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Research Article

A New Biomarker for Intensive Care Unit Patients: suPAR

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Abstract

Objective: The aim of the current study was to demonstrate the relationship between the suPAR, APACHE II, C-reactive protein (CRP), procalcitonin (PCT) values and the mortality rates of patients under follow-up in the intensive care unit who met the SIRS criteria.

Materials and Methods: Patients were selected from the intensive care units for this single-center, prospective study. Inpatientswho had at least two SIRS criteria, were ≥18 years of age, and spent a duration of ≥72 hours in the intensive care unit were included in the study. The lowest/worst APACHE II score in the first 24 hours, as well as the suPAR, CRP, PCT, lactate values on the days 1 and 5were determined.

Results: An evaluation of the ROC curves for the APACHE II score and the suPAR, CRP, PCT and lactate values measured for the patients in intensive care during the first 24 hours indicated that the APACHE II score had the highest AUC (AUC: 0.824), while the next highest AUCs were observed with suPAR1 (AUC: 0.673), PCT1 (AUC: 0.628), lactate1 (AUC: 0.528), CRP1 (AUC: 0.526). An evaluation of the ROC curves for the suPAR, CRP, PCT and lactate values measured on day 5 indicated that the PCT5 value had the highest AUC (AUC: 0.769), while the next highest AUC values were observed with lactate 5 (AUC: 0.733), suPAR5 (AUC: 0.687) and CRP5 (AUC: 0.648).

Conclusion: These findings suggest that suPAR levels can be used to predict mortality on admission day but not for follow up.

Keywords: APACHE II; Mortality; Sepsis; SIRS; suPAR

Introduction

Bacterial infections and sepsis are the most common causes of mortality and morbidity in intensive care units [1,2]. Early detection of progress to sepsis and reducing the mortality rate are highly important for patients in intensive care units (ICU).

Various biomarkers and scoring systems are used to determine the prognosis of patients in intensive care units. Among these, APACHE II (Acute Physiology and Chronic Health Evaluation II), C-reactive protein (CRP), procalcitonin (PCT) and lactate are among the most important biomarkers.

The APACHE II scoring system is the gold standard to evaluate high-risk patients in intensive care units. This system classifies the patients and provides information about their prognosis. However, this method can yield inaccurate results. For instance, the relative APACHE II score of a young patient who has severe sepsis, but no organ failure is calculated as low [3,4].

CRP and PCT are among the common parameters used to monitor patients in critical condition in intensive care units [5]. However, CRP measurement is not ideal for monitoring sepsis; CRP levels are also elevated in postoperative conditions, autoimmune and rheumatologic diseases and non-infectious conditions such as myocardial infarction. On the other hand, PCT is significantly elevated in bacteremia and sepsis. PCT and CRP have low prognostic value in terms of evaluating the expected life span of sepsis patients [6].

Lactate level is another parameter that is important during progression to SIRS and early sepsis. Tissue hypoxia-dependent hyperlactatemia is observed. Given that oxygen transport to cells is decreased after sepsis, it is difficult to interpret lactate levels.

Soluble urokinase-type plasminogen activator receptor (suPAR) is a protein-derived potential biomarker for infectious diseases [7]. Urokinase-type plasminogen activator receptor (suPAR) is expressed in neutrophils, lymphocytes, monocytes, macrophages, endothelial cells and malignant cells, and is called suPAR [8,9]. Elevated suPAR levels allow for the prediction of mortality in patients with bacteremia, SIRS, sepsis, and septic shock [9-12].

For the successful treatment of sepsis and SIRS, it is necessary to perform the intervention rapidly and in a timely manner. Thus, the aim of the present study was to analyze suPAR, APACHE II, CRP, PCT, lactate levels in intensive care unit patients who complied with the SIRS criteria, and to determine the association of these parameters with mortality.

Materials and Methods

The study was designed as a prospective and single-center study, and was performed at Cukurova University School of Medicine

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Department of Infectious Diseases and Clinical Microbiology between February 2013 and October 2013.

