on the prognosis both alone and in combination. In this study, du-

ring the first 30 days, when the mortality rate was compared with the other group; the mean serum sodium level and eGFR were significantly lower and the serum glucose level was significantly higher in the patients who died. When PESI compatibility with these parameters was examined, it was concluded that the serum sodium level and eGFR were lower and the serum glucose level was higher in PESI class V compared to the other PESI classes, and this difference was statistically significant.

The hyponatremia develops in severe PTE cases. Furthermore, BNP (Brain natriuretic peptide) and natriuretic peptide levels increase [8]. In our study, hyponatremia was present in 27.6% of 112 patients with acute PTE and the mortality rate during first 30 days was significantly higher in these cases than the patients with normal serum sodium levels (p:0.001). The serum sodium level at the time of admission was below 135 mmol/L and the risk of death was increased 48 times (p:0.001). Similarly, in another study, 30-day mortality rates in PTE cases were reported to be 28.5% in patients with serum sodium level below 130 mmol/L and 8% in patients with a normal sodium level (p <0.001). Hyponatremia has also been shown to be a poor prognostic factor in patients with acute and chronic cardiopulmonary disease such as left heart failure, acute myocardial infarction, pulmonary arterial hypertension, and pneumonia [5].

In studies investigating the usability of renal dysfunction for prognosis in patients with acute PTE, it has been emphasized that, hemodynamics of coronary and pulmonary circulation, as well as other organs such as kidney, are also affected due to PTE, and this increases mortality. In a study, it was shown that in patients with acute PTE, mortality was increased significantly in cases with a plasma creatinine level above 2 mg/dl during the first 7 days [9]. Similarly, in another study, mortality in the first 30 days was significantly increased in patients with eGFR<60 ml/min [6]. In our study, the mortality rate in the first 30 days was significantly higher in acute PTE patients with eGFR <60 ml/min. Based on these data, the mortality rate is approximately 6 times higher if acute renal damage arises along with the development of PTE in acute PTE patients who had no previously diagnosed renal failure.

It is known that the increase in serum glucose level and hyperinsulinemia enhance the procoagulant effect and reduce the fibrinolytic activity and there is a significant relationship between high serum glucose level and 30-day mortality due to PTE in the cases who had no diagnosis of diabetes. In addition, a significant relationship between the elevation in serum glucose level and the severity of the disease has been reported [10]. Increased hepatic gluconeogenesis and insulin resistance due to elevated stress hormones such as catecholamine, cortisol and growth hormone are indicated in severe PTE. The mortality rate in the first 30 days was 9.6% in a study involving 13621 cases with PTE. This rate is 5.6% in patients with a serum glucose level below 110 mg/dl, 8.4% in those with 110-140 mg/dl and 12% in cases with a serum glucose level above 140 mg/dl [5]. Similarly, the mortality rate in the first 30 days was 6.5% in patients with serum glucose levels below 110 mg/dl and 10.3% in those with serum glucose levels between 110 and 140 mg/dl.

The mean serum sodium level and eGFR in the group with high mortality were significantly lower and the serum glucose level was higher compared to the other group. When the compatibility of these markers with PESI was studied, it was found that serum sodium level and eGFR were lower and serum glucose level was higher in PESI class V compared to other classes, and this difference was statistically significant (p <0.001). (Figure 1. Serum sodium and glucose correlation with PESI).
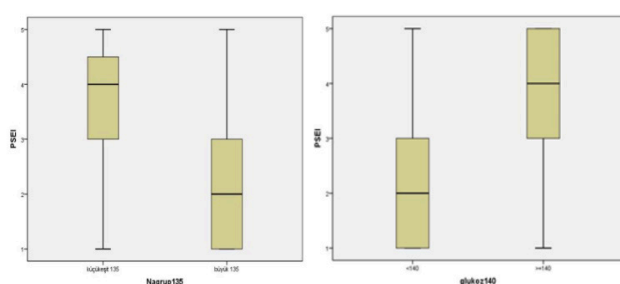

Figure 1. Serum sodium and glucose correlation with PESI.

In our study, when the three parameters, serum sodium level <135 mmol/L, glucose >140 mg/dl and eGFR <60 ml/min, were found in a patient, the sensitivity for the first 30-day mortality was 42.3% and the specificity was 100%. When we examined the impact of hyponatremia, low eGFR

and hyperglycemia on the prognosis separately, the highest sensitivity was detected in serum sodium level and the highest specificity was found in eGFR. (Table 3. Results of ROc analysis for parameters). In 11 of 112 patients (9.8%) in our study, three markers coexisted, and the mortality rate in these patients during the first 30 days was 100% (p<0.001). However, since the probability of coexistence of three markers is unlikely, it should be kept in mind that sensitivity in predicting mortality is 100% if this coexistence is present even though this is not a required condition for prognostic evaluation in acute PTE.

Table 3. Results of ROc analysis for parameters

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Sodium	%84.6	%89.5	%71	%95.1
eGFR	%80.8	%90.7	%72.4	%94
Glucose	%73.1	%84.9	%59.4	%91.3
Together	%42.3	%100	%100	%85.1

When the prognostic values of these three markers were compared, the area under the curve was measured and cut off value was considered as AUC> 0.8 (areas under the receiver operating characteristic curves), serum sodium level was ascertained as having the best prognostic value. When we examined the impact of each marker as an independent variable on prognosis by logistic regression analysis, eGFR and serum sodium level were found to be independent risk factors for prognosis (Figure 2. Receiver operating characteristic (ROC) curve analysis for parameters).
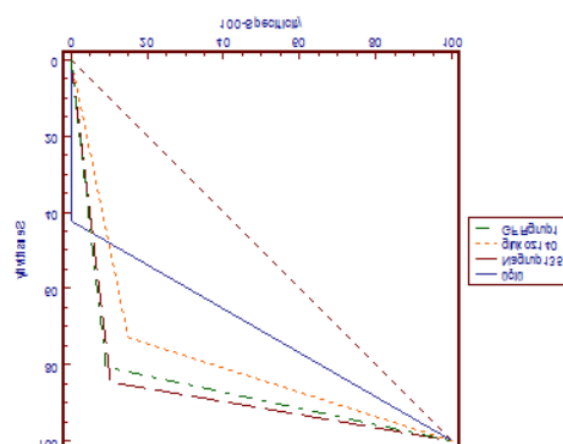

Figure 2. Receiver operating characteristic (ROC) curve analysis for parameters

Conclusion: RVD, troponin level and PESI are used in the prognostic evaluation of acute PTE cases. The necessity of and specialized physician and a special device for evaluation of right ventricle, unavailability of troponin test in every center, requirement of many parameters for PESI score hinder the accessibility of these markers in daily practice. In our study, we found that serum sodium, glucose and eGFR levels, which have the advantage of being easily applied in every center, were compatible with RVD, troponin and PESI parameters, all previously proven prognostic factors in determining the mortality risk in acute PTE. We believe that serum sodium, serum glucose and eGFR levels may be used separately or in combination in the determination of acute PTE prognosis in a group of patients with no specific comorbidity, such as diabetes mellitus and chronic kidney disease. Among these parameters, we recommend the serum sodium level as the best marker for diagnostic performance. Planning further comprehensive studies on this issue will enhance the sensitivity of our results.

Conflict of Interest: The authors have no conflicts of interest relevant for this article.

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