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ORIGINAL ARTICLE

Fibrinogen-to-albumin ratio is associated with the prognosis of patients with septic acute kidney injury

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ABSTRACT

Background. The fibrinogen-to-albumin ratio (FAR), a novel inflammatory biomarker, is strongly associated with the incidence of sepsis. Nonetheless, there is a lack of research regarding the FAR and prognosis in individuals with septic acute kidney injury (SAKI). The aim of this study was to assess the correlation between the FAR upon intensive care unit (ICU) admission and overall mortality in patients with SAKI.

Methods. All patient information was retrieved from the Medical Information Mart for Intensive Care-IV (MIMIC-IV) database. All patients were divided into four distinct categories according to the FAR. The primary endpoints for this study were the 30-day and 365-day all-cause death rates, whereas the secondary endpoints were the 60-day, 90-day and 180-day all-cause death rates. The FAR was quartile, and the Kaplan–Meier curve was used to evaluate the outcomes across the groups. To evaluate the correlation between the FAR and outcomes, we used a Cox proportional hazards regression model and restricted cubic splines (RCSs).

Results. Among the 6208 participants, the average age was 65 years, with 3659 (58.94%) identified as male. Patients exhibiting elevated FAR values demonstrated an increased risk of all-cause mortality at 30, 60, 90, 180 and 365 days, as evidenced by the Kaplan–Meier curves (log-rank $P < .001$). SAKI patients with elevated FAR values had a greater risk of all-cause mortality at 30, 60, 90, 180 and 365 days than did those with lower FAR values, as demonstrated by Cox proportional hazards regression analysis. With inflection points at 35.14 for 30-day mortality and 34.8 for 365-day mortality, the RCS analysis revealed that the FAR and all-cause mortality were related in an inverted N-type pattern. In instances where FAR levels were below 35.14 mg/g, a reduction of 1 unit in the FAR correlated with a 6.5% increase in the risk of 30-day all-cause mortality [hazard ratio (HR) 0.935; 95% confidence interval (CI) 0.923, 0.948]. In instances where FAR levels were below 34.8 mg/g, a reduction of 1 unit in the FAR correlated with a 6.2% increase in the risk of 365-day all-cause mortality (HR 0.938; 95% CI 0.927, 0.949).

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Conclusion. In severely ill patients with SAKI, elevated FAR levels are strongly correlated with an increased risk of all-cause mortality at 30, 60, 90, 180 and 365 days. FAR may serve as a reliable metric for assessing and managing patients with SAKI in the ICU.

Keywords: all-cause mortality, fibrinogen-to-albumin ratio (FAR), inflammatory biomarker, prognosis, septic acute kidney injury

KEY LEARNING POINTS

What was known:

- Fibrinogen-to-albumin ratio (FAR), a novel inflammatory biomarker, is strongly associated with the incidence of sepsis; nonetheless, there is a lack of research regarding the FAR and prognosis in individuals with septic acute kidney injury (SAKI).
- The aim of this study was to assess the correlation between the FAR upon intensive care unit (ICU) admission and overall mortality in patients with SAKI.

This study adds:

- In severely ill patients with SAKI, elevated FAR levels are strongly correlated with an increased risk of all-cause mortality at 30, 60, 90, 180 and 365 days.
- FAR may serve as a reliable metric for assessing and managing patients with SAKI in the ICU.

Potential impact:

- FAR may be a new inflammatory biomarker in SAKI.

INTRODUCTION

Sepsis, characterized by organ malfunction, is a potentially fatal condition induced by immune response disorders, and its pathophysiological process is more complex than that of simple infection [1]. Although the survival rate of patients with mild sepsis has been significantly improved, severe patients still need to be monitored and treated in the intensive care unit (ICU), and the mortality rate is as high as 20%. The mortality rate is even higher for severe patients with complications [2]. Acute kidney injury (AKI) frequently occurs as an outcome of sepsis. There are approximately 98 million cases of septic acute kidney injury (SAKI) worldwide each year [3]. In the ICU, the incidence of SAKI is 51%, and the number of deaths accounts for 41% of ICU deaths [3]. Patients who survive SAKI are prone to various complications, including chronic kidney disease and even death [3]. Recognizing indicators that help assess the prognosis of SAKI and pinpointing appropriate therapeutic strategies is crucial because severe morbidity and mortality are linked to SAKI.

Fibrinogen is a serum glycoprotein that plays a central role in the coagulation cascade as a key coagulation factor in the coagulation pathway. In addition, fibrinogen is also involved in inflammatory responses, and its level is associated with the occurrence and development of tumors [4]. An elevated fibrinogen level is significantly correlated with increased mortality from sepsis [5]. Recent studies confirmed that fibrinogen is a positive acute-phase response protein, marked by increased levels during systemic inflammatory responses [6]. In contrast, albumin is recognized as a negative acute-phase response protein [7]. Studies have shown that the serum albumin concentration is a reliable indicator of prognosis in patients with sepsis [8]. The fibrinogen-to-albumin ratio (FAR) combines information from coagulation function and nutritional status and has become an emerging biomarker of inflammation. FAR has been demonstrated to have distinctive implications in the diagnosis and prognosis of pathologies such as stroke-associated pneumonia [9], colorectal cancer [10] and antineutrophil cytoplasmic antibody–associated vasculitis [11]. By monitoring the FAR, clinicians can obtain comprehensive information about a patient's inflammatory status and overall nutritional status, which can help clinicians assess the condition more accurately and guide treatment strategies.

Currently, there is very little research regarding the correlation between the FAR and sepsis incidence. A retrospective investigation indicated that an elevated FAR was an independent predictor of both the presence and severity of newborn sepsis [12]. Nevertheless, this research has several drawbacks, such as the potential for errors arising from the use of outdated diagnostic criteria. Furthermore, the link between the FAR and SAKI remains largely unexplored and requires additional investigation. We performed a retrospective analysis to assess the prognostic value of the FAR in SAKI patients, utilizing data from the Medical Information Mart for Intensive Care-IV database version 2.0 (MIMIC-IV v2.0).

MATERIALS AND METHODS

Source of data

Retrospective analysis was included in the study. The raw data were obtained from the critical care database (MIMIC-IV v2.2). The MIMIC-IV database contains comprehensive data on ICU patients, including demographic information, biochemistry results, vital signs, patient diagnoses and survival status. We have successfully completed the assessments of the Collaborative Institutional Training Initiative (CITI). Given the anonymity of the patients and the absence of protected information in the database, a waiver of informed consent was approved. One of the authors, W.W., obtained access to the database after passing the CITI exam (certificate number 56 452 808).

Ethics approval and consent to participate

The MIMIC-IV database was approved by the Massachusetts Institute of Technology (Cambridge, MA, USA) and consent was obtained for the original data collection.