Informed consent forms were obtained from the patients or their relatives. Ethics approval was obtained from the institutional ethics committee (Date: 14.02.2013, Project title: A NEW BIOMARKER FOR INTENSIVE CARE UNITPATIENTS: suPAR). Twenty-nine patients from the internal intensive care unit and 29 patients from the reanimation unit were included in the study. A survey was created for the patients, and the required information was recorded on the survey form.

1. Inclusion criteria wereMeeting a minimum two of the criteria:

a. Body temperature > 38 C° or< 36 C°

b. Heart rate > 90 beats/minute

c. Respiration rate > 20/minute or PaCO2 < 32 mm-Hg

d. White blood cell count > 12000 / µL or < 4000 / µL or > 10% immature neutrophils

2. Age ≥ 18 years

3. Intensive care unit stays ≥ 72 hours.

Patients who met these three criteria were included in the study. Terminal cancer patients, patients who received massive blood transfusions, and patients with ongoing pregnancy were excluded from the study.

All patients underwent general evaluation (age, gender, diagnosis, and comorbid conditions). Blood biochemistry, whole blood count, and arterial blood gas measurement were performed for all patients. The APACHE II score was calculated within the first 24 hours of admission to the ICU.

The APACHE II score was calculated by evaluating acute physiological score [body temperature, heart rate, mean arterial pressure, respiration rate, oxygenation, arterial pH, sodium, potassium, creatine, hematocrit, leukocyte count, neurological score (15-Glaskow coma scale)], age, and chronic health condition.

To measure suPAR levels on days 1 and 5 in the ICU, 3 cc blood samples were collected from the peripheral vein into EDTA-containing tubes. Blood samples were centrifuged at 3,000 rpm for 10 minutes, and plasma samples were separated with the help of a Pasteur pipette. Samples were stored at (-) 80°C until the analysis of suPAR levels. Plasma samples were analyzed by a commercial ELISA kit according to the manufacturer's instructions (Viro Gates A/S, Denmark).

To measure procalcitonin and CRP levels on days 1 and 5 in the ICU, 5 cc blood samples were collected from the peripheral vein into biochemistry tubes. Blood samples were centrifuged at 4,000 rpm for 5 minutes, and immediatelyanalyzed. A chemiluminescent method was used to analyze PCT levels on a SNIBE MAGLUMI 1000 auto analyzer. A nephelometric method was used to analyze CRP levels on a BECKMAN Coulter IMMAGE 800 auto analyzer. PCT values > 0.5 ng/mL, and CRP values > 0.8 mg/dL were considered significant.

To measure lactate levels on days 1 and 5 in ICU, 1 cc blood samples were collected from the artery into a heparin-containing syringe. Blood samples were analyzed in an ABL 800 blood gas analyzer using ion-selective electrode (amperometric) method. Blood samples were collected in the morning between 8:00 am and 10:00 am.

Table 1: Main clinical features.

Number of patients (n)	58	Malignancy n (%) Yes No	 21 (36.2%) 37 (63.8%)
Age Mean±SD Median (min-max)	 57.54±18.15 59 (20-87)	Diabetes Mellitus n (%) Yes No	 11 (19%) 47 (81%)
Gender Male Female	 26 (44.8%) 32 (55.2%)	Hypertension n (%) Yes No	 17 (29.3%) 41 (70.7%)
APACHE II Median (min-max)	 23 (3-39)	Kidney failure n (%) Yes No	 15 (25.9%) 43 (74.1%)
Hospital stay (days) Median (min-max)	 13 (5-110)	Trauma n (%) Yes No	 2 (3.4%) 56 (96.6%)
MV days Median (min-max)	 13.71 (1-110)	Operation n (%) Yes No	 13 (22.4%) 45 (77.6%)
Final condition n (%) Survivor Exitus	 19 (32.8%) 39 (67.2%)	Infection n (%) Yes No	 40 (69%) 18 (31%)

