Original article

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# Prognostic role of soluble urokinase plasminogen activator receptor (suPAR) in ICU outcomes after adult cardiac surgery: A single-center prospective cohort study

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**Abstract**

***Objective*: To determine the prognostic value of soluble urokinase plasminogen activator receptor (suPAR) on morbidity and mortality related to the intensive care unit (ICU) length of stay, hospital length of stay, and postoperative complications in adult cardiac surgery patients.**

***Design*: This study used an analytic observational design with a prospective cohort approach.**

***Setting*: This study was conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar, from December 2024 to March 2025.**

***Patients*: This study involved 40 adult cardiac surgery patients who met the inclusion criteria.**

***Measurements*: SuPAR levels were measured in blood samples obtained before induction of anesthesia and 24 hours postoperatively using an enzyme-linked immunosorbent assay (ELISA). Other data collected included age, gender, body mass index (BMI), presence of comorbidities, New York Heart Association (NYHA) cardiac classification, type of adult cardiac surgical operation, and European System for Cardiac Operative Risk Evaluation (EuroSCORE) II. In addition, postoperative data were collected, and mortality was followed for 30 days postoperatively using Kaplan-Meier survival analysis.**

***Results*: SuPAR levels showed significant associations with length of hospitalization, length of hospital stay, and duration of mechanical ventilation ($p<0.05$). Patients with a longer length of stay consistently had higher suPAR levels. Significant differences were also found between preoperative and postoperative suPAR levels regarding mortality ($p<0.05$). Preoperative suPAR showed acceptable performance in predicting mortality, as indicated by the area under the curve (AUC). Kaplan-Meier survival analysis showed that higher suPAR levels were associated with a lower probability of 30-day postoperative survival. However, suPAR showed no significant association in predicting postoperative stroke or deep sternal wound infection.**

***Conclusions*: SuPAR has significant prognostic value for predicting ICU length of stay, hospital length of stay, mechanical ventilation duration, and mortality in adult cardiac surgery patients. However, no significant association was found between suPAR and postoperative stroke or deep sternal wound infection. Therefore, suPAR serves as an important biomarker to assess prognosis in adult cardiac surgery patients.**

**Keywords**: Soluble urokinase plasminogen activator receptor, ICU outcomes, adult cardiac surgery.

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## Introduction

Postoperative mortality is one of the leading causes of death in the world. (1) European studies reported a high perioperative mortality rate of approximately 3% in elective surgery, 5% in urgent surgery, and up to 10% in emergency department surgery. Comorbidities such as cirrhosis, congestive heart failure, and coronary artery disease are the main risk factors associated with postoperative mortality. (2) A large-scale analysis involving over 600,000 patients revealed that individuals with heart failure undergoing complex surgical procedures faced a 90-day mortality rate exceeding 10%. (2)

In addition, patients undergoing cardiac surgery have a high risk of developing multisystem complications after surgery, which contributes to prolonging intensive care unit (ICU) and hospital length of stay. (3,4) The ability to predict patients at high risk of complications before or after surgery is critical in clinical decision-making. Reliable prognostic biomarkers will allow the identification of patients at increased risk, enabling them to receive intensive monitoring and early intervention. Conversely, patients with low risk can be prioritized for faster recovery. (5)

Multiple risk stratification tools, including the European System for Cardiac Operative Risk Evaluation **(**EuroSCORE) I, EuroSCORE II, and the Society of Thoracic Surgeons (STS) score, have been established to optimize clinical decision-making, guide tailored therapeutic strategies, and improve outcomes in patients undergoing cardiothoracic surgery. (6) In addition to clinical scores, biomarkers have also been evaluated for their ability to predict surgical outcomes, although results vary. (7,8) The majority of studies focus on preoperative risk stratification, while studies related to postoperative risk assessment are limited.

The soluble urokinase plasminogen activator receptor (suPAR) is a circulating form of the membrane-bound urokinase plasminogen activator receptor (uPAR), which plays a key role in plasminogen activation, extracellular proteolysis, and cell migration. (9) Emerging evidence highlights suPAR as a promising biomarker with significant diagnostic and prognostic utility in cardiovascular diseases, critical illness, and sepsis. (10) Cardiothoracic surgery with the use of cardiopulmonary bypass (CPB) elicits a systemic inflammatory response that increases the levels of various inflammatory and infectious biomarkers. Although studies on suPAR in cardiothoracic surgery are limited, a recent study found that suPAR was a predictor of perioperative complications in patients with aortic stenosis. Also, it showed that it predicted the incidence of acute kidney injury after cardiac surgery. (11)

Therefore, this study was conducted to evaluate suPAR as a prognostic marker of mortality and morbidity, as measured by ICU and hospital length of stay, and postoperative complications, in adult patients undergoing cardiac surgery.

