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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

The Relationship Between Procalcitonin Level and Short Term Mortality in Emergency Department

Acil Serviste Prokalsitonin Düzeyi ile Kısa Dönem Mortalite Arasındaki İlişki

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ABSTRACT

Aim: Procalcitonin (PCT) is a biomarker for infection, which has grown in popularity in recent years. In our study, we investigated whether there was a relationship between procalcitonin levels and seven-day mortality in all patients whose procalcitonin levels were measured in the emergency department (ED).

Material and Methods: In this single-center, cross-sectional, analytic, retrospective study, the patients whose PCT levels were measured in Dokuz Eylül University Hospital adult emergency department between 01.01.2016 and 31.03.2016 were included. PCT level and other parameters were evaluated in the survived and non- survived groups,

Results: We analyzed 499 patients whose PCT levels were measured. The median age was 74 (IQR: 63-82) years, and 54% were male. Of the 499 patients, 6 (1.2%) had a low procalcitonin level (median 0.03: IQR 0.02-0.04), 407 (81.6%) had an intermediate procalcitonin level (median 0.26; IQR 0.16-0.54) and 86 (17.2%) had a high procalcitonin level (median 5.54; IQR 3.20-15.31). When the PCT level-high group was compared with the other groups; systolic blood pressure (SBP), diastolic blood pressure (DBP), platelet count, pCO2 were lower and pulse rate, WBC, lactate, base excess values were higher. It was found that 249 (49.9%) of the patients were discharged from the ED, 112 (22.4%) were hospitalized, 66 (13.2%) were hospitalized in the intensive care unit, and 72 (14.4%) died. The PCT level was higher in the non-survivor group than in the survivor group (0.29 ngr/mL vs 1.07 ngr/mL, p<0.001). Univariate analysis showed that the non-survivor group had higher age, pulse, respiratory rate, procalcitonin levels, lactate and base deficiency levels, and lower SBP, DBP, oxygen saturations, and pH. The AUC for PCT was 0.722 (CI% 0.660-0.784) in the ROC curve In the multivariate logistic regression analysis, age, SBP, oxygen saturation, and lactate were independent risk factors for mortality in ED.

Conclusion: High PCT levels are associated with increased mortality in patients admitted to the ED. Patients with high- PCT levels showed higher mortality and were hospitalized in the intensive care unit. Advanced age, low systolic blood pressure, low oxygen saturation and high lactate levels are independent risk factors for mortality in ED admissions.

Keywords: Procalcitonin, mortality, emergency department, hospitalization

ÖZ

Amaç: Prokalsitonin (PKT), enfeksiyonu gösteren biyobelirteçtir ve son yıllarda popüleritesi artmaktadır. Çalışmamızda acil serviste (AS) prokalsitonin düzeyi ölçülen hastalarda prokalsitonin düzeyleri ile yedi günlük mortalite arasında ilişki olup olmadığını araştırdık.

Gereç ve Yöntemler: Tek merkezli, kesitsel, analitik, retrospektif bu çalışmaya Dokuz Eylül Üniversitesi Hastanesi erişkin acil servisinde 01.01.2016-31.03.2016 tarihleri arasında PKT düzeyi ölçülen hastalar dahil edildi. Yaşayan ve ölen hasta gruplarında PKT düzeyi ve diğer parametreler değerlendirildi.

Bulgular: PKT düzeyi ölçülen 499 hastayı analiz ettik. Yaş ortalama 74 (ÇAA 63-82) ve % 54'ü erkekti. Prokalsitonin düzeyleri 499 hastanın 6'sında (%1,2) hafif yüksek (ortanca 0,03: ÇAA 0,02-0,04), 407'sinde (%81,6) orta yüksek (ortanca 0,26; ÇAA 0,16-0,54) ve 86'sında (%17,2) ciddi yüksek (ortanca 5,54; ÇAA 3,20-15,31) seviyelerde idi. PKT düzeyi yüksek olan grup diğer gruplarla karşılaştırıldığında; sistolik kan basıncı (SKB), diyastolik kan basıncı (DKB), trombosit sayısı, pCO2 daha düşük iken; nabız, beyaz küre, laktat, baz açığı değerleri daha yüksekti. Hastaların 249'unun (%49,9) acil servisten taburcu edildiği, 112'sinin (%22,4) servise yattığı, 66'sının (%13,2) yoğun bakımda yattığı ve 72'sinin (%14,4) öldüğü belirlendi. Ölen grubun PKT düzeyleri, yaşayan gruba göre daha yüksekti (0,29 ngr/mL'ye karşı 1,07 ngr/mL, p<0,001). Tek değişkenli analizde, ölen grubun yaş, nabız, solunum hızı, prokalsitonin seviyeleri, laktat ve baz açığı değerleri daha yüksek ve SKB, DKB, oksijen satürasyonu ve pH değerlerinin daha düşük olduğu gösterildi. ROC eğrisinde PKT için eğri altında kalan alan değeri 0,722 (%95 GA 0,660-0,784) idi. Çok değişkenli lojistik regresyon analizinde, yaş, SKB, oksijen satürasyonu ve laktat acil serviste mortalite için bağımsız risk faktörleri olarak tespit edildi.