Statistical analysis

SPSS v.15.0 (SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis. Continuous variables were represented with mean and standard deviation. Numbers and percentages were used to express the categorical variables. The Kolmogorov-Smirnov test was used to compare the mean levels of biomarkers on day 1 and day 5. In case of histograms, the non-parametric Wilcoxon rank test was used to evaluate the variables that did not fit a normal distribution. Receiver operating characteristic (ROC) curves were used to analyze the accuracy of suPAR to predict mortality. According to this method, the following criteria should be met for the best test: sensitivity=100%; false negativity=0 (1-Specificity=0); area under the curve (AUC)=1; and diagnostic value of AUC (p value)<0.05. The Youden index, which uses the point with the highest sensitivity and specificity in the ROC curve, was used to determine the cut-off values. To determine the accuracy of the diagnostic test, the sensitivity, specificity, PPV, and NPV values were calculated at a 95% confidence interval, and were presented in a table. P values <0.05 were considered statistically significant.

Findings

Twenty-nine patients (50%) from the internal intensive care unitand 29 patients (50%) from the reanimation unit were included in the study. Twenty-six patients (44.8%) were male and 32 patients (55.2%) were female. The mean age was 57.54±18.15 years. The median APACHE II score (min-max) at the time of admission to intensive care unit were 23 (range: 3-39).

Patients' co morbid diseases were evaluated in this study. Accordingly, infection was observed in 40 patients (69%), malignancy was observed in 21 patients (36.2%), hypertension was observed in 17 patients (29.3%), kidney failure was observed in 15 patients (25.9%), surgery was observed in 13 patients (22.4%), and trauma was observed in two patients (3.4%).

Patients' final conditions were evaluated as alive or exitus.

Table 2: Levels of vital biomarkers on day 1 and day 5 (Wilcoxon Rank Test).

	Day 1 Mean±SD Median(Min-Max)	Day 5 Mean±SD Median(Min-Max)	Z	p
suPAR (ng/dL)	16.06±6.06 17.52 (3.99-22.50)	17.13±5.82 17.13 (3.77-22.50)	-0.646	0.518
CRP (mg/dL)	14.16±14.76 8.29 (0.14-58.20)	12.75±11.03 10.20 (0.18-46)	-1.754	0.079
Procalcitonin (ng/mL)	12.08±25.48 1.17 (0.04-100)	8.03±19.74 1.05 (0.02-100)	-2.507	0.012
Lactate (mmol/L)	3.07±2.70 2.35 (0.40-14.60)	2.21±1.84 2.00 (0.20-13)	-1.497	0.134
Leukocyte count (µL)	14.13±8.79 14.10 (0.10-51.60)	12.09±7.74 11.20 (0.10-38.80)	-2.349	0.019

Accordingly, 39 patients (67.2%) were exitus. The main clinical features of the patients are shown in Table 1.

suPAR, CRP, PCT, lactate and leukocyte count were analyzed during the first 24 hours and on day 5. When we compared the mean leukocyte count and the mean PCT level on day 1 and day 5, day 1 levels were significantly higher in both parameters (leukocyte count p=0.019; PCT p=0.012). However, we did not find any significant changes in suPAR (p=0.518), CRP (p=0.079), and lactate (p= 0.134) levels (Table 2).

The area under the curve (AUC) and significance (p<0.05) were calculated for all biomarkers on day 1 and day 5. Given that AUCs for PCT1(AUC: 0.628; p=0.117), CRP1 (AUC: 0.526; p=0.747), lactate1 (AUC: 0.528; p=0.734), white blood cells1 (WBC1) (AUC: 0.453; p=0.568), and CRP5 (AUC: 0.648; p=0.070), and WBC5 (AUC: 0.548; p=0.556) were not significant; sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were not calculated for these parameters. The cut-off, sensitivity, specificity, PPV, NPV, and AUC values for significant biomarkers are summarized in Table 3.

The ROC curves for APACHE II score, suPAR, CRP, PCT, lactate, and WBC in first 24 hours are shown in Figure 1A. According to the ROC curves, the APACHE II score had the highest AUC (AUC: 0.824), followed by suPAR (AUC: 0.673), PCT (AUC: 0.628), lactate (AUC: 0.528), CRP (AUC: 0.526), and WBC (AUC: 0.453), respectively.

ROC curves for APACHE II at the time of admission to ICU, suPAR, CRP, PCT, lactate, and WBC at day 5 are shown in Figure 1B. When we evaluated the APACHE II score at admission and ROC curves on day 5, the APACHE II score had the highest AUC (AUC: 0.824), which was followed by PCT (AUC: 0.769), lactate (AUC: 0.733), suPAR (AUC: 0.687), CRP (AUC: 0.648), and WBC (AUC: 0.548), respectively.

Discussion

Sepsis and SIRS represent the most important causes of mortality in patients in ICU [1,2]. Thus, different scoring systems and biomarkers have been used to determine the progression to sepsis in early stages. Among these, the APACHE II scoring system is the most significant method. Moreover, CRP, PCT and lactate are commonly used as biomarkers. On the other hand, suPAR is a new biomarker that allows us to predict mortality and morbidity in patients in ICUs. In this regard, we analyzed suPAR, APACHE II, CRP, PCT, and lactate levels in patients who were in the ICU and who met the SIRS criteria, and determined the association between these parameters and mortality.

APACHE II scoring is the gold standard to evaluate high-risk patients in ICUs. Parameters that are associated with poor prognosis in first 24 hours are used in this scale. This scoring system provides the risk classification of patients, and gives information about mortality and prognosis. The score ranges between 0-71 and high APACHE II scores are significantly correlated with mortality [13,14]. Knaus et al. analyzed 5815 patients in the ICU; for all nonoperative patients, the authors found that the APACHE II score ranges between 20-35, and mortality ranges between 40-75% [13]. Uçgun et al. found that a high APACHE II score (≥21), hypotension, and respiratory failure requiring mechanical ventilator support is among the factors that affect mortality [14]. Khwankeaw and Bhurayanontachai conducted a retrospective study in Thailand, and aimed to identify the factors that are correlated with mortality in AML and lymphoma patients in the ICU [15]. One hundred forty-five patients were included in the study, and the mortality rate in the ICU was calculated as 55.2%. In conclusion, having an APACHE II score >27, mechanical ventilator use, vasopressor use, and neutropenia had 80% sensitivity, and 75% specificity was associated with 82% mortality. Giamarellos-Bourboulis et al. conducted a prospective, multicenter cohort study on 1914 patients (62.2% sepsis, 37.8% severe sepsis/septic shock) to investigate the effects of APACHE II score and suPAR level on prognosis [16]. Blood samples were collected from 1914 patients on day 1. Blood samples were collected from 367 patients on days 1, 3, 7, and 10. The results were evaluated in four groups: Group 1: APACHE II <17, suPAR<12, and mortality 5.5%; Group 2: APACHE II <17, suPAR ≥12, mortality 17.4%; Group 3: APACHE II ≥17, suPAR<12, mortality 37.4%; and Group 4: APACHE II ≥17, suPAR ≥12, mortality 51.7%. ROC curves were as follows: suPAR (AUC: 0.708, p<0.0001), APACHE II (AUC: 0.822, p<0.0001), and suPAR+APACHE II (AUC: 0.831, p<0.0001). Overall, APACHE II had higher predictive value to predict mortality compared to suPAR. Moreover, the combination of suPAR and the APACHE II score had significantly higher predictive power compared to suPAR or APACHE II alone. Suberviola et al. conducted a prospective, observational, single-center study in Spain to investigate the effects of suPAR and pro-adrenomedulin (proADM) levels on mortality in sepsis patients in the ICU. In

Table 3: The cut-off, sensitivity, specificity, PPV, NPV and AUC values of vital biomarkers in terms of mortality.