## Methods

*Study design, population, and sampling method*

This study used an analytical observational research design with a prospective cohort approach, conducted on adult patients undergoing cardiac surgery at Dr. Wahidin Sudirohusodo Hospital, Makassar, from December 2024 until the sample size was reached. Inclusion criteria included patients aged 18 years or older who underwent heart surgery, had complete preoperative and postoperative suPAR examinations, and were willing to participate in the study by signing informed consent. Sampling was done by consecutive sampling, where all patients who met the inclusion criteria were included until the sample size was reached.

*Data collection*

Blood samples were collected to measure suPAR levels using matrix tubes containing 150 µl of ethylenediaminetetraacetic acid (EDTA) for plasma, at the time before anesthesia induction and at 24 hours postoperatively. Measurement of suPAR was performed using the Human suPAR kit (Bioassay Technology Laboratory, Shanghai, China) and analyzed in the Hasanuddin University Medical Research Center, Makassar.

Patients' history, clinical examination, and laboratory data (age, sex, body mass index [BMI], presence of comorbidities, cardiac disorder classification according to the New York Heart Association [NYHA] classification, type of adult cardiac surgery, and EuroSCORE II) were recorded from electronic medical records. Postoperative data, including duration of CPB, duration of aortic cross-clamping, duration of surgery, duration of mechanical ventilation, length of ICU stay, length of hospital stay, incidence of complications, and mortality, were also recorded. Patient mortality was followed for 30 days postoperatively. All patient data were collected directly by the investigators.

*Data analysis*

Continuous variables were compared using the t-test or Mann-Whitney test, as appropriate, while the discriminatory ability of suPAR was assessed via receiver operating characteristic (ROC) curve analysis. Statistical significance was defined as $p<0.05$.

*Ethical approval*

This study has obtained ethical approval from the Health Research Ethics Committee of Hasanuddin University before the implementation of the survey, with recommendation number 1066/UN 4.6.4.5.31/ PP36/2024.

## Results

*Sample characteristics*

The total sample in this study consisted of 40 patients who met the inclusion criteria and were scheduled to undergo adult cardiac surgery.

**Table 1** presents the baseline characteristics of the patients. The median age of patients was 45 years (18–74), with the majority being male (45%). Mean BMI was 22.4±4.47 kg/m², and median EuroSCORE II was 1.53% (0.70–6.44%). The most common comorbidities were hypertension (15 patients), previous myocardial infarction (15 patients), type 2 diabetes mellitus (6 patients), and pulmonary hypertension (10 patients). The most common type of surgery was coronary artery bypass graft (CABG) (16 patients). The median preoperative suPAR level was 5.74 ng/ml and increased postoperatively to 8.52 ng/ml. The median duration of CPB was 112±45.47 minutes, and the aortic clamp time was 81±29.69 minutes. Median ventilator duration was 28 hours, ICU stay was 70 hours, and hospital stay was 9 days.

**Table 2** shows the comparison of suPAR levels with ICU length of stay, hospital length of stay, and mechanical ventilator duration. Patients with prolonged ICU stays had higher preoperative suPAR levels (7.31±1.45 ng/ml) than the fixed group (4.21±1.38 ng/ml, p=0.001). Similar results were found in hospital length of stay and ventilator duration, with higher preoperative and postoperative suPAR levels in the prolonged stay group ($p<0.05$).

**Table 3** presents the area under the ROC curves (AUC) values for preoperative suPAR and EuroSCORE II on predicting prolonged ICU length of stay, hospital length of stay, and mechanical ventilator use. Preoperative suPAR had high AUC values to predict prolongation of ICU length of stay (AUC 0.900, 95% CI: 0.81–0.99), prolongation of hospital length of stay (AUC 0.817, 95% CI: 0.67–0.97), and prolongation of mechanical ventilator use (AUC 0.895, 95% CI: 0.79–0.99). Meanwhile, EuroSCORE II also had significant AUC values for prolongation of ICU length of stay (0.802) and mechanical ventilator use (0.857), but lower for prediction of hospital length of stay (0.631).