Population selection criteria

The sepsis criteria followed the definition of the Sepsis 3.0 criteria, characterized by a suspected infection alongside a Sequential Organ Failure Assessment (SOFA) score of ≥2 [1] and AKI, in compliance with the criteria of Kidney Disease: Improving Global Outcomes (KDIGO) [13]. Patients were diagnosed with AKI according to the KDIGO criteria, defined by any of the following conditions: an increase in serum creatinine (Scr) by ≥0.3 mg/dL (26.5 μmol/L) within 48 h, an Scr elevation to ≥1.5 times the baseline value, known or presumed to have occurred within the past 7 days, or a urine output of <0.5 mL/kg/h for more than six consecutive hours. In cases where baseline Scr was not recorded before ICU admission, the initial Scr value after admission was adopted as the baseline reference. The exclusion criteria were as follows: (i) had numerous ICU admissions; (ii) were under 18 years of age; (iii) had an ICU stay <24 h; (iv) had no survival outcome; (v) had missing data on the first day of admission (fibrinogen, albumin); (vi) had abnormal data; and (vii) had chronic kidney disease. We incorporated the initial ICU admission data from the first hospitalization for patients with multiple admissions. A total of 6208 patients were included in the final study cohort and categorized into four groups based on the quartiles of the FAR data (Supplementary data, Fig. S1). This method ensures that the sample size of each group is relatively balanced. It also facilitates comparison of clinical outcomes among patients with different FAR levels, thereby minimizing bias.

Data extraction

We employed Navicat software to retrieve data from the MIMIC-IV, including demographic information, vital signs, comorbidities, therapies, laboratory data, scoring systems and prognostic data during follow-up. All hematological parameters were assessed for the first time following patient admission to the ICU. The formula for determining the FAR was as follows: serum fibrinogen (mg/dL)/serum albumin (mg/dL) [14]. Any variable exhibiting >20% missing data was excluded from the analysis. For variables with ≤20% missing data, imputation was conducted utilizing the random forest method to ensure data integrity and reliability.

Outcomes

The MIMIC-IV database encompasses mortality rates for the prognosis of SAKI patients. The primary endpoint for the current study was the 30-day and 365-day all-cause death rates, whereas the supplementary endpoints were the all-cause mortality rates at 60, 90 and 180 days.

Statistical analysis

This study used R 4.4.1 statistical analysis software. Continuous variables with a normal distribution are presented as the means ± standard deviations, and t tests were used to evaluate them. Skewed continuous data were represented as mean (first quartile, third quartile) [M (Q_1, Q_3)], and the rank sum test was employed for multiple sample groups. Categorical data are presented as *n* (%), and the chi-square test or Fisher's exact test was employed. Intergroup comparisons were considered statistically significant when $P < .05$.

We stratified the data by the FAR and used Kaplan–Meier curves to determine the occurrence rates of the primary and secondary outcomes. The associations between the FAR and mortality at 30, 60, 90, 180 and 365 days were evaluated via univariate Cox analyses. Variables that were clinically significant or demonstrated a univariate association with the outcome were included in the multivariate Cox proportional hazard regression model. We cautiously selected the variables for the end model according to the quantity of available occurrences. Model 1 alone incorporated the FAR, whereas Model 2 accounted for age, SOFA score, body mass index (BMI), sex, marital status, hypertension and diabetes. We utilized the lowest quartile of the FAR as the reference for both models.

To further elucidate the correlation of the dosage effect with the risk of major and secondary outcome events, the FAR was also investigated as a continuous variable via restricted cubic splines (RCSs). The inflection points between the FAR and 30-day, 60-day, 90-day, 180-day and 365-day mortality rates were determined via the recursive algorithm in the event that the correlations were nonlinear. A two-segment Cox proportional risk model was implemented on both sides of the inflection point to further investigate the correlations between the FAR and 30-day, 60-day, 90-day, 180-day and 365-day mortality rates. Furthermore, based on sex, age, hypertension and diabetes, a stratified analysis was conducted.

RESULTS

Baseline characteristics of the study participants

The study included 41 647 sepsis patients from the MIMIC-IV database, of whom 6208 patients with SAKI satisfied the inclusion criteria (Supplementary data, Fig. S1) and were further evaluated.

The average age of the patients who participated in the study was 65 years (18–101 years), and men made up 58.94% of the total participants. The study participants' baseline characteristics were investigated according to the quartiles of the FAR at admission (Q1: <52.88 mg/g, Q2: 52.89–84.63 mg/g, Q3: 84.64–155 mg/g, and Q4: >155 mg/g) and are detailed in Table 1. The mean FAR values in the four groups were 41.085, 65.845, 111.11 and 221.07 mg/g, respectively. The participants with the lowest FAR were younger and presented a reduced prevalence of dementia, cerebrovascular disease, chronic pulmonary disease, diabetes, paraplegia, cancer and peptic ulcer disease. These patients had a higher prevalence of peripheral vascular disease and mild liver disease, as well as severe liver disease. Additionally, there was a lower utilization rate of norepinephrine and epinephrine than aspirin and furosemide. Furthermore, they presented lower heart rates; respiratory rates; PaCO2, temperature, glucose, hematocrit, hemoglobin, creatinine, platelet, white blood cell, anion gap, blood urea nitrogen, alkaline phosphatase, red blood cell and fibrinogen levels; and elevated levels of calcium, basophil, eosinophil, monocyte, neutrophil, international normalized ratio, prothrombin time, partial thromboplastin time, alanine aminotransferase, aspartate aminotransferase, lactate, PaO2 and albumin than did the other groups. In the Q2 group, the 30-day mortality rates were 25.84%, 23.32%, 29.18% and 30.03% ($P < .01$); the 60-day mortality rates were 30.09%, 26.80%, 34.60% and 36.66% ($P < .01$); the 90-day mortality rates were 31.44%, 28.03%, 37.64% and 39.29% ($P < .01$); the 180-day

Table 1: Baseline characteristics of patients grouped according to FAR quartiles.