	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	95% CI	P
APACHE II	22	89.47	71.79	93.33%	60.71%	0.824	55.1 - 85.0	0.000
PCT day 5	0.627	73.68	74.36	85.29%	58.33%	0.769	57.9 - 86.9	0.001
Lactate day 5	1	52.63	89.74	79.55%	71.43%	0.733	75.8 - 97.1	0.004
suPAR day 5	14.296	57.89	79.49	79.49%	57.89%	0.687	63.5 - 90.7	0.022
suPAR day 1	21.41	94.74	46.15	94.74%	46.15%	0.673	30.1 - 62.8	0.033

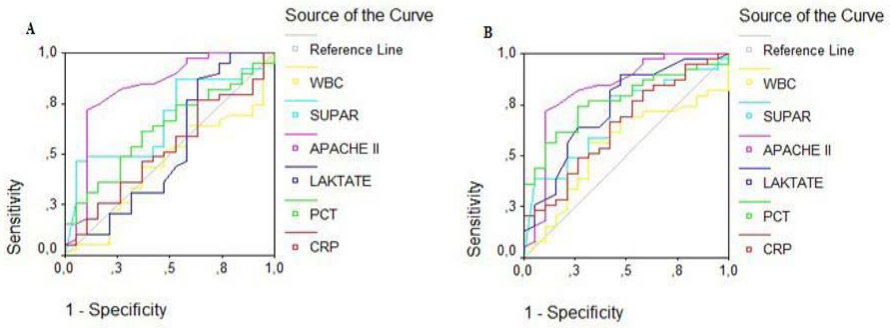

Figure 1: A: ROC curves for APACHE II, suPAR, PCT, lactate and WBC on day 1. B: ROC curves for APACHE II, suPAR, PCT, lactate and WBC on day 5.

this study, the authors analyzed APACHE II and SOFA scores, and CRP and PCT levels in 137 patients (90 males and 47 females; mean age: 62.6±15.9 years) [17]. The authors compared the AUCs to determine the correlation between these parameters and mortality, and found that AUCs for APACHE II and suPAR were 0.82 and 0.67, respectively. Overall, the results suggested that APACHE II score was superior compared to suPAR, in terms of indicating mortality. Donadello et al. conducted prospective, observational study on 161 adult males (62.4%) and 97 adult females (37.6%). The median scores at admission (min-max) was as follows: APACHE II, 17 (range: 9-23) and SOFA 6 (range: 3-9) [18]. At the time of admission to the ICU, 94 patients (36%) had severe sepsis and 49 patients had septic shock. At the end of the 28-day follow-up period, ROC curves for mortality showed that AUCs for APACHE II and suPAR were 0.863 and 0.723, respectively. Overall, APACHE II had more predictive value to predict the mortality of patients who were followed-up in the intensive care unit. In our study, we found that the AUCs for suPAR1, suPAR5, and APACHE II were 0.673, 0.687, and 0.824, respectively. The highest AUC was observed in APACHE II. The AUC for suPAR levels on day 5 was higher compared to AUC for suPAR levels on day 1. When we compared AUCs, we found that APACHE II was superior compared to suPAR in terms of indicating mortality in SIRS patients, which was consistent with the literature.

CRP is a common marker to evaluate the prognosis of patients with sepsis and SIRS. Previous studies have shown that the predictive value of CRP to predict mortality is lower compared to suPAR. Suberviola et al. demonstrated that suPAR (AUC: 0.67) was superior compared to CRP (AUC: 0.50) in terms of indicating mortality in sepsis patients [17]. Raggam et al. found that suPAR levels are superior compared to CRP in terms of evaluating mortality in SIRS patients [19]. In another prospective study, Donadello et al. followed-up 258 patients with sepsis for 28 days, and the authors found that suPAR has more power to predict mortality compared to CRP [18]. Wittenhagen et al. investigated the correlation between elevated suPAR levels and mortality in *Streptococcus pneumonia* bacteremia (SPB) patients [9]. The authors found that suPAR is an independent predictor of mortality in SPB patients (cut-off >10 ng/mL; specificity: 98%, sensitivity: 38%, PPV: 60%, NPV: 88%); however, they reported that there is no correlation between CRP and suPAR. Another study investigated the association between elevated suPAR levels and mortality in staphylococcus aureus bacteremia (SAB) patients, and found that suPAR has a greater predictive value compared to CRP [12]. Similarly, our results were consistent with the literature. AUCs for suPAR1 and suPAR5 were higher compared to AUCs for CRP1 and CRP5. Thus, suPAR had more prognostic value to indicate mortality in SIRS patients.

