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SURGICAL MEDICAL SCIENCES / CERRAHİ TIP BİLİMLERİ

Can the Fibrinogen-Albumin Ratio be a Predictor of Mortality in Dialysis Patients?

Fibrinojen-Albümin Oranı Diyaliz Hastalarında Mortalitenin Bir Belirleyicisi Olabilir mi?

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Abstract

Objectives: Renal failure is linked to both acute and chronic inflammatory processes for a number of reasons, particularly in end-stage renal disease. Although it has demonstrated potential as an inflammatory marker in a number of diseases, the fibrinogen-to-albumin ratio's (FAR) predictive significance in critically ill dialysis patients is yet unknown. The purpose of this study was to look into FAR as a possible mortality predictive indicator in this particular patient population.

Materials and Methods: A retrospective analysis of 226 patients admitted to the intensive care units of internal medicine and anesthesia, undergoing dialysis between 12.12.2021 and 15.12.2023, was conducted. Inclusion criteria were age ≥18, diagnosis of albumin or kidney disease, and availability of complete clinical and laboratory data. Exclusion criteria included anemia unrelated to kidney disease and inability to access relevant data. Demographic, clinical, and laboratory variables were collected, and statistical analyses were performed.

Results: The study revealed significant associations between mortality and lower body mass index, higher APACHE II score, elevated creatinine levels, lower glomerular filtration rate, higher albumin levels, and increased FAR. With an 81.75% sensitivity, 39.00% specificity, 62.80% positive predictive value, and 62.90% negative predictive value, the FAR cut-off point for mortality was found to be 241. Area under the curve of 58.1% was shown by receiver operating characteristic analysis.

Conclusion: FAR shows promise as a prognostic indicator for mortality in intensive care dialysis patients. While further prospective and multicenter studies are needed to validate its clinical usability, FAR could contribute to enhanced prognostic assessments and improved patient care in this specific population.

Key Words: Fibrinogen albumin ratio, mortality, acute kidney injury, chronic kidney disease

Öz

Amaç: Böbrek yetmezliği, özellikle son dönem böbrek hastalığında, çeşitli faktörlere bağlı akut ve kronik enflamatuvar süreçlerle ilişkilidir. Fibrinojen albümin oranı (FAR) çeşitli hastalıklarda enflamatuvar bir belirteç olarak umut vaat etmektedir, ancak yoğun bakım diyaliz hastalarında prognostik değeri belirsizliğini korumaktadır. Bu çalışmanın amacı, bu spesifik hasta popülasyonunda mortalite için potansiyel bir prognostik indeks olarak FAR'yi araştırmaktır.

Gereç ve Yöntem: Dahiliye ve anestezi yoğun bakım ünitelerine 12.12.2021 ile 15.12.2023 tarihleri arasında diyalize giren 226 hastanın retrospektif analizi yapıldı. Dahil edilme kriterleri yaş ≥18, albümin veya böbrek hastalığı tanısı ve tam klinik ve laboratuvar verilerinin mevcut olmasıydı. Dışlama kriterleri arasında böbrek hastalığı ile ilişkili olmayan anemi ve ilgili verilere erişememe yer aldı. Demografik, klinik ve laboratuvar değişkenleri toplandı ve istatistiksel analizler yapıldı.

Bulgular: Çalışmada mortalite ile düşük vücut kitle indeksi, yüksek APACHE II skorları, yüksek kreatinin seviyeleri, düşük glomerüler filtrasyon hızı, yüksek albümin seviyeleri ve artmış FAR arasında anlamlı ilişkiler tespit edilmiştir. Mortalite için FAR kesme noktası %81,75 duyarlılık, %39 özgüllük,

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%62,80 pozitif prediktif değer ve %62,90 negatif prediktif değer ile 241 olarak belirlenmiştir. ROC analizine göre eğri altındaki alan %58,1 bulundu.

Sonuç: FAR, yoğun bakım diyaliz hastalarında mortalite için prognostik bir gösterge olarak umut vaat etmektedir. Klinik kullanılabilirliğini doğrulamak için daha ileri prospektif ve çok merkezli çalışmalara ihtiyaç duyulsa da, FAR bu spesifik popülasyonda gelişmiş prognostik değerlendirmelere ve iyileştirilmiş hasta bakımına katkıda bulunabilir.