Sonuç: Acil servise başvuran hastalarda yüksek PKT seviyeleri artmış mortalite ile ilişkilidir. PKT düzeyi yüksek olan hastalarda yoğun bakım ünitesine yatış ve ölüm daha fazladır. Acil servis başvurusunda ileri yaş, düşük sistolik kan basıncı, düşük oksijen satürasyonu ve yüksek laktat seviyeleri mortalite için bağımsız risk faktörleridir.

Anahtar Kelimeler: Prokalsitonin, mortalite, acil servis, hastaneye yatış

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Introduction

Procalcitonin (PCT) is the prohormone of calcitonin synthesized from the thyroid gland. It is also secreted from neuroendocrine cells in the liver, lungs, pancreas and intestines (1,2). PCT increases within three hours of response to stimulation and is eliminated within 24 to 35 hours (3). PCT correlates with bacterial infection and not elevate viral infections and systemic immunological diseases (4). It is recommended to measure PCT in the diagnosis and follow-up of sepsis in the sepsis guideline (5). PCT increases in other conditions such as multiple trauma, heart failure, pyelonephritis, pancreatitis, appendicitis, mesenteric ischemia, osteomyelitis, inhalation burns, ARDS, septic arthritis, infective endocarditis, tuberculosis, cardiogenic shock, rhabdomyolysis, liver transplant rejection or renal failure (6-10).

It has been reported that the PCT level correlates with the severity of the inflammation and is associated with the prognosis of the patient in many diagnostic groups (4,8-10). Previous studies were showed that lactate is an independent risk factor for showing 10-day mortality in the ED (11). However, we found that no similar research was conducted for PCT in the literature.

Our aim in this study is to investigate the relationship between PCT levels and short-term (7-day) mortality in all patients whose PCT levels were measured in the ED.

Material and Methods

Study design and setting

This is a single-center, cross-sectional, analytic, retrospective study. The study was conducted at the Dokuz Eylül University Hospital Department of Emergency Medicine between 01/01/2016- 31/03/2016, after the ethics approval from the Dokuz Eylül University Ethics Committee (14.07.2016 / 2799-GOA). The ED at Dokuz Eylül University Hospital is a 45-bed tertiary hospital ED with 86,000 patients per year.

Participants

All patients > 18 years of age who measured PCT levels at admission to the ED were included in the study. Patients with missing information were excluded from the study.

Data collection and processing:

Information such as age, gender, diagnosis of the patients in the ED, laboratory parameters, vital signs, seven-day outcomes was screened from the electronic patient information management system. ICD-10 diagnostic codes were used as diagnosis groups. Procalcitonin levels were classified as PCT level-low (<0.05 ngr / mL), PCT level-intermediate (0.5-2.0 ngr / mL), PCT level-high (> 2.0 ngr / mL).

Statistical analysis

Study data were recorded in the "Statistical Package for Social Sciences for Windows 22.0". Normality analyzes were evaluated with the Kolmogorov-Smirnov test. When comparing the values of the patients such as age and laboratory, the T-test or Mann-Whitney test was used according to normality analysis. The Chi-square test was used to compare categorical variables. The receiver operating characteristic (ROC) analysis was performed and area under the curve (AUC) values were calculated for surviving and non-surviving patients. P Values <0.05 were considered statistically significant. Univariate analysis was performed to evaluate the factors affecting mortality. p Values> 0.2 among these parameters were evaluated by multivariate logistic regression analysis whether they were independent risk factors for mortality.