**Table 4** shows the comparison of preoperative suPAR levels to postoperative morbidity. Patients who underwent reoperation had higher preoperative suPAR levels (7.91±2.04 ng/ml) than those who did not (5.12±1.86 ng/ml, p=0.021). In patients with postoperative acute kidney injury, preoperative suPAR levels were also higher (6.91±1.06 ng/ml) than in those without acute kidney injury (4.91±2.12 ng/ml, p=0.002). There was no significant difference between preoperative suPAR levels and the incidence of postoperative stroke (p=0.208) or deep sternal wound infection (p=0.750).

**Table 5** shows the difference in suPAR levels between patients who died and those who survived. The preoperative suPAR levels of patients who died were higher (6.55±2.03 ng/ml) than those who lived (5.25±1.85 ng/ml), with p=0.008. Similarly, postoperative suPAR levels in the deceased group (9.57±2.03 ng/ml) were higher than those in the living group (7.89±3.29 ng/ml, p=0.038).

**Table 6** presents the AUC for preoperative suPAR and EuroSCORE II in predicting mortality. Preoperative suPAR levels had an AUC of 0.757 (95% CI: 0.59–0.91), while EuroSCORE II had a higher AUC of 0.903 (95% CI: 0.81–0.99) in predicting patient mortality.

**Figure 1** shows the relationship between preoperative suPAR and EuroSCORE II with prolonged ICU stay. Both suPAR and EuroSCORE II increased proportionally with longer ICU stays, indicating their role as risk stratification markers for postoperative recovery.

**Figure 2** illustrates the association between preoperative suPAR and EuroSCORE II with mortality. Patients with higher suPAR and EuroSCORE II had higher mortality, demonstrating that both biomarkers are predictive of adverse outcomes.

**Figure 3** shows that preoperative suPAR levels were divided into four quartile groups. The lowest suPAR quartile group (blue) had the highest survival probability, indicating that patients with the lowest suPAR levels had the greatest likelihood of survival. In contrast, the highest suPAR quartile group (orange) showed the lowest survival rate, with a sharp decline occurring within the first few postoperative days, reflecting a higher risk of mortality. This demonstrates that patients with the highest suPAR levels had the worst outcomes. From **Figure 3**, it can be concluded that there is an association between suPAR levels and survival probability. The higher the suPAR level (approaching quartile 4), the lower the survival probability within 30 days of adult cardiac surgery.

## Discussion

The results of this study show that the baseline characteristics of the sample, such as age, gender, BMI, and comorbid history, are in line with the character-

istics of adult cardiac surgery patients in previous studies, and that these conditions contribute to an increased risk of postoperative complications and mortality. (12,13) The median preoperative suPAR level was 5.74 ng/ml and increased postoperatively to 8.52 ng/ml, supporting suPAR's role as an inflammatory biomarker elevated under conditions of surgical stress and systemic inflammation. (14)

This study showed that preoperative and postoperative suPAR levels were significantly associated with ICU and hospital length of stay and mechanical ventilator use. Patients with higher preoperative suPAR levels tended to have prolonged length of stay, as reported by Eugen-Olsen et al., who found that suPAR correlated with disease severity and ICU length of stay. (15) The preoperative suPAR AUC value in predicting prolongation of ICU length of stay (0.900), hospital length of stay (0.817), and ventilator duration (0.895) showed good diagnostic performance, similar to Backes et al.'s study, which found suPAR AUC>0.8 for the prediction of postoperative complications. (16)

This study also found higher preoperative suPAR levels in patients who underwent reoperation ($p=0.021$) and in those with postoperative acute kidney injury ($p=0.002$). This supported Hayek et al.'s study, which showed that suPAR played a role in the pathophysiology of acute kidney injury by activating podocytes and inducing renal inflammation. (17) However, no significant difference was found between suPAR levels and the incidence of postoperative stroke or deep sternal wound infection. This was consistent with Okonta et al.'s report that risk factors for stroke and sternal wound infection were multifactorial and not always directly related to systemic inflammation. (18)

In addition, preoperative and postoperative suPAR levels also showed a significant association with mortality. Kaplan-Meier analysis showed that patients with the highest quartile suPAR levels had the lowest 30-day postoperative survival probability. This finding was in line with Chenevier-Gobeaux et al.'s meta-analysis, which reported an increased risk of mortality in patients with high suPAR. (19) The AUC value of preoperative suPAR in mortality prediction (0.757) was moderate, whereas EuroSCORE II showed higher predictive performance (AUC 0.903), consistent with the EuroSCORE II validation study in cardiac surgery patients. (20)

Overall, suPAR has potential as a prognostic biomarker for predicting morbidity and mortality in adult cardiac surgery patients, especially for early risk stratification and postoperative management optimization.

However, this study has a relatively small sample size, which may affect the validity of the results. In addition, suPAR levels were not measured serially, and there was potential bias because the exact cause of the increase in suPAR levels in each patient was unknown. Further research with a prospective multicenter cohort design and multivariate analysis is recommended to strengthen these findings.

**Limitation**

Despite statistical significance, the relatively wide confidence intervals in some AUC values warrant caution when interpreting suPAR's predictive power in smaller subgroups. The predominantly Asian population limited the applicability to other ethnic groups. suPAR measurements were limited to two perioperative time points, potentially obscuring temporal patterns. Additionally, unmeasured confounders and the lack of comparative biomarker data may have influenced outcomes. The 30-day follow-up period further precluded evaluation of late effects.

**Conclusion**

SuPAR levels are a reliable predictor of morbidity and mortality risk in adult cardiac surgery patients. SuPAR correlates strongly with length of stay and ventilator duration and shows good diagnostic accuracy for mortality. Therefore, suPAR has potential as a routine, non-invasive tool for early detection and prognostication.

**Conflict of interest**

All authors have no conflict of interest regarding this article. This research did not receive research funding from any party.

**Table 1**. Characteristics of research subjects

| Characteristics | Patients (n=40) |
|---|---|
| Age (years) | 45 (18–74) |
| Gender (male) | 18 |
| BMI (kg/m$^2$) | 22.4±4.47 |
| EuroSCORE II (%) | 1.53 (0.70–6.44) |
| Comorbidities<br>- DM type 2<br>- Hypertension<br>- Previous myocardial infarction<br>- Pulmonary hypertension | <br>6<br>15<br>15<br>10 |
| Procedure type<br>- CABG<br>- 1 non-CABG procedure<br>- 2 procedures<br>- 3 procedures | <br>16<br>12<br>8<br>4 |
| SuPAR<br>- Preoperative (ng/ml)<br>- Postoperative (ng/ml) | <br>5.74 (0.52–10.55)<br>8.52 (2.98–14.55) |
| Cardiopulmonary bypass duration (min) | 112±45.47 |
| Aortic cross-clamp time (min) | 81±29.69 |
| Duration of mechanical ventilator use (hours) | 28 (18–216) |
| Length of ICU stay (hours) | 70 (42–406) |
| Length of hospital stay (days) | 9 (4–28) |

Legend: BMI=body mass index; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; DM=diabetes mellitus; CABG=coronary artery bypass graft; suPAR=soluble urokinase plasminogen activator receptor; ICU=intensive care unit.
Numerical data (BMI, cardiopulmonary bypass duration, aortic cross-clamp time) are displayed with mean±standard deviation. Numerical data (age, EuroScore II, SuPAR, duration of mechanical ventilator use, length of ICU stay, and length of hospital stay) are presented as median (min-max). Categorical data (gender, comorbidities, and procedure type) are shown as frequencies (n).

**Table 2**. Comparison of suPAR levels against ICU and hospital length of stay and mechanical ventilation duration

| | Fixed | Prolonged | p-value |
|---|---|---|---|
| ICU length of stay<br>- suPAR preop (ng/ml)<br>- suPAR postop (ng/ml) | <br>4.21±1.38<br>6.03±1.88 | <br>7.31±1.45<br>11.09±1.99 | <br>0.001<br>0.001 |
| Hospital length of stay<br>- suPAR preop (ng/ml)<br>- suPAR postop (ng/ml) | <br>4.52±1.87<br>6.47±2.43 | <br>6.69±1.67<br>10.17±2.79 | <br>0.002<br>0.001 |
| Mechanical ventilation duration<br>- suPAR preop (ng/ml)<br>- suPAR postop (ng/ml) | <br>4.06±1.68<br>6.77±2.54 | <br>7.39±1.52<br>10.97±2.41 | <br>0.001<br>0.001 |

Legend: suPAR=soluble urokinase plasminogen activator receptor; ICU=intensive care unit.
Data were processed using the Mann-Whitney U test.

**Table 3**. Preoperative suPAR and EuroSCORE II on the prolongation of stay and mechanical ventilator

| AUC | ICU length of stay | Hospital length of stay | Prolongation of mechanical ventilation |
|---|---|---|---|
| SuPAR | 0.900 (0.81–0.99) | 0.817 (0.67–0.97) | 0.895 (0.79–0.99) |
| EuroSCORE II | 0.802 (0.66–0.94) | 0.631 (0.44–0.83) | 0.857 (0.74–0.97) |

Legend: suPAR=soluble urokinase plasminogen activator receptor; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; AUC=area under the curve; ICU=intensive care unit.
Data are shown as AUC with a 95% confidence interval.

**Table 4**. Comparison of preoperative suPAR levels to postoperative morbidity

| Postoperative morbidity | Preoperative suPAR (ng/ml) | p-value |
|---|---|---|
| Reoperation<br>- Yes (n=6)<br>- No (n=34) | <br>7.91±2.04<br>5.12±1.86 | 0.021 |
| Postoperative stroke<br>- Yes (n=2)<br>- No (n=38) | <br>5.34±2.08<br>7.36±0.54 | 0.208 |
| Deep sternal wound infection<br>- Yes (n=1)<br>- No (n=39) | <br>5.47±2.07<br>8.09±3.16 | 0.750 |
| Postoperative acute kidney injury<br>- Yes (n=12)<br>- No (n=28) | <br>6.91±1.06<br>4.91±2.12 | 0.002 |

Legend: suPAR=soluble urokinase plasminogen activator receptor.
Data were processed using the Mann-Whitney U test.

**Table 5**. Comparison of suPAR levels on mortality

| Mortality | No (n=26) | Yes (n=14) | p-value |
|---|---|---|---|
| SuPAR preop (ng/ml) | 5.251±1.85 | 6.55±2.03 | 0.008 |
| SuPAR postop (ng/ml) | 7.89±3.29 | 9.57±2.03 | 0.038 |

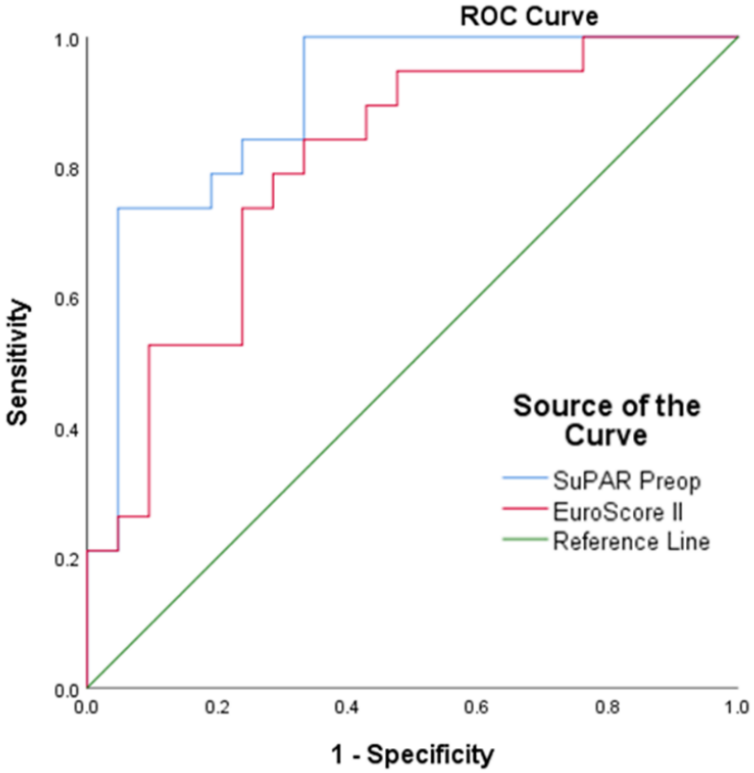
Legend: suPAR=soluble urokinase plasminogen activator receptor.
Data were processed using the Mann-Whitney U test.