In normal and healthy individuals, PCT (prohormone) is transformed into calcitonin (active form) as a result of intracellular proteolytic reaction, and is secreted from the C cells of the thyroid gland. Serum PCT levels are extremely low in healthy individuals (<0.05 ng/ml) [20,21]. In case of viral infections and inflammatory events, PCT levels increase up to 1.5 ng/ml. On the other hand, PCT levels can exceed 100 ng/ml in case of severe bacterial infections and inflammation. PCT levels increase slightly during viral infections and systemic immunological diseases. Contrary to cytokines and CRP, PCT levels do not increase significantly in inflammation and viral infections which suggest that PCT is more specific to bacterial infections [22]. Raggam et al. investigated the correlation between mortality rates in SIRS patients and suPAR levels. In this study, which included 902 adults, patients were followed up for 31 months [19]. Mortality rates were calculated at the 48th hour (36 of 902 died), and on day 30 (117 of 902 deceased) and on day 90 (151 of 902 deceased). The authors found that suPAR had greater predictive power to indicate mortality compared to PCT (AUC: 0.777, 0.671, and 0.638). Another study investigated the effects of biomarkers on mortality and the prognosis of sepsis patients who were staying in the ICU. This study showed that PCT has a lower prognostic value (AUC: 0.44) compared to suPAR (AUC: 0.67) [17]. In our study, AUC values for suPAR1 and suPAR5 were higher compared to AUC value for PCT1. On the other hand, AUC for PCT5 was higher compared to AUCs for suPAR1 and suPAR5. suPAR1 and suPAR5 had higher power to predict mortality in SIRS patients compared to PCT1; on the other hand, PCT5 had greater power to predict mortality compared to suPAR1 and suPAR5. suPAR levels have more power to predict mortality in SIRS patients in the early stages, whereas PCT levels have greater power to predict mortality during follow-up.

Lactate is a key intercellular metabolite that plays a role in metabolic events. Lactic acid is the most common molecule in biological fluids, and it is dispersed in these fluids in its cationic form. It has a widespread distribution in intermediary metabolism of living systems. According to various clinicians, lactate is associated with high mortality rate in acute patients [23,24]. Hyperlactatemia can reflect tissue hypoxia in SIRS or early sepsis. Hyperlactatemia

is considered to be an indicator of mortality in patients in the ICU, especially in cases of sepsis, organ failure, trauma, and SIRS [25-32]. In addition, it is used for the management of patients in the ICU.

Chen and Li investigated APACHE II, SOFA, and mortality in emergency department sepsis (MEDS) scores, and lactate levels in adult sepsis patients who were admitted to the emergency service, and have calculated the mortality rates at the end of a 28-day period [33]. Lactate levels, and APACHE II, SOFA, and MEDS scores were significantly higher in deceased patients compared to survivors ($p<0.001$). AUC values for MEDS, APACHE II, SOFA, and lactate were 0.74, 0.74, 0.75, and 0.79, respectively. When lactate was combined with MEDS, APACHE II, and SOFA, AUCs were calculated as 0.81, 0.81, and 0.82, respectively. Compared to individual scoring systems, the combination of different systems yielded significantly higher AUCs ($p<0.05$). Overall, lactate level is an important prognostic marker to predict mortality in patients who are admitted to emergency service, and its combination with MEDS, APACHE II, and SOFA scoring systems increase its power to predict mortality. To our knowledge, there are no studies on the association between lactate and suPAR, and mortality. When we evaluated the AUCs for different biomarkers, we found that AUCs for suPAR1 and suPAR5 were significantly higher compared to lactate1. However, AUC for lactate5 was significantly higher compared to AUC for suPAR1 and suPAR5. These results suggest that suPAR has greater prognostic value to predict mortality in SIRS patients in the ICU in the early stages, whereas lactate has greater prognostic value during follow-up.

The activation of plasminogen to plasmin via uPA and tissue plasminogen activator (tPA) is the key step in fibrinolysis. tPA has a relatively unique role in coagulation; on the other hand, uPA regulates cell migration, adhesion, proliferation, and plays a role in various inflammatory and immune responses. The effect of uPA depends on binding to its receptor uPAR, which is expressed on the surface of endothelial cells, activated T cells, granulocytes, and macrophages. This, in turn, leads to local proteolysis and fibrinolysis. The proteolytic cleavage of uPAR from the cell surface leads to the secretion of suPAR, which is the chemotactively active form of uPAR. Previous studies have shown that serum suPAR levels are elevated during various infectious diseases and malignancies, and suPAR levels can serve as an effective biomarker in adults to predict patients' prognosis and treatment efficacy [34].

Various studies have been conducted on suPAR. The majority of these studies have focused on the power of suPAR to predict sepsis and mortality in sepsis patients. According to a study in Spain, suPAR levels are superior compared to CRP and PCT in terms of indicating mortality prognosis in patients in ICU; however, APACHE II and SOFA scores were superior in terms of indicating mortality [17]. Raggam et al. compared suPAR, IL-6, CRP, and PCT levels in the mortality of SIRS patients, and found that suPAR level at the 48th hour has a significantly high predictive value on mortality [19]. Moreover, when bacteremia and suPAR levels were evaluated together, they had a significantly higher predictive value on mortality at days 30 and 90. In conclusion, suPAR levels in early stages of SIRS have a significant predictive value to predict mortality. Wittenhagen et al. and Mölkänen et al. found that suPAR has greater power to predict mortality in patients with bacteremia, compared to PCT and CRP [9,12]. Donadello et al. conducted a study on sepsis patients who were admitted to the ICU to evaluate the mortality at the end of a 28-day follow-up period [18]. In conclusion, APACHE II is more powerful to predict mortality compared to suPAR, and suPAR is more powerful compared to CRP. Rabna et al. conducted a prospective cohort study in West Africa on 863 patients (TBC (-), age >15 years) to investigate the correlation between urine and plasma suPAR levels and mortality [35]. The third month follow-up revealed that 38 patients were deceased, whereas 825 patients survived. suPAR levels in urine were an effective indicator of mortality prognosis in HIV (+) individuals (AUC: 0.75), whereas such an effect was not seen in HIV(-) individuals. Koch et al. conducted a prospective study in Germany, and investigated the correlation between suPAR levels and mortality in an internal ICU [36]. Two hundred seventy-three patients (172 males and 101 females; median age: 64 years (range: 18-90 years)) and 43 controls (28 males and 15 females; median age: 53 years (range: 24-68 years)) were included in the study. Altogether, the authors found that suPAR levels do not have sufficient predictive value with respect to ICU stay. Gustafsson et al. investigated the effects of suPAR on the prognosis of patients with severe sepsis [37]. Twenty-seven patients with sepsis (10 males and 17 females) were included in the study, and were followed-up for 90 days for mortality. For the control group, 11 males and 11 females from neurosurgery ICU were included. Blood samples were collected within the first 24 hours in the ICU to analyze IL-6, IL-10, PCT, CRP, and MPO levels, and SOFA score was calculated. A comparison of suPAR levels between the sepsis group and the control group revealed that there was no significant difference in mortality rates between the groups (deceased n=12; suPAR median: 15.4 ng/mL; min-max: 6.8-36.1; survivors n=15; suPAR median: 11.7 ng/mL; min-max: 5.9-25.5). In conclusion, there is no significant correlation between suPAR levels and mortality, which is likely to result from the small sample size.

The major limitation of our study is the small sample size. Also control patients could not be used for comparing in SIRS.

In the present study, we compared the existing scoring system (APACHE II) and biomarkers, and a new biomarker (suPAR), to predict mortality in patients in ICU. suPAR levels are significantly better compared to day 1 levels of existing biomarkers, including CRP, PCT, and lactate but worse than APACHE II scoring system. At the same time our findings suggest that suPAR levels have no significant superiority over PCT and lactate levels on day 5. These findings suggest that suPAR levels can be used to predict mortality on admission day but not for follow up. As a conclusion more studies with bigger sample size should be designed to show its value better in sepsis and mortality.

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