Results

Baseline characteristics

During the study period, procalcitonin level was measured in 507 of 29,588 patients who have been admitted to ED. Eight patients were excluded from the study according to exclusion criteria. Finally, 499 patients were included in the study. According to procalcitonin categories; Low PCT levels were measured in 6 (1.2%) patients, intermediate levels in 407 (81.6%) patients, and high values in 86 (17.2%) patients (Figure 1). It was found that 249 (49.9%) of the patients were discharged from the ED, 112 (22.4%) were hospitalized in the ward, 66 (13.2%) were hospitalized in the intensive care unit, and 72 (14.4%) die. There were two patients hospitalized in the ward in the PCT level –low group.

The median age was 74 (IQR: 63-82) years, and 269 patients (54%) were male. Of the 499 patients, 6 (1.2%) had a low PCT level (median 0.03: IQR 0.02-0.04), 407 (81.6%) had an intermediate procalcitonin level (median 0.26; IQR 0.16-0.54) and 86 (17.2%) had a high procalcitonin level (median 5.54; IQR 3.20-15.31). When the PCT level-high group was compared with the other groups; systolic blood pressure (SBP), diastolic blood pressure (DBP), platelet count, pco2 were lower and pulse rate, WBC, lactate, base excess values were higher. Table 1 presents the baseline characteristics of enrolled patients.

Procalcitonin level and seven-day outcomes

When patients are grouped as survivor and non-survivor groups according to the seven-day outcomes; demographic characteristics, vital signs and laboratory parameters are shown in Table 2. The median PCT level was higher in the non-survivor group than the survivor group (0.29 ngr/mL vs 1.07 ngr/mL, p<0.001).

The AUC for procalcitonin was 0.722 (0.660-0.784) in the ROC curve (Figure-2). The specificity and sensitivity for different cut-off values of procalcitonin were shown in Table 3.

Univariate analysis showed that the non-survivor group had higher age, pulse, respiratory rate, procalcitonin levels, lactate and base deficiency levels, and lower SBP, DBP, oxygen saturations, and pH (Table 2). In the multivariate logistic regression analysis, age, SBP, oxygen saturations, and lactate were independent risk factors for mortality in ED (Table 3).

Procalcitonin levels of the patients according to the diagnosis groups are shown in Table-4. The highest procalcitonin values were measured in the urinary system and digestive system disorders, respectively.

Discussion

In our study, we examined the short-term mortality of patients whose procalcitonin levels were measured in the ED. According to the results of our study, we found that the

	Initial PCT Level on ED Admission			
	PCT level - low (<0.05 ngr/mL) n=6	**PCT level- intermediate (0.5-2.0 ngr/mL) n= 407**	**PCT level – high (>2.0 ngr/mL) n=86**	**P**
Age, median (IQR)	68.5 (37.8 -86.3)	74.0 (64.0-32.0)	72.5 (63.0-84.0)	0.816
Male, n(%)	1 (16.7)	209 (51.4)	59 (68.6)	0.003
Outcomes				
Survivors n(%)	6 (100)	362 (88.9)	59 (68.6)	<0.001
Non- survivors n(%)	0	45 (11.1)	27 (31.4)	
Vital Signs				
SBP (mmHg)	136 (111-151)	126 (110-136)	116 (94-132)	0.001
DBP (mmHg)	80 (76-87)	80 (70-85)	70 (56-82)	<0.001
Pulse rate (beats/min)	84 (82-92)	88 (82-106)	98 (82-116)	0.013
Respiratory rate (beats/min)	18 (16-21)	19 (16-22)	20 (17-24)	0.182
Oxygen saturation %	96 (93-98)	96 (90-98)	94 (90-97)	0.164
Laboratory				
Procalcitonin (ngr/ml)	0.03 (0.02-0.04)	0.26 (0.16-0.54)	5.54 (3.20-15.31)	<0.001
Complete Blood Count				
WBC (10^3/µl)	10 (8-13)	11 (8-14)	14 (9-21)	0.002
Hemoglobin (gr/dl)	12 (10-14)	12 (10-13)	11 (10-13)	0.226
Platelet (10^3/µl)	261 (236-341)	229 (175-307)	188 (133-271)	0.001
Blood gas				
pH	7.43 (7.36-7.48)	7.41 (7.35-7.46)	7.43 (7.36-7.48)	0.481
PCO2	37 (36-46)	37 (31-43)	30 (23-36)	<0.001
Lactate (mmol/l)	1.4 (1.3-1.6)	1.5 (1.1-2.4)	2.0 (1.4-4.0)	0.001
Base excess (mmol/l)	0.9 ([-0.95]-3.45)	-0.8 ([-4.00]-2.02)	-3.6 ([-9.00]-[-1.00])	<0.001

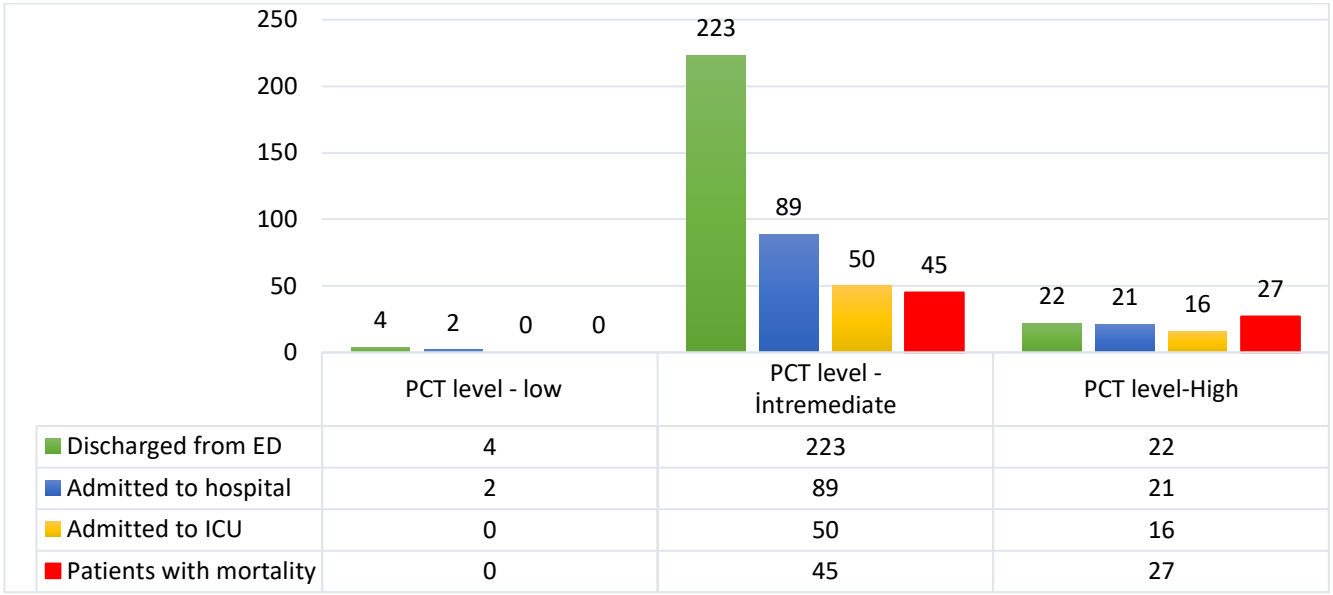
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White blood cell

Table 1. Baseline characteristics of patients

	survivors		**non- survivors**		**Odss ratio (95% CI)**	**P**
	N	**Median (IQR)**	**N**	**Median (IQR)**		
Age	427	73 (63-81)	72	81.5 (66-86)	1.032 (1.012-1.053)	0.001
Vital signs						
SBP (mmHg)	427	126 (112-136)	72	106 (81-131)	0.975 (0.965-0.985)	0.002
DBP (mmHg)	427	80 (70-85)	72	68 (51-82)	0.961 (0.946-0.977)	<0.001
Pulse rate (beats/min)	427	87 (82-105)	72	102.5 (82-125)	1.020 (1.009-1.031)	<0.001
Respiratory rate (beats/min)	427	19 (16-22)	72	22 (18.3-28)	1.151 (1.097-1.208)	<0.001
Oxygen saturation %	427	96 (91-98)	72	90 (80-96)	0.937 (0.914-0.961)	<0.001
Laboratory						
Procalcitonin (ngr/ml)	427	0.29 (0.16-0.73)	72	1.07 (0.32-5.30)	1.033 (1.013-1.054)	0.001
Complete Blood Count						
WBC (10^3/µl)	427	11 (8.1-14.3)	72	14.2 (9.3-22.4)	1.016 (0.995-1.038)	0.133
Hemoglobin ((gr/dl)	427	11.8 (10.4-13.4)	72	11.2 (9.7-12.3)	0.860 (0.767-0.963)	0.262
Platelet (10^3/µl)	427	225 (170-301)	72	222 (138-308)	0.999 (0.996-1.001)	0.262
Blood Gas					0.960 (0.993-0.987)	
pH	319	7.42 (7.37-7.46)	64	7.41 (7.29-7.47)	0.063 (0.006-0.614)	0.017
PCO2	319	36.6 (30.4-42.8)	64	30.4(26.2-38.8)		0.004
Lactate (mmol/l)	319	1.5 (1.0-2.3)	64	2.7 (1.4-5.8)	1.302 (1.180-1.436)	<0.001
BE (mmol/l)	319	-1.0 ([-]4.1-1.9)	64	-3.1 ([-]3.1 -0.5)	0.900 (0.841-0.935)	<0.001

CI = confidence interval, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White blood cell

Table-2: Characteristics of survivor and non- survivor patients



ED, Emergency Department; ICU Intensive Care Unit

Figure 1: Seven-day outcomes of patients according to PCT categories

Parameter	OR	95% CI		P value
		Lower	Higher	
Age	1.027	1.002	1.053	0.038
SBP (mmHg)	0.985	0.974	.0996	0.008
Pulse rate (beats/min)	1.006	0.993	1.019	0.380
Respiratory rate (beats/min)	1.074	0.994	1.161	0.071
Oxygen saturation %	0.951	0.910	0.994	0.026
Procalcitonin (ngr/ml)	1.018	0.993	1.044	0.156
Hemoglobin (gr/dl)	0.921	0.798	1.062	0.257
pH	1.436	0.408	5.048	0.573
pCO2	0.979	0.945	1.014	0.232
BE (mmol/l)	1.001	0.992	1.010	0.863
Lactate (mmol/l)	1.209	1.056	1.383	.006

Hosmer–Lemeshow goodness-of-fit $p = 0.873$

Table 3. Multivariate analysis of the variables as a seven –day mortality

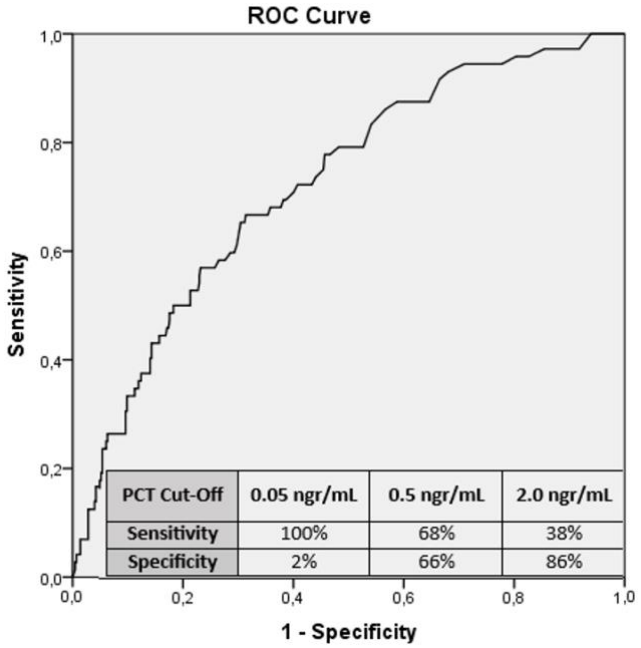


Figure 2. ROC curve and sensitivity-specificity values according to procalcitonin level

procalcitonin levels of non-survivor patients were significantly higher than the survivor patients. Literature has shown that procalcitonin levels are showing mortality in sepsis, heart insufficiency and pneumonia (6,8,9). These studies are mostly on infectious diseases. Arora and his friends` systematic composition and meta-analysis showed that procalcitonin levels in the early sepsis phase are significantly lower in surviving patients than the non-survive patients (12). In our study, we took all patients who has measured procalcitonin levels without discriminating the other diagnosis.

There are lots of parameters that are showing the disease severity and mortality for a patient who is coming to emergency services. These are mostly scoring systems that need complex measurements (13-15). But these score systems are not used in routines and common. In emergency services, we need easily accessible and simple parameters for measuring mortality. Procalcitonin is an easily measurable biomarker that gives you results in about 1 hour with 4 ml of blood. Because of easily accessible and applicable, procalcitonin is more advantageous than other scoring systems. The success of procalcitonin in predicting mortality may change emergency service practice. However, in our study, the majority of the patients were diagnosed with infection and pulmonary diseases. Therefore, more comprehensive studies are needed in patients diagnosed other than infection.

In our study, it was found that systolic blood pressure, diastolic blood pressure, oxygen saturation, thrombocyte and pCO2 values were lower in the non-survivor patients compared to the survivor patients. Their age, pulse rate, respiratory rate, base deficit, lactate and procalcitonin levels

ICD group	n	Median (IQR)
Diseases of the respiratory system (J00-J99)	207	0.32 (0.17-0.90)
Certain infectious and parasitic diseases (A00-B99)	114	0.43 (0.19-2.30)
Diseases of the circulatory system (I00-I99)	47	0.22 (0.14-0.40)
Diseases of the genitourinary system (N00-N99)	31	0.68 (0.34-1.31)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	28	0.20 (0.12-0.47)
Diseases of the nervous system (G00-G99)	26	0.18 (0.11-0.30)
Neoplasms (C00-D49)	16	0.26 (0.16-0.58)
Diseases of the digestive system (K00-K95)	17	0.60 (0.24-2.75)
Endocrine, nutritional and metabolic diseases (E00-E89)	8	0.46 (0.15-1.98)
Diseases of the musculoskeletal system and connective tissue (M00-M99)	5	0.28 (0.09-0.70)

Table 4. Procalcitonin values according to ICD-10 group

were higher in the non-survivor patients. High mortality in patients with unstable vital signs (such as hypoxic, hypotensive, tachycardia) is an expected condition. Also, lactate, which is an indicator of hypoperfusion, was higher in the patient group who died. In the study of Pedersen et. al., it was stated that lactate is a parameter showing the seven-day mortality in the emergency department (11). This study included infection, trauma, cardiac diseases, digestive diseases, neurological diseases and respiratory system diseases groups. In our study, we made a similar assessment for procalcitonin, inspired by this study. Procalcitonin also predicts mortality in emergency service patients such as lactate regardless of the diagnosis group. However, in the multivariate analysis, we found that age, systolic blood pressure, oxygen saturation and lactate values are independent risk factors for mortality.

When we examine procalcitonin levels categorically in our study; in the group with low procalcitonin levels (<0.05 ng/ml), there were no patients hospitalized in the intensive care unit or who died. On the other hand, in the group with high procalcitonin levels (>2.0 ng/ml) were more patients hospitalized in the intensive care unit (%18.6) or died (%34.6). In this group, systolic blood pressure, diastolic blood pressure, platelet level and pCO2 levels were lower; heart rate, WBC, lactate and base deficit were higher.

In recent years, procalcitonin has been used to exclude non-infectious conditions and to determine the severity of infection in patients in whom the diagnosis of infection cannot be made clear in the emergency department. However, there is no single reliable cut-off value for procalcitonin in the literature. In our study, we found the AUC value 0.722 according to the roc curve. According to this, mortality was not encountered with procalcitonin values below <0.05 ng/ml, while the sensitivity for death was %38 and specificity was %86 for values >2.0 ng/ml.

Limitations

Our results cannot be generalized for the pediatric patient. This study was carried out only in one center; it was also another limitation of the study, the number of patients with the non-infectious diagnosis was small.

Conclusion

High PCT levels are associated with increased mortality in patients admitted to the ED. Patients with high- PCT levels showed higher mortality and were hospitalized in the intensive care unit. In these patients, SBP, DBP, thrombocyte and pCO2 levels are lower, while pulse rate, WBC, lactate and base deficiency values are higher. Advanced age, low systolic blood pressure, low oxygen saturation and high lactate levels are independent risk factors for mortality in ED admissions.

Conflict of Interest: The authors declare no conflict of interest regarding this study.

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Authors' Contributions: OBC and NC. wrote the article. OBC conceived the idea. OBC and DG. collected data. BB analyzed data. NC assisted with study design and revised the article. All authors have read and approved the final manuscript.

Ethical Approval: Approval was obtained from Dokuz Eylul University Clinical Researches Ethical Committee Date:14.07.2016, Decision No:2799-GOA.

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