**Table 6**. Relationship between suPAR and EuroSCORE II levels on mortality

| | AUC |
|---|---|
| SuPAR level | 0.757 (0.59–0.91) |
| EuroSCORE II | 0.903 (0.81–0.99) |

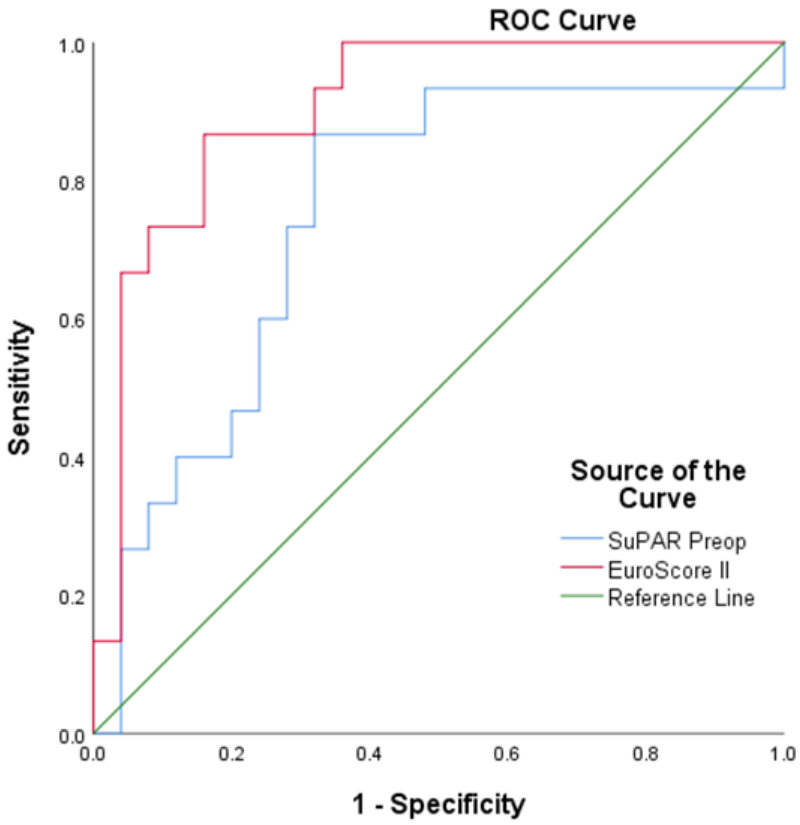
Legend: suPAR=soluble urokinase plasminogen activator receptor; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; AUC=area under the curve.
Data are shown as AUC with a 95% confidence interval.

**Figure 1**. Preoperative suPAR and EuroSCORE II in relation to prolonged ICU stay



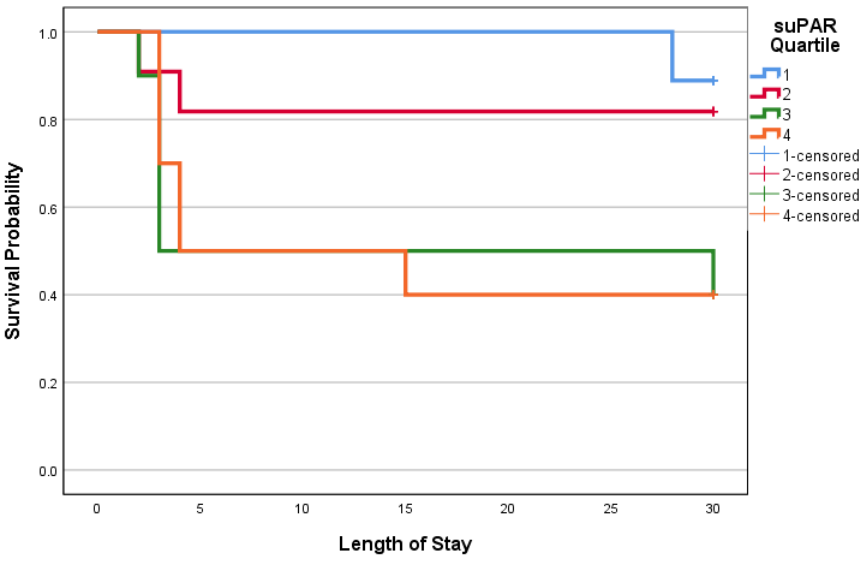

Legend: suPAR=soluble urokinase plasminogen activator receptor; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; ICU=intensive care unit; ROC=receiver operating characteristic.

**Figure 2**. Preoperative suPAR and EuroSCORE II in relation to mortality




Legend: suPAR=soluble urokinase plasminogen activator receptor; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; ICU=intensive care unit; ROC=receiver operating characteristic.

**Figure 3**. Probability of suPAR levels on survival according to length of stay




Legend: suPAR=soluble urokinase plasminogen activator receptor.

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