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ORIGINAL RESEARCH

Fibrinogen-to-Albumin Ratio as a Novel Predictor of Intracerebral Hemorrhage in Maintenance Hemodialysis Patients

Xiaojie He[1,*], Yaqing Wang[2,*], Yuqing Wang[1,*], Xiaodong Li[3]

[1]Graduate School of Hebei Medical University, Shijiazhuang, Hebei, 050017, People's Republic of China; [2]Graduate School of Chengde Medical University, Chengde, Hebei, 06700, People's Republic of China; [3]Department of Nephrology, Baoding No. 1 Central Hospital of Hebei Medical University, Baoding, Hebei, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaodong Li, Department of Nephrology, Baoding No.1 Central Hospital of Hebei Medical University, Baoding Great Wall North Street No 320, Baoding, Hebei, 071000, People's Republic of China, Email lxd_765@sina.com

Objective: Intracerebral hemorrhage (ICH) is a life-threatening complication in patients undergoing maintenance hemodialysis (MHD), yet reliable biomarkers for early risk stratification remain scarce. The fibrinogen-to-albumin ratio (FAR), a composite inflammatory and nutritional marker, may offer predictive value for ICH in this high-risk population.

Methods: This retrospective study analyzed a total of 536 MHD patients (ICH group: n=207; non-ICH group: n=329) from June 2019 to June 2024. FAR was calculated based on laboratory parameters. Multivariate Logistic regression analysis was used to identify independent risk factors for ICH, and ROC curve analysis and restricted cubic spline (RCS) modeling were used to assess the predictive performance of FAR for cerebral hemorrhage in maintenance hemodialysis patients. Finally, the DeLong test was used to compare the differences in area under curve (AUC).

Results: Logistic regression analysis revealed that FAR ([OR] 1.07, 95% [CI] 1.03–1.10, $p<0.001$) was the independent predictor of ICH. Trend testing showed a dose-response correlation between FAR (*p for trend* <0.001) and ICH risk. RCS showed a non-linear correlation between FAR and ICH risk (*non-linear* $p=0.029$). ROC analysis demonstrated FAR's superior accuracy (AUC=0.75) compared to fibrinogen (AUC=0.67) and albumin (AUC=0.49), identifying 12.2 as the optimal cutoff (sensitivity=0.73, specificity=0.60). The DeLong's test confirm that FAR exhibits significantly superior discriminatory performance.

Conclusion: FAR may predict the occurrence of ICH in MHD patients. This study explores the application value of FAR in predicting ICH risk in MHD patients, providing a new biomarker for early identification of high-risk patients in clinical practice.

Keywords: fibrinogen to albumin ratio, intracerebral hemorrhage, fibrinogen, albumin, maintenance hemodialysis

Introduction

Intracerebral hemorrhage (ICH) is a non-traumatic brain parenchymal hemorrhage primarily caused by the rupture of blood vessels due to high blood pressure and small artery sclerosis. Accounting for 10–15% of all stroke cases, ICH is a significant cause of disability and death worldwide.[1] ICH has the highest mortality rate among all subtypes, with over 40% of patients dying within a month, while the rest may experience severe disability.[2]

Globally, dialysis is the most common renal replacement therapy.[3] ICH is one of the most severe complications in patients undergoing maintenance hemodialysis (MHD). It has been reported that lipid metabolism and inflammatory response are important factors in regulating the progression of ICH, as well as subsequent brain injury and brain function repair.[4] Despite the continuous development of dialysis technology and the gradual improvement of nursing standards, the risk of brain damage in MHD patients is about six times higher than that of healthy individuals, with a mortality rate as high as 41–47%.[5]

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In MHD patients, traditional factors related to dialysis, such as micro inflammatory state, malnutrition, acceleration of calcification of renal tubules, response to anticoagulants, and low blood pressure during dialysis, accelerated atherosclerosis, which led to a significant increase in brain outflow rate in MHD patients.[6] Due to factors such as antioxidant and anti-inflammatory effects, as well as impaired renal filtration function,[7] MHD patients are in a state of mild inflammation during the early stages. This may lead to internal injury and atherosclerosis.[8] This may increase the incidence rate and mortality of brain tube diseases.[9] Inflammation and acute stress are important components of the brain's pathological and physiological pathways.[10]

Elevated fibrinogen promotes hypercoagulability and endothelial activation, while hypoalbuminemia reduces oncotic pressure, exacerbating endothelial leakage and oxidative stress. The FAR ratio quantifies this imbalance: higher fibrinogen amplifies thrombotic and inflammatory cascades, whereas lower albumin diminishes vascular repair capacity. This combination heightens susceptibility to microvascular rupture, particularly in hemodialysis patients with preexisting uremic vasculopathy.[11] Unlike CRP or IL-6, which solely reflect inflammation, FAR captures the interplay between systemic inflammation and malnutrition, which both prevalent in MHD patients.[12]

Research indicates that the fibrinogen to albumin ratio (FAR) is a promising new inflammatory marker, previously shown to be associated with atherosclerosis, acute lacunar stroke, and cancer.[13–15] It has been widely used for evaluating the prognosis of tumors, coronary heart disease, acute kidney injury and inflammation related diseases, and brain stroke.[16] However, there are currently no relevant reports on predictive analysis of FAR for ICH in MHD patients. Therefore, the aim of this study is to analyze the value of FAR in predicting ICH risk in MHD patients.