Anahtar Kelimeler: Fibrinojen albümin oranı, mortalite, akut böbrek hasarı, kronik böbrek hastalığı

Introduction

In individuals with end-stage kidney disease, both acute and chronic inflammatory processes are widespread. This can be attributed to multiple factors, including the uremic environment, heightened levels of circulating proinflammatory cytokines, oxidative and carbonyl stress, protein-energy wasting, elevated rates of infections (particularly associated with dialysis access), the existence of comorbid conditions, and other contributing elements (1).

In recent studies, findings indicate that the fibrinogen-to-albumin ratio (FAR), an innovative inflammatory marker, is linked to unfavorable outcomes in diverse conditions such as peritonitis-induced sepsis (2), myocardial infarction (3), ischemic stroke (4), knee synovitis (5), and gastric cancer (6). Despite these associations, the applicability of FAR as a prognostic factor for outcomes and mortality in intensive care patients undergoing dialysis remains unclear.

The study aimed to investigate the potential of FAR as a prognostic indicator in intensive care unit dialysis patients. By examining its utility in this specific patient population, the research could contribute to the development of more effective prognostic assessment tools and ultimately enhance patient care and outcomes.

Materials and Methods

Study Design

This retrospective, non-randomized study adhered to the principles of the Declaration of Helsinki and obtained approval from the Local Ethics Committee of Giresun Training and Research Hospital (decision no.: 37, dated: 18.12.2023).

Between 18.12.2021 and 25.12.2023, a retrospective archive of patients hospitalised in the intensive care unit of internal medicine and anaesthesia and who received dialysis screening was carried out.

Inclusion Criteria: Age ≥18 years, diagnosis of albumin or kidney disease, availability of complete clinical and laboratory data.

Exclusion Criteria: Anemia due to conditions other than kidney disease, inability to access clinical and laboratory data, patients who died within 24 hours of admission to intensive care.

Demographic and clinical variables, including gender, age, body mass index (BMI), underlying disease, reason for intensive care unit (ICU) admission, dialysis duration, acute kidney injury (AKI) and chronic kidney disease (CKD) status, chronic chronic kidney failure duration, ICU outcome, ICU length of stay, creatinine, fibrinogen, albumin, C-reactive protein (CRP), procalcitonin, glucose, and estimated glomerular filtration rate (GFR) levels, as well as APACHE II score.

Primary Hypothesis: To determine if the FAR can be used as a new and useful prognostic index for predicting mortality in dialysis patients admitted to the ICU.

Statistical Analysis

The research variables underwent descriptive statistical analysis, utilizing box plot diagrams and the Shapiro-Wilk test to assess data normality. For comparing the two groups, the independent sample t-test was applied to continuous data, while the Mann-Whitney U test was employed for categorical variables. Pearson correlation analysis was utilized to evaluate the association between FAR and other variables. Receiver operating characteristic (ROC) analysis and cut-off value determination were performed to identify the optimal FAR value for predicting mortality. Reports included the area under the curve and the 95% confidence interval (CI). Significance was established at $p<0.05$.

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Results

A total of 226 participants were involved in the study conducted at Giresun Training and Research Hospital from December 18, 2021, to December 25, 2023. The age range of the patients was 21 to 98 years, with a mean age of 71.80±15.30 years. The gender distribution showed 60.2% men and 39.8% women. The mean BMI was 24.84±3.45, with 52.7% normal weight, 39.4% overweight, and 8% obese individuals (Table 1).

No statistically significant differences in survivorship or mortality were found based on age and gender distribution (p>0.05). However, BMI values were significantly lower in cases of mortality (p<0.01). Deceased patients exhibited lower occurrences of AKI and CKD (p<0.01), with routine hemodialysis (HD) being more prevalent in these cases (p<0.01) (Table 2).

APACHE II ratings were substantially higher in cases of mortality (p<0.01). Creatinine levels were significantly elevated in cases of mortality (p<0.01), while carbide measures showed no significant differences (p>0.05). Mortality was associated with lower GFR levels (p<0.01) and higher albumin levels (p<0.05). Fibrinogen levels did not significantly differ based on survival (p>0.05).

Patients with mortality had higher CRP levels (p<0.05), while procalcitonin levels showed no substantial differences (p>0.05). The FAR was significantly higher in cases of mortality (p<0.01) (Table 3).

The FAR cut-off point for mortality, determined through ROC analysis, was 241 or above, with 81.75% sensitivity, 39% specificity, 62.80% positive predictive value, and 62.90% negative predictive value (Table 4). The ROC curve indicated a statistically significant correlation between mortality and the FAR cut-off value (p=0.001; p<0.01). Patients with a FAR of 241 or above had a 2.863-fold increased probability of dying, as indicated by an odds ratio of 2.863 (95% CI: 1.56-5.42) (Figure 1).

Table 1: Distribution of descriptive characteristics

Age	Mean±SD	71.80±15.30
Gender	Female Male	90 (39.8) 136 (60.2)
BMI	Mean±SD	24.84±3.45
	Normal Overweight Obese	119 (52.7) 89 (39.4) 18 (8.0)

BMI: Body mass index, SD: Standard deviation

Discussion

The study aimed to explore the relationship between various clinical and biochemical factors, focusing particularly on the FAR, and mortality in a cohort of 226 cases. Significant associations between mortality and variables such as lower BMI, higher APACHE II scores, elevated creatinine levels, lower GFR, higher Albumin levels, and notably, an increased FAR were observed.

The key findings included the identification of a FAR cut-off point of 241 and above as a potential prognostic marker for mortality risk. The clinical implications are substantial, as FAR emerges as a novel prognostic marker, providing clinicians with a tool to assess mortality risk and enhance risk stratification. The integration of FAR into routine assessments may contribute to a more comprehensive approach to patient care.

The significance of FAR extends beyond this study, with its emergence as a prognostic factor across various medical

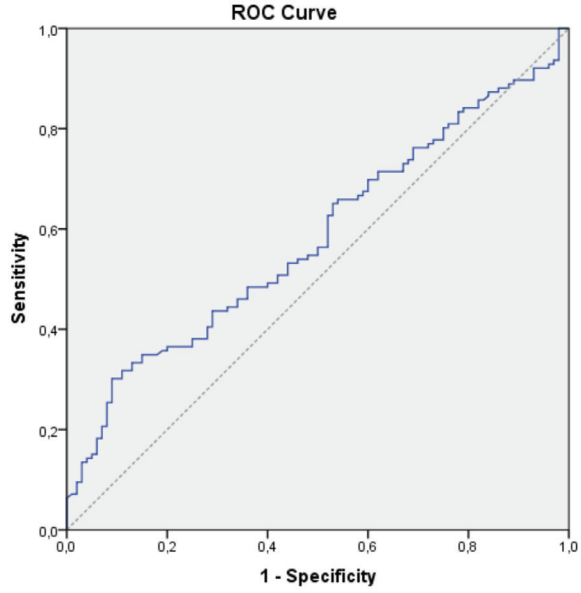

Figure 1: ROC curve for the FAR ratio in detecting mortality

Table 2: Evaluation of socio-demographic characteristics according to mortality

		Survivors (n=100)	Non-survivors (n=126)	p-value
Age	**Mean±SD**	70.24±15.21	73.09±15.32	[a]**0.172**
Gender	**Woman**	40 (40.0)	50 (39.7)	[c]**0.961**
	Male	60 (60.0)	76 (60.3)	
BMI	**Mean ± SD**	25.52±3.39	24.29±3.42	[a]**0.008****
AKI	**%**	83 (83.0)	78 (61.9)	[c]**0.001****
CKD	**%**	85 (85.0)	76 (60.3)	[c]**0.001****
AKI&CKD	**%**	55 (55.0)	73 (57.9)	[c]**0.658**
Routine HD	**%**	61 (61.0)	103 (81.7)	[c]**0.001**

[a]Student's t-test, bMann-Whitney U test, *p<0.05, **p<0.01
SD: Standard deviation, BMI: Body mass index, GFR: Glomerular filtration rate, CRP: C-reactive protein, FAR: Fibrinogen-albumin ratio, HD: Hemodialysis

conditions. In critically ill patients with AKI, FAR proves promising, showing an association with increased in-hospital mortality risk. This suggests that FAR could enhance predictive accuracy in diverse diseases (7).

In the context of CKD, FAR exhibits connections with the severity of coronary artery disease and early renal damage in hypertensive patients (8). Further exploration into end-stage renal disease (ESRD), specifically in patients on peritoneal dialysis, solidifies FAR as a robust prognostic index in this population, indicating its potential as a valuable biomarker for predicting outcomes in ESRD patients (8-11).

Interestingly, the study observed a significantly lower presence of acute and chronic kidney injury in those who died compared to survivors, while the rate of routine HD was significantly higher in the former cases.

The search results highlight the relevance of FAR in diverse medical contexts beyond kidney diseases (12). Studies in spontaneous intracerebral hemorrhage patients and those with sepsis showcase FAR's prognostic value, associating higher FAR with increased risks of in-hospital mortality (12,13). Its significance is also demonstrated in patients undergoing primary percutaneous coronary intervention and those with IgA nephropathy, emphasizing its broad applicability (14,15).

FAR, proposed as an indicator of inflammation and malnutrition, combines the inflammatory mediator function of fibrinogen and the reflective nature of nutritional status, vascular tone, and oxygen-carrying capacity in albumin. Its value in predicting mortality has been evident across various diseases, such as peritoneal dialysis and acute decompensated heart failure patients with diabetes (16-18).

Despite its potential, the value of FAR in predicting prognosis in patients hospitalized in intensive care and receiving dialysis remains unclear, with limited studies available (7,11,17,19-21). A meta-analysis conducted by Rathore et al. (22) found FAR to be better than albumin, fibrinogen, and CRP in predicting mortality in intensive care unit patients, with a different cut-off value. In this study, FAR's cut-off value was 241, providing 81.75% sensitivity and 39% specificity in predicting mortality.

In our study, the presence of AKI and CKD was found to be significantly lower in those who died compared to those who survived ($p<0.01$). While the association of ABH & CKD did not show a significant difference according to mortality ($p>0.05$), the rate of routine HD was significantly higher in mortality cases ($p<0.01$).

In our study, there was no significant difference between urea measurements according to mortality ($p>0.05$), while creatinine levels were statistically significantly higher in mortality cases ($p<0.01$). GFR levels were statistically significantly lower in mortality cases ($p<0.01$). This is consistent with other studies in the literature (23,24).

The use of FAR in predicting the prognosis of dialysis patients in intensive care presents several advantages. FAR is a ratio of two easily accessible, inexpensive, and routinely measured parameters, reflecting the combined effect of inflammation

Table 3: Evaluation of biochemical variables according to mortality

	Survivors (n=100) Mean ± SD	Non-survivors (n=126) Mean ± SD	[a]p-value
APACHE II score	29.31±6.94	34.47±7.38	**<0.001****
Urea	166.58±93.82	185.35±81.71	**0.110**
Creatinine	4.46±1.69	5.56±2.96	**<0.001****
GFR (median)	14.17±9.69 (10.7)	11.84±10.27 (9.07)	**[b]0.006****
Albumin	2.81±0.59	3.01±0.6	**0.010***
Fibrinogen	472.52±162.2	519.031209.63	**0.061**
FAR	163.79±65.72	193.48191.07	**0.005****
CRP	122.84±106.64	156.721108.81	**0.020***
Procalcitonin	8.78±17.09 (1.07)	10.6±23.0 (2.83)	0.066

[a]Student's t-test, [b]Mann-Whitney U test, *p<0.05, **p<0.01
GFR: Glomerular filtration rate, CRP: C-reactive protein, FAR: Fibrinogen-albumin ratio

Table 4: Diagnostic screening tests and ROC curve results for FAR

Diagnostic Scan				ROC Curve			
	Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	95% Confidence interval	p-value
FAR	241	81.75	39.00	62.80	62.90	0.514-0.647	0.031

ROC: Receiver operating characteristic curve, FAR: Fibrinogen-albumin ratio

and malnutrition. It stands out as a stable and less affected parameter than other inflammatory or nutritional markers, potentially contributing to improved treatment choices and outcomes in dialysis patients.

Study Limitations

However, the study has limitations, including its retrospective, single-center design with a small sample size. Changes in FAR over time, the impact of other inflammatory or nutritional markers, and the association of FAR with endpoints other than mortality were not assessed. While the study demonstrates an association of FAR with prognosis and mortality in patients hospitalized in intensive care and receiving dialysis, it does not establish a causal relationship.

Future research should focus on prospective, multicenter, and large-sample studies to better understand FAR's association with prognosis and mortality in this patient population. Comparative studies with other biomarkers, monitoring changes in FAR over time, investigating its relationship with other endpoints, and evaluating its usability in clinical practice are crucial for further insights.

Conclusion

In patients receiving dialysis and admitted to the intensive care unit, this study shows a substantial correlation between FAR and mortality. The management of dialysis patients in critical care may be affected by the discovery of FAR as a possible new biomarker for mortality prediction. However, more investigation is necessary to confirm its applicability in clinical settings and fully examine its potential with a range of patient types.

Ethics

Ethics Committee Approval: Ethical approval from the Giresun Training and Research Hospital Local Ethics Committee was obtained with decision number 37 on 18.12.2023.

Informed Consent: Retrospective study.

Authorship Contributions

Concept: T.A., Design: T.A., Data Collection and/or Processing: B.Y., Analysis and/or Interpretation: T.A., B.Y., Writing: T.A., B.Y.

Conflict of Interest: According to the authors, there are no conflicts of interest related to this study.

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