Variables	Total ($n = 6208$)	Q1 ($n = 1552$)	Q2 ($n = 1552$)	Q3 ($n = 1549$)	Q4 ($n = 1555$)	P
Demographics						
Age, M (Q_1, Q_3)	65.00 (54.00, 74.00)	63.00 (54.00, 72.00)	65.00 (54.00, 74.00)	65.00 (54.00, 76.00)	66.00 (54.00, 76.00)	**<.001**
Gender, *n* (%)						**<.001**
1	3659 (58.94)	966 (62.24)	935 (60.24)	896 (57.84)	862 (55.43)	
2	2549 (41.06)	586 (37.76)	617 (39.76)	653 (42.16)	693 (44.57)	
Height, cm, M (Q_1, Q_3)	170.00 (163.00, 176.95)	172.42 (165.00, 178.00)	170.00 (163.00, 178.00)	170.00 (163.00, 176.34)	168.00 (163.00, 175.00)	**<.001**
Weight kg, M (Q_1, Q_3)	82.95 (70.00, 98.96)	82.00 (70.15, 97.00)	83.20 (70.00, 99.41)	82.20 (69.00, 99.00)	83.83 (70.00, 100.00)	.266
Marital status, *n* (%)						**.016**
1	1925 (31.01)	458 (29.51)	451 (29.06)	511 (32.99)	505 (32.48)	
2	3232 (52.06)	843 (54.32)	841 (54.19)	751 (48.48)	797 (51.25)	
3	571 (9.20)	126 (8.12)	145 (9.34)	167 (10.78)	133 (8.55)	
4	480 (7.73)	125 (8.05)	115 (7.41)	120 (7.75)	120 (7.72)	
Vital signs						
Heart rate mean, M (Q_1, Q_3)	89.00 (78.00, 102.00)	85.00 (77.00, 97.00)	86.00 (78.00, 99.00)	90.00 (78.00, 103.00)	94.09 (81.00, 108.00)	**<.001**
SBP mean, M (Q_1, Q_3)	109.47 (102.00, 118.00)	110.00 (103.00, 117.00)	110.00 (103.00, 118.00)	109.00 (102.00, 118.00)	109.00 (102.00, 118.00)	.902
DBP mean, M (Q_1, Q_3)	60.00 (54.00, 66.00)	59.00 (53.00, 64.00)	59.00 (54.00, 65.00)	60.00 (55.00, 67.00)	61.00 (55.00, 67.00)	**<.001**
MBP mean, M (Q_1, Q_3)	75.00 (70.00, 80.00)	74.00 (69.00, 80.00)	75.00 (70.00, 80.00)	75.00 (70.00, 81.00)	75.00 (70.00, 81.00)	**.006**
RR mean, M (Q_1, Q_3)	19.00 (17.00, 23.00)	18.00 (16.00, 21.00)	18.00 (17.00, 21.00)	20.00 (17.00, 24.00)	22.00 (19.00, 25.00)	**<.001**
Temperature mean, M (Q_1, Q_3)	36.80 (36.58, 37.20)	36.70 (36.50, 36.90)	36.80 (36.50, 37.10)	36.80 (36.60, 37.20)	37.00 (36.70, 37.50)	**<.001**
Laboratory data						
Spo2, %, mean, M (Q_1, Q_3)	97.00 (96.00, 99.00)	98.00 (96.00, 99.00)	98.00 (96.00, 99.00)	97.00 (96.00, 99.00)	97.00 (95.00, 98.00)	**<.001**
Glucose, g/dL, M (Q_1, Q_3)	135.00 (118.00, 167.00)	131.00 (119.00, 155.00)	134.00 (120.00, 161.00)	137.00 (116.00, 173.00)	142.00 (114.00, 178.00)	**<.001**
Hematocrit, %, M (Q_1, Q_3)	26.80 (22.90, 32.00)	25.00 (21.80, 29.00)	26.30 (22.60, 31.10)	27.40 (23.30, 33.00)	29.10 (24.90, 34.30)	**<.001**
Hemoglobin, g/dL, M (Q_1, Q_3)	8.90 (7.60, 10.60)	8.40 (7.20, 9.80)	8.90 (7.50, 10.40)	9.06 (7.50, 10.80)	9.50 (8.00, 11.20)	**<.001**
Platelets, K/μL, M (Q_1, Q_3)	123.00 (72.00, 185.00)	91.00 (54.00, 127.00)	116.00 (68.00, 160.00)	142.00 (84.00, 204.00)	175.00 (103.00, 251.00)	**<.001**
WBC, K/μL, M (Q_1, Q_3)	15.10 (10.60, 20.90)	14.50 (10.70, 19.40)	15.10 (10.70, 20.20)	15.70 (10.80, 21.80)	15.50 (10.10, 22.20)	**.001**
Anion gap, mmol/L, M (Q_1, Q_3)	16.00 (13.00, 20.00)	15.00 (12.00, 20.00)	15.00 (13.00, 20.00)	17.00 (14.00, 20.00)	17.00 (14.00, 20.00)	**<.001**
Bicarbonate, mmol/L, M (Q_1, Q_3)	20.00 (16.00, 23.00)	21.00 (17.00, 23.00)	21.00 (17.00, 23.00)	19.00 (16.00, 23.00)	19.00 (16.00, 23.00)	**<.001**
BUN, mg/dL, M (Q_1, Q_3)	23.00 (16.00, 37.00)	21.00 (15.00, 33.00)	21.00 (15.00, 34.00)	26.00 (17.00, 39.00)	28.00 (18.00, 44.00)	**<.001**
Calcium, mg/dL, M (Q_1, Q_3)	7.90 (7.30, 8.30)	8.10 (7.60, 8.44)	8.01 (7.50, 8.36)	7.80 (7.20, 8.30)	7.60 (7.10, 8.10)	**<.001**
Chloride, mEq/L, M (Q_1, Q_3)	103.00 (98.00, 106.00)	103.00 (99.00, 107.00)	103.00 (99.00, 107.00)	102.00 (98.00, 106.00)	101.00 (97.00, 105.00)	**<.001**
Creatinine, mg/dL, M (Q_1, Q_3)	1.20 (0.90, 1.90)	1.10 (0.90, 1.90)	1.10 (0.90, 1.70)	1.30 (0.90, 1.90)	1.30 (0.90, 2.10)	**<.001**
Sodium, mEq/L, M (Q_1, Q_3)	136.00 (133.00, 139.00)	137.00 (134.00, 139.00)	136.00 (134.00, 139.00)	136.00 (133.00, 139.00)	136.00 (133.00, 139.00)	.118
Potassium, mEq/L, M (Q_1, Q_3)	4.60 (4.20, 5.10)	4.60 (4.30, 5.10)	4.60 (4.30, 5.10)	4.60 (4.20, 5.20)	4.50 (4.10, 5.10)	**.001**
Basophils, K/μL, M (Q_1, Q_3)	0.09 (0.02, 3.78)	0.80 (0.02, 3.79)	0.18 (0.02, 3.72)	0.10 (0.01, 4.03)	0.05 (0.00, 3.59)	**<.001**
Eosinophils, K/μL, M (Q_1, Q_3)	0.41 (0.01, 12.10)	2.85 (0.07, 14.36)	1.40 (0.04, 13.02)	0.45 (0.01, 11.17)	0.09 (0.00, 8.78)	**<.001**
Lymphocytes, K/μL, M (Q_1, Q_3)	55.67 (1.34, 153.93)	81.84 (1.72, 172.57)	71.66 (1.63, 167.10)	56.10 (1.37, 147.14)	18.40 (0.91, 134.27)	**<.001**
Monocytes, K/μL, M (Q_1, Q_3)	20.00 (0.75, 58.17)	24.98 (0.63, 52.37)	19.98 (0.76, 52.37)	24.32 (0.87, 63.45)	6.00 (0.72, 63.75)	**<.001**
Neutrophils, K/μL, M (Q_1, Q_3)	459.36 (11.24, 1077.50)	571.38 (100.12, 989.80)	492.36 (11.06, 1022.39)	510.98 (12.61, 1152.63)	80.40 (11.37, 1157.63)	**<.001**

Table 1: Continued

Variables	Total ($n = 6208$)	Q1 ($n = 1552$)	Q2 ($n = 1552$)	Q3 ($n = 1549$)	Q4 ($n = 1555$)	*P*
INR, M (Q_1, Q_3)	1.60 (1.30, 2.10)	1.80 (1.50, 2.60)	1.60 (1.40, 2.10)	1.60 (1.30, 2.00)	1.40 (1.30, 1.80)	**<.001**
PT, s, M (Q_1, Q_3)	17.35 (14.80, 22.90)	19.40 (16.10, 27.70)	17.50 (15.00, 22.70)	16.90 (14.30, 21.80)	15.80 (13.80, 19.95)	**<.001**
PTT, s, M (Q_1, Q_3)	39.50 (31.50, 59.90)	45.70 (34.50, 67.10)	40.20 (31.90, 60.92)	38.50 (31.10, 60.10)	35.40 (29.80, 50.15)	**<.001**
ALT, U/L, M (Q_1, Q_3)	54.83 (27.00, 134.38)	62.66 (32.82, 176.83)	56.00 (29.38, 136.31)	53.41 (25.00, 137.36)	45.00 (22.00, 103.20)	**<.001**
ALP, U/L, M (Q_1, Q_3)	95.00 (70.87, 139.00)	88.86 (71.21, 120.34)	88.16 (69.00, 122.03)	101.14 (71.00, 149.00)	107.28 (71.00, 160.00)	**<.001**
AST, U/L, M (Q_1, Q_3)	97.02 (46.51, 249.00)	122.19 (64.92, 368.38)	107.00 (54.00, 273.03)	89.00 (41.00, 248.00)	70.00 (34.00, 172.00)	**<.001**
Lactate, mmol/L, M (Q_1, Q_3)	3.00 (2.01, 5.00)	3.50 (2.50, 6.00)	3.20 (2.23, 5.40)	2.81 (1.90, 4.72)	2.40 (1.60, 3.80)	**<.001**
PH, M (Q_1, Q_3)	7.30 (7.22, 7.35)	7.30 (7.23, 7.35)	7.30 (7.23, 7.35)	7.31 (7.22, 7.36)	7.30 (7.21, 7.36)	.132
PaO2, mmHg, M (Q_1, Q_3)	83.00 (64.13, 109.00)	87.00 (68.00, 112.01)	87.00 (67.00, 114.00)	82.00 (65.00, 109.00)	76.00 (60.00, 101.00)	**<.001**
PaCO2, mmHg, M (Q_1, Q_3)	34.00 (30.00, 38.00)	33.00 (30.00, 36.13)	34.00 (30.00, 37.00)	34.00 (30.00, 38.00)	36.00 (31.00, 40.00)	**<.001**
Base excess, mmol/L, M (Q_1, Q_3)	−4.00 (−9.00, −1.00)	−5.00 (−9.00, −2.00)	−4.00 (−9.00, −2.00)	−4.00 (−9.00, −1.00)	−4.00 (−9.00, −0.97)	**<.001**
Total CO_2, mmol/L, M (Q_1, Q_3)	26.00 (22.00, 28.00)	26.00 (23.00, 28.00)	26.00 (23.00, 28.00)	25.00 (22.00, 28.00)	25.00 (22.00, 28.00)	**<.001**
RBC, K/μL, M (Q_1, Q_3)	3.26 (2.76, 3.89)	3.00 (2.55, 3.50)	3.19 (2.72, 3.77)	3.36 (2.83, 4.00)	3.51 (3.02, 4.14)	**<.001**
Albumin, g/dLl, M (Q_1, Q_3)	3.00 (2.50, 3.60)	3.60 (2.98, 4.10)	3.20 (2.70, 3.80)	2.90 (2.50, 3.40)	2.50 (2.20, 2.90)	**<.001**
Fibrinogen, mg/dL, M (Q_1, Q_3)	257.00 (172.00, 432.00)	139.00 (104.00, 171.00)	215.00 (177.00, 250.00)	332.00 (269.00, 397.00)	591.00 (479.00, 724.00)	**<.001**
Scoring system						
Charlson Comorbidity Index, M (Q_1, Q_3)	5.00 (4.00, 7.00)	5.00 (4.00, 6.00)	5.00 (4.00, 7.00)	6.00 (4.00, 7.00)	5.00 (4.00, 7.00)	**<.001**
APSIII, M (Q_1, Q_3)	65.00 (43.00, 90.00)	58.00 (36.00, 88.00)	57.00 (37.00, 82.00)	66.00 (49.00, 90.00)	73.00 (54.00, 94.00)	**<.001**
SAPSII, M (Q_1, Q_3)	42.00 (34.00, 54.00)	40.00 (32.00, 52.00)	41.00 (32.00, 53.00)	44.00 (35.00, 56.00)	45.00 (36.00, 56.00)	**<.001**
OASIS, M (Q_1, Q_3)	38.00 (32.00, 46.00)	35.00 (29.00, 42.00)	36.00 (30.00, 43.00)	40.00 (33.00, 46.00)	42.00 (35.00, 48.00)	**<.001**
SOFA score, M (Q_1, Q_3)	4.00 (3.00, 6.00)	4.00 (3.00, 7.00)	4.00 (3.00, 6.00)	4.00 (2.00, 5.00)	4.00 (2.00, 5.00)	**<.001**
Comorbidities, *n* (%)						
Hypertension						.158
0	2644 (42.59)	695 (44.78)	637 (41.04)	645 (41.64)	667 (42.89)	
1	3564 (57.41)	857 (55.22)	915 (58.96)	904 (58.36)	888 (57.11)	
Myocardial infarction						**<.001**
0	5077 (81.78)	1344 (86.60)	1227 (79.06)	1203 (77.66)	1303 (83.79)	
1	1131 (18.22)	208 (13.40)	325 (20.94)	346 (22.34)	252 (16.21)	
Congestive heart failure						**<.001**
0	4507 (72.60)	1253 (80.73)	1126 (72.55)	1018 (65.72)	1110 (71.38)	
1	1701 (27.40)	299 (19.27)	426 (27.45)	531 (34.28)	445 (28.62)	
Peripheral vascular disease						**<.001**
0	5395 (86.90)	1300 (83.76)	1335 (86.02)	1358 (87.67)	1402 (90.16)	
1	813 (13.10)	252 (16.24)	217 (13.98)	191 (12.33)	153 (9.84)	
Dementia						**<.001**
0	6066 (97.71)	1546 (99.61)	1535 (98.90)	1488 (96.06)	1497 (96.27)	
1	142 (2.29)	6 (0.39)	17 (1.10)	61 (3.94)	58 (3.73)	
Cerebrovascular disease						**.004**
0	5441 (87.64)	1391 (89.63)	1373 (88.47)	1346 (86.89)	1331 (85.59)	
1	767 (12.36)	161 (10.37)	179 (11.53)	203 (13.11)	224 (14.41)	

Table 1: Continued

Variables	Total ($n = 6208$)	Q1 ($n = 1552$)	Q2 ($n = 1552$)	Q3 ($n = 1549$)	Q4 ($n = 1555$)	P
Chronic pulmonary disease						**<.001**
0	4759 (76.66)	1252 (80.67)	1183 (76.22)	1173 (75.73)	1151 (74.02)	
1	1449 (23.34)	300 (19.33)	369 (23.78)	376 (24.27)	404 (25.98)	
Rheumatic disease						**.034**
0	5980 (96.33)	1501 (96.71)	1490 (96.01)	1506 (97.22)	1483 (95.37)	
1	228 (3.67)	51 (3.29)	62 (3.99)	43 (2.78)	72 (4.63)	
Peptic ulcer disease						**.002**
0	5926 (95.46)	1505 (96.97)	1472 (94.85)	1461 (94.32)	1488 (95.69)	
1	282 (4.54)	47 (3.03)	80 (5.15)	88 (5.68)	67 (4.31)	
Mild liver disease						**<.001**
0	4405 (70.96)	891 (57.41)	1023 (65.91)	1155 (74.56)	1336 (85.92)	
1	1803 (29.04)	661 (42.59)	529 (34.09)	394 (25.44)	219 (14.08)	
Diabetes without CC						**<.001**
0	4736 (76.29)	1258 (81.06)	1183 (76.22)	1154 (74.50)	1141 (73.38)	
1	1472 (23.71)	294 (18.94)	369 (23.78)	395 (25.50)	414 (26.62)	
Diabetes with CC						**.008**
0	5913 (95.25)	1502 (96.78)	1474 (94.97)	1471 (94.96)	1466 (94.28)	
1	295 (4.75)	50 (3.22)	78 (5.03)	78 (5.04)	89 (5.72)	
Paraplegia						**<.001**
0	5972 (96.20)	1525 (98.26)	1501 (96.71)	1476 (95.29)	1470 (94.53)	
1	236 (3.80)	27 (1.74)	51 (3.29)	73 (4.71)	85 (5.47)	
Malignant cancer						**<.001**
0	5229 (84.23)	1369 (88.21)	1351 (87.05)	1271 (82.05)	1238 (79.61)	
1	979 (15.77)	183 (11.79)	201 (12.95)	278 (17.95)	317 (20.39)	
Severe liver disease						**<.001**
0	5059 (81.49)	1041 (67.07)	1184 (76.29)	1333 (86.06)	1501 (96.53)	
1	1149 (18.51)	511 (32.93)	368 (23.71)	216 (13.94)	54 (3.47)	
Metastatic solid tumor						**<.001**
0	5847 (94.18)	1516 (97.68)	1499 (96.59)	1423 (91.87)	1409 (90.61)	
1	361 (5.82)	36 (2.32)	53 (3.41)	126 (8.13)	146 (9.39)	
AIDS						**.030**
0	6159 (99.21)	1544 (99.48)	1532 (98.71)	1535 (99.10)	1548 (99.55)	
1	49 (0.79)	8 (0.52)	20 (1.29)	14 (0.90)	7 (0.45)	
Therapies, *n* (%)						
Norepinephrine						**<.001**
0	3461 (55.75)	1014 (65.34)	976 (62.89)	783 (50.55)	688 (44.24)	
1	2747 (44.25)	538 (34.66)	576 (37.11)	766 (49.45)	867 (55.76)	
Epinephrine						**<.001**
0	3162 (50.93)	893 (57.54)	859 (55.35)	739 (47.71)	671 (43.15)	
1	3046 (49.07)	659 (42.46)	693 (44.65)	810 (52.29)	884 (56.85)	

Table 1: Continued

Variables	Total ($n = 6208$)	Q1 ($n = 1552$)	Q2 ($n = 1552$)	Q3 ($n = 1549$)	Q4 ($n = 1555$)	*P*
Aspirin						**<.001**
0	4587 (73.89)	1035 (66.69)	1039 (66.95)	1192 (76.95)	1321 (84.95)	
1	1621 (26.11)	517 (33.31)	513 (33.05)	357 (23.05)	234 (15.05)	
Metformin						.435
0	6201 (99.89)	1551 (99.94)	1548 (99.74)	1548 (99.94)	1554 (99.94)	
1	7 (0.11)	1 (0.06)	4 (0.26)	1 (0.06)	1 (0.06)	
Dopamine						**<.001**
0	6025 (97.05)	1524 (98.20)	1514 (97.55)	1473 (95.09)	1514 (97.36)	
1	183 (2.95)	28 (1.80)	38 (2.45)	76 (4.91)	41 (2.64)	
Furosemide						**<.001**
0	4368 (70.36)	991 (63.85)	1013 (65.27)	1145 (73.92)	1219 (78.39)	
1	1840 (29.64)	561 (36.15)	539 (34.73)	404 (26.08)	336 (21.61)	
ACEI						**.045**
0	2138 (34.44)	531 (34.21)	526 (33.89)	503 (32.47)	578 (37.17)	
1	4070 (65.56)	1021 (65.79)	1026 (66.11)	1046 (67.53)	977 (62.83)	
ARB						.105
0	5886 (94.81)	1471 (94.78)	1454 (93.69)	1477 (95.35)	1484 (95.43)	
1	322 (5.19)	81 (5.22)	98 (6.31)	72 (4.65)	71 (4.57)	
Beta blockers						**<.001**
0	2185 (35.20)	493 (31.77)	494 (31.83)	592 (38.22)	606 (38.97)	
1	4023 (64.80)	1059 (68.23)	1058 (68.17)	957 (61.78)	949 (61.03)	
CRRT						**<.001**
0	5158 (83.09)	1276 (82.22)	1333 (85.89)	1297 (83.73)	1252 (80.51)	
1	1050 (16.91)	276 (17.78)	219 (14.11)	252 (16.27)	303 (19.49)	
Invasive ventilation						.170
0	1527 (24.60)	385 (24.81)	380 (24.48)	407 (26.28)	355 (22.83)	
1	4681 (75.40)	1167 (75.19)	1172 (75.52)	1142 (73.72)	1200 (77.17)	
Noninvasive ventilation						**.007**
0	5964 (96.07)	1511 (97.36)	1495 (96.33)	1476 (95.29)	1482 (95.31)	
1	244 (3.93)	41 (2.64)	57 (3.67)	73 (4.71)	73 (4.69)	
HFNC						**<.001**
0	5638 (90.82)	1441 (92.85)	1420 (91.49)	1416 (91.41)	1361 (87.52)	
1	570 (9.18)	111 (7.15)	132 (8.51)	133 (8.59)	194 (12.48)	
Outcome						
Status 30, *n* (%)						**<.001**
0	4526 (72.91)	1151 (74.16)	1190 (76.68)	1097 (70.82)	1088 (69.97)	
1	1682 (27.09)	401 (25.84)	362 (23.32)	452 (29.18)	467 (30.03)	
Status 60, *n* (%)						**<.001**
0	4219 (67.96)	1085 (69.91)	1136 (73.20)	1013 (65.40)	985 (63.34)	
1	1989 (32.04)	467 (30.09)	416 (26.80)	536 (34.60)	570 (36.66)	

Table 1: Continued

Variables	Total ($n = 6208$)	Q1 ($n = 1552$)	Q2 ($n = 1552$)	Q3 ($n = 1549$)	Q4 ($n = 1555$)	*P*
Status 90, *n* (%)						<.001
0	4091 (65.90)	1064 (68.56)	1117 (71.97)	966 (62.36)	944 (60.71)	
1	2117 (34.10)	488 (31.44)	435 (28.03)	583 (37.64)	611 (39.29)	
Status 180, *n* (%)						<.001
0	3897 (62.77)	1020 (65.72)	1095 (70.55)	907 (58.55)	875 (56.27)	
1	2311 (37.23)	532 (34.28)	457 (29.45)	642 (41.45)	680 (43.73)	
Status 365, *n* (%)						<.001
0	3718 (59.89)	1000 (64.43)	1041 (67.07)	851 (54.94)	826 (53.12)	
1	2490 (40.11)	552 (35.57)	511 (32.93)	698 (45.06)	729 (46.88)	

Q1: <52.88 mg/g; Q2: 52.89–84.63 mg/g; Q3: 84.64–155 mg/g; Q4: >155 mg/g. Bold P-values indicate statistical significance ($P < 0.05$).
SINGLE 1, MARRIED 2, WIDOWED 3, DIVORCED 4, MALE 1; Status 0 survival, Status 1 death; Therapies 0 No; Therapies 1 Yes.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RR, respiratory rate; SpO2, oxygen saturation; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; WBC, white blood cell; RBC, red blood cell; PH, potential of hydrogen; ALP, alkaline phosphatase; BUN, blood urea nitrogen; Cr, creatinine; PaCO2, carbon dioxide partial pressure; PaO2, partial pressure of arterial oxygen; diabetes with CC, diabetes mellitus with complications; diabetes without CC, diabetes without complications; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRRT, continuous renal replacement therapy; HFNC, high-flow nasal cannula; OASIS, Oxford Acute Severity of Illness Score; SAPSII, Simplified Acute Physiology Score II; APSIII, Acute Physiology Score III.

mortality rates were 34.28%, 29.45%, 41.45% and 43.73% ($P < .01$); and the 365-day mortality rates were 35.57%, 32.93%, 45.06% and 46.88% ($P < .01$). All mortality rates in the Q2 group were lower than those in the other three groups, with no significant differences observed between the Q3 and Q4 groups.

Study outcomes

The Kaplan–Meier curve demonstrated that the four groups had varying prevalence rates of 30-day mortality and 365-day mortality, as determined by FAR quartiles (Fig. 1). Additionally, the rates of 60-, 90- and 180-day mortality varied among the four groups (Supplementary data, Fig. S2). Patients with lower FAR values demonstrated superior survival rates at 30, 60, 90, 180 and 365 days than did those with elevated FAR values (log-rank $P < .001$). Compared with those of the Q1 and Q2 groups, the survival rates of the Q3 and Q4 groups were lower at 30, 60, 90, 180 and 365 days. Nonetheless, the survival rates at 30, 60, 90 and 365 days did not significantly differ between the Q1 and Q2 groups. Compared with the Q1 group, the Q2 group presented a greater 180-day survival rate.

Correlations between the FAR and clinical outcomes in individuals with SAKI

Two Cox regression models were implemented to examine the independent effects of the FAR on mortality (Table 2). After adjusting for age, SOFA score, BMI, sex, marital status, hypertension status and diabetes status (Model 2), from lowest to highest FAR categories (<52.88 mg/g, 52.89–84.63 mg/g, 84.64–155 mg/g, >155 mg/g), the adjusted hazard ratio (HR) and 95% confidence interval (CI) for 30-day all-cause mortality were as follows: 1.00 (reference), 0.92 (0.80–1.07), 1.21 (1.05–1.38) and 1.22 (1.07–1.40), respectively. For 365-day all-cause mortality, the adjusted HRs and 95% CIs were as follows: 1.00 (reference), 0.93 (0.83–1.05), 1.38 (1.23–1.54) and 1.43 (1.28–1.60). We discovered that SAKI individuals with elevated FAR levels (>84.63 mg/g) presented an increased risk of all-cause death at 30 days and 365 days compared with those with FAR ≤84.63 mg/g. Additionally, as indicated in Supplementary data, Table S1, we observed a correlation between the FAR and all-cause mortality at 60, 90 and 180 days, yielding similar results.

The identification of nonlinear correlations

The RCS curves were generated to identify the nonlinear relationship that exists between the FAR and all-cause mortality at 30, 60, 90, 180 and 365 days. The analysis revealed inverted N-shaped relationships between the FAR and 30-day and 365-day all-cause mortality (Fig. 2A and B), in addition to 60-day, 90-day, and 180-day all-cause mortality (Supplementary data, Fig. S3A–C). The nonlinear relationship between the FAR and all-cause mortality in SAKI patients was investigated via a two-piecewise Cox proportional hazards model alongside the standard Cox proportional hazards model. Both *P*-values for the log-likelihood ratio were <.05 (Table 3, Supplementary data, Table S2). At 30, 60, 90, 180 and 365 days, the all-cause mortality inflection points were 35.14, 34.84, 34.87, 35 and 34.8 mg/g, respectively. In instances where FAR levels were <35.14 mg/g, a reduction of 1 unit in the FAR correlated with a 6.5% increase in the risk of 30-day all-cause mortality (HR 0.935; 95% CI 0.923, 0.948). In instances where FAR levels were below 34.8 mg/g, a reduction of 1 unit in the FAR correlated with a 6.2% increase in the risk of 365-day all-cause mortality (HR 0.938; 95% CI 0.927, 0.949). A FAR below

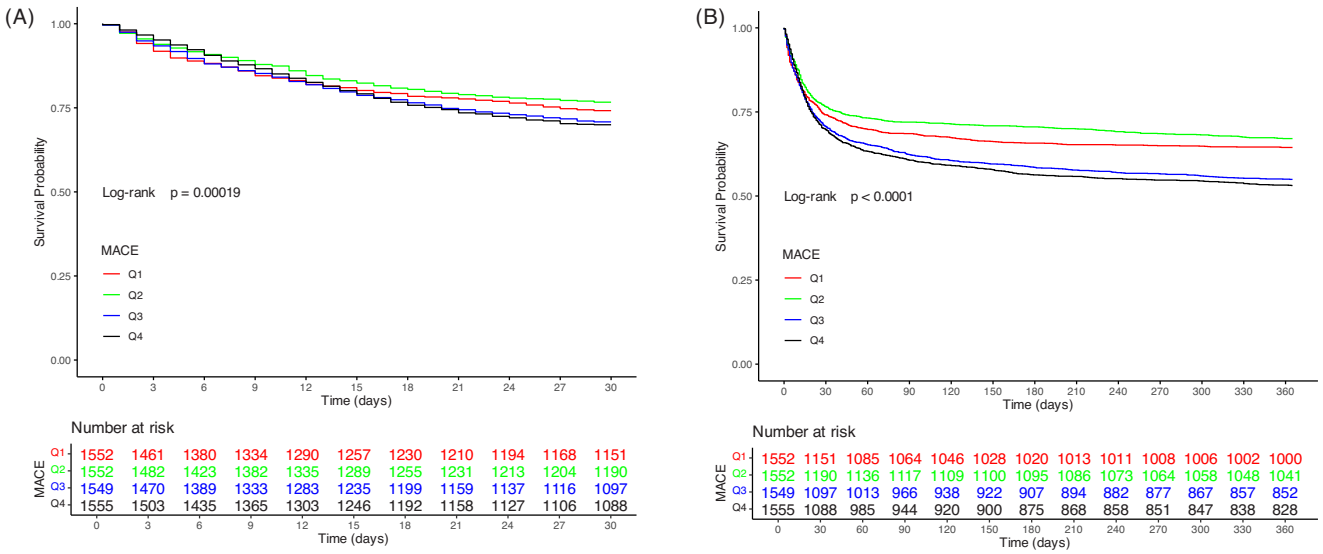

Figure 1: Kaplan–Meier survival analysis curves for all-cause mortality. Kaplan–Meier curves and cumulative incidence of 30-day (**A**) and 365-day (**B**) all-cause mortality stratified by FAR.

Table 2: Cox proportional hazard models for 30-day and 365-day all-cause mortality.

	Model 1		Model 2	
Variables	HR (95% CI)	P	HR (95% CI)	P
30-day mortality				
FAR quantile				
1	1.00 (Reference)		1.00 (Reference)	
2	0.88 (0.77–1.02)	.085	0.92 (0.80–1.07)	.279
3	1.14 (0.99–1.30)	.061	1.21 (1.05–1.38)	.007
4	1.16 (1.02–1.33)	.029	1.22 (1.07–1.40)	.004
HR for trend	1.01 (1.01–1.01)		1.01 (1.01–1.01)	
P for trend		<.001		<.001
365-day mortality				
FAR quantile				
1	1.00 (Reference)		1.00 (Reference)	
2	0.90 (0.80–1.01)	.077	0.93 (0.83–1.05)	.246
3	1.31 (1.17–1.47)	<.001	1.38 (1.23–1.54)	<.001
4	1.37 (1.22–1.53)	<.001	1.43 (1.28–1.60)	<.001
HR for trend	1.01 (1.01–1.01)		1.01 (1.01–1.01)	
P for trend		<.001		<.001

Model 1: crude.
Model 2: adjust: age, SOFA score, BMI, gender, marital status, hypertension, diabetes.

34.84, 34.87 or 35 mg/g indicated that a 1 unit reduction in the FAR was associated with increases of 6.6%, 6.6% and 6.3% in the risk of all-cause mortality at 60, 90 and 180 days, respectively (HR 0.934, 95% CI 0.922–0.946; HR 0.934, 95% CI 0.923–0.946; and HR 0.934, 95% CI 0.922–0.946, respectively).

Subgroup analysis and *P*-values for interactions

Subgroup analyses were carried out for sex, age, diabetes status and hypertension status to further investigate whether the relationships between the FAR and 30-day and 365-day all-cause mortality remained consistent under varying conditions. Within the subgroups of patients aged ≥60 years, those aged <60 years and males, the HRs of 30-day and 365-day mortality from all causes were statistically significant. The HR of 365-day all-cause mortality was also statistically significant in the female subgroup (Fig. 3 and Supplementary data, Fig. S4). There was a statistically significant relationship ($P < .05$) between FAR and 30-day all-cause mortality in patients without diabetes and hypertension, as well as in hypertension patients (Fig. 3). However, in patients with diabetes and hypertension, the relationship between FAR and 365-day all-cause mortality was statistically significant, as was the case in patients without diabetes ($P < .05$) (Supplementary data, Fig. S4). The interaction effects between age, hypertension, and the FAR were significant (Fig. 3 and Supplementary data, Fig. S4).

DISCUSSION

This study represents a retrospective analysis of the correlation between FAR levels and all-cause mortality in individuals who are seriously ill with SAKI. Kaplan–Meier survival analysis indicated that patients with elevated FAR values experienced a poor prognosis. The RCS curve revealed an inverted N-shaped relationship between the FAR and all-cause mortality at 30, 60, 90, 180 and 365 days. Elevated FAR levels in seriously ill SAKI patients are associated with increased mortality rates. Following adjustments for various variables, SAKI patients with elevated FAR levels continued to demonstrate an increased mortality risk. These findings indicate that the FAR could function as a prognostic marker for SAKI patients. This would enable physicians to obtain FAR levels through laboratory tests, allowing for immediate and quantitative assessment of clinical severity and prognosis, ultimately decreasing patient mortality.

Sepsis is the leading cause of AKI in seriously ill patients. However, the exact pathophysiologic mechanisms that cause SAKI are unclear. It is generally agreed that SAKI involves three main changes: microvascular dysfunction, inflammation and the metabolic response to inflammatory injury [15]. Disseminated intravascular coagulation, biological reprogramming of tubular epithelial cells and systemic vasodilation are the original mechanism of SAKI. Additionally, secondary injury occurs due

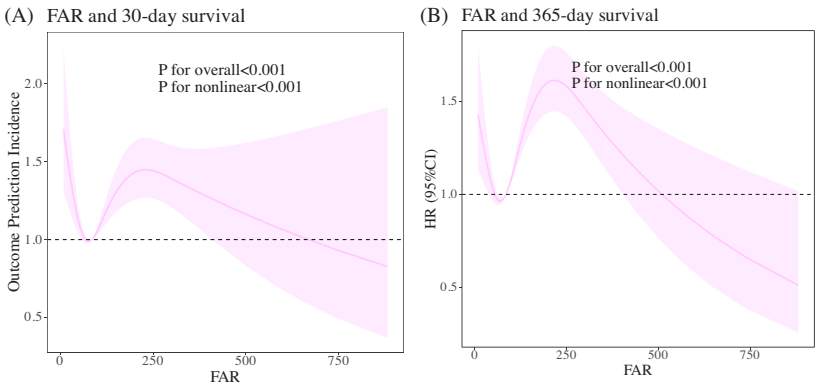

Figure 2: RCS regression analysis of FAR with all-cause mortality. RCS regression analysis of FAR with 30-day (**A**) and 365-day (**B**) all-cause mortality.

Table 3: Threshold effect analysis of FAR on 30-day and 365-day all-cause mortality in SAKI patients.

	HR (95% CI), *P*-value
30-day mortality	
Fitting by the standard linear model	1.001 (1–1.001), .003
Fitting by the two-piecewise linear model	
Infection point	35.14
FAR <35.14 mg/g	0.935 (0.923–0.948), <.01
FAR ≥35.14 mg/g	1.001 (1.001–1.002), <.01
P for Log-likelihood ratio	<.01
365-day mortality	
Fitting by the standard linear model	1.001 (1.001–1.002), <.01
Fitting by the two-piecewise linear model	
Infection point	34.8
FAR <34.8 mg/g	0.938 (0.927–0.949), <.01
FARI ≥34.8 mg/g	1.002 (1.001–1.002), <.01
P for Log-likelihood ratio	<.001

The inflection of threshold effect analysis of FAR on 30-day all-cause mortality was 35.14 mg/g; the inflection of threshold effect analysis of FAR on 365-day all-cause mortality was 34.8 mg/g.

to the administration of fluid resuscitation, which may result in venous congestion and intra-abdominal hypertension, further leading to AKI [16]. Although the mechanism of SAKI is still unclear, the systemic inflammatory response plays a major role in the progression of SAKI.

Serum albumin is crucial for several physiological functions. It helps maintain acid–base balance and plasma colloidal osmotic pressure. Additionally, it scavenges free radicals, reduces inflammation and prevents coagulation. By performing these roles, serum albumin significantly contributes to overall health [17]. Furthermore, the serum albumin concentration is related to the prognosis of sepsis patients [18]. Hypoproteinaemia is considered an independent risk factor for the prediction of AKI [19]. According to certain studies, albumin has a renoprotective mechanism [20]. Initially, albumin may mitigate oxidative damage. Moreover, albumin plays a crucial role in preserving renal perfusion and glomerular filtration. Ultimately, additional research has demonstrated that albumin can increase the synthesis of DNA in renal tubular cells. Albumin plays a paramount role in safeguarding the kidneys and sustaining renal function. Low albumin levels frequently suggest a dismal prognosis in patients with SAKI.

Fibrinogen is a serum glycoprotein produced by the liver. As an important coagulation factor, it is involved in inflammatory responses. Studies have shown that increased fibrinogen levels indicate better overall survival in critically ill patients with sepsis. Increased fibrinogen levels are a response to the acute phase of inflammation, indicating that the body is beneficial for compensation [21]. However, another study demonstrated that elevated fibrinogen levels are strongly correlated with an increase in sepsis-related mortality [5]. We believe that the fibrinogen level alone may not be an effective prognostic predictor for sepsis. The combination of fibrinogen and albumin may be more effective than a single biomarker, either fibrinogen or albumin. However, few studies have investigated the predictive role of the FAR in SAKI patients.

Recent studies have shown that a wide range of parameters, such as age, sex, etiology, inflammatory markers and life support treatment, have an impact on the prognosis of individuals with SAKI. However, the FAR has the highest sensitivity and specificity and is the most valuable predictor of death in SAKI patients [22]. The findings of this study revealed that the higher the FAR is, the worse the prognosis of SAKI patients. This finding is consistent with our results, but this study had a small sample size, the follow-up time was short and only a prediction model was proposed based on the nomogram. The observational data from the MIMIC-IV database were retrospectively evaluated in our study, and subgroup analysis combined with RCS curves was used to ascertain the associations between the FAR and 30-, 60-, 90-, 180- and 365-day all-cause mortality. The results are reliable, and the conclusions are more credible.

In the present study, patients with SAKI who had greater FAR values had a higher mortality rate than those with lower FAR values. Increased FAR values may result from elevated fibrinogen levels and/or reduced albumin levels. During sepsis, hypoalbuminemia is likely to occur due to increased peripheral clearance of albumin, and hyperfibrinogenemia is likely to occur due to increased fibrinogen production caused by inflammatory stimulation [23]. Elevated fibrinogen levels contribute to coagulation abnormalities, while decreased albumin levels diminish antioxidant capacity, jointly promoting renal injury. Elevated FAR indicates the concurrent presence of inflammatory storms and coagulopathy, increasing the risk of endothelial dysfunction and microcirculatory disturbances, which are the pathophysiologic mechanisms that cause SAKI [24]. Collectively, high FAR is associated with increased mortality in SAKI patients.

The FAR serves as a reliable predictor of the prognosis of SAKI patients. Nonetheless, limited research exists regarding the predictive value of FAR levels for SAKI prognosis, indicating the need for additional clinical trials to explore its relevance.

Variable	Count	Percent (%)	HR (95% CI)	P value	P for interaction
Gender					0.794
Male	3659	58.9	1.001 (1.000 to 1.001)	0.027	
Female	2549	41.1	1.001 (1.000 to 1.001)	0.092	
Age					<0.001
≥60	3938	63.4	1.002 (1.001 to 1.003)	<0.001	
<60	2270	36.6	0.998 (0.997 to 0.999)	<0.001	
Diabetes					0.781
No	4559	73.4	1.001 (1.000 to 1.001)	0.018	
Yes	1649	26.6	1.001 (1.000 to 1.002)	0.072	
Hypertension					<0.001
No	2644	42.6	0.999 (0.998 to 1.000)	0.008	
Yes	3564	57.4	1.002 (1.002 to 1.003)	<0.001	
Overall	6208	100	1.001 (1.000 to 1.001)	0.003	

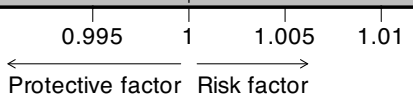

Figure 3: Forest plots of stratified analyses of FAR and 30-day all-cause mortality.

This study examined the correlation between FAR and the prognosis of SAKI patients, as well as the potential mechanisms involved. As a new indicator, the FAR can more significantly and powerfully predict the prognosis of a disease by combining the inflammation, coagulation and nutritional status of patients. Moreover, the FAR is also a simple parameter indicator used to collect data from patients upon ICU admission, which makes it possible for physicians to identify high-risk patients sooner. Patients with high FAR levels should receive special treatment, including anti-infection and nutritional support therapy, to reduce the mortality rate.

There are some constraints to our investigation. First, the retrospective analysis was a single-center study. Drawing firm conclusions about causality from observational data is challenging. Even with the adjustment of variables and execution of subgroup analysis, it is not possible to exclude all confounding factors. Furthermore, our sample size is not particularly large, and a large-scale cohort study is indispensable. Additionally, no exact values were provided for the range of FAR levels. Moreover, the present research cannot determine the time of SAKI occurrence and the primary reason for death. In the future, other possible prognostic factors can also be explored in depth, hence enhancing the precision of SAKI prognosis prediction.

CONCLUSION

The current study revealed that the FAR serves as a potential predictor of 30-day, 60-day, 90-day, 180-day and 365-day all-cause mortality in severe SAKI individuals. Additionally, in seriously ill individuals with SAKI, there was a nonlinear correlation between the FAR and the probability of all-cause death. FAR has the potential to serve as an accurate measure for assessing and managing patients with SAKI in the ICU.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

L.Y.Z., Y.Z. and Y.X.Z. contributed equally to this work. L.Y.Z. and Y.Z. designed the study, Y.X.Z. and L.W. drafted the manuscript. Y.Z., J.D.C. and W.W. extracted the data from the MIMIC-IV database. H.D.Z., M.M.G., R.J.H. and Y.Q.S. analyzed the data. H.G., J.X. and R.X. guided the literature review. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data underlying this article are available in the article and in its online supplementary material. The datasets are available in the physionet (https://physionet.org/content/mimiciv/0.4/).

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

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