Materials and Methods

Study Design and Population

In this retrospective study, we selected 536 maintenance hemodialysis patients admitted between June 2019 and June 2024 as the research subjects, and divided them into an observation group (ICH group, n=207) and a control group (Non-ICH group, n=329) based on whether ICH occurred. All enrolled patients underwent conventional in-center hemodialysis three times per week, with each session lasting 4 hours. The dialysis parameters included a blood flow rate of 300–400 mL/min, dialysate flow rate of 500 mL/min, and standard bicarbonate-based dialysate. Patients on peritoneal dialysis or alternative modalities were excluded. Unfractionated heparin (UFH) was administered as the primary anticoagulant (initial bolus: 50 IU/kg; maintenance dose: 1000 IU/hour). For patients with contraindications to heparin, regional citrate anticoagulation (RCA) was utilized. Patients with bleeding complications within the preceding 3 months were excluded. The research conducted in this study adhered strictly to the principles outlined in the Helsinki Declaration and obtained approval from the Ethics Committee at Baoding No.1 Central Hospital (approval number:2024178).

The inclusion criteria are as follows: (1) All participants are aged ≥ 18 years and have no gender restrictions. (2) Dialysis duration >3 months. (3) Within one week after the onset of cerebral infarction, the brain had undergone at least one head CT scan or MRI that diagnosed spontaneous cerebral infarction, and the cerebral infarction occurred during dialysis.

The exclusion criteria are as follows: (1) Missing FIB, ALB, or other incomplete clinical data. (2) Existence of chronic/acute liver failure. (3) ICH related to brain trauma, aneurysms, vascular malformations, Moyamoya disease, malignant tumors, fluid diseases, and the use of anticoagulants or antiplatelet drugs in violation of medical advice. (4) Patients with combined mental illness, surgery, severe trauma, and severe infection. (5) Received treatment with defibrase or human albumin. (6) History of cerebral infarction in the past, to avoid confounding by preexisting cerebrovascular pathology. Figure 1 illustrates the participant selection process, with 536 patients screened and 207 included in the ICH group.

Data Collection

We conducted a comprehensive survey of all enrolled patients and reviewed their medical records upon admission. The baseline demographic characteristics of the patients, including age, gender, and body mass index (BMI), were collected and recorded. Clinical data included the history of hypertension (Use of antihypertensive medications or systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg on two separate occasions prior to enrollment)[17] diabetes

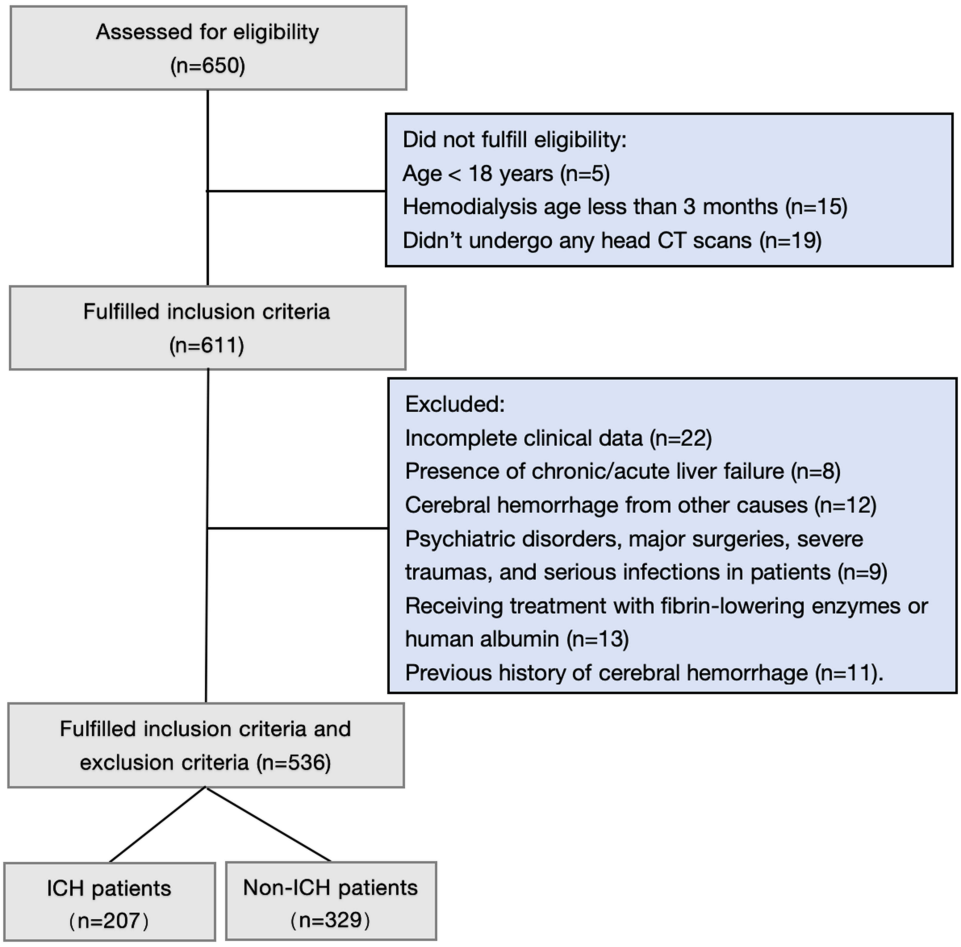

Figure 1 The flow chart of participants selection.
Abbreviations: MHD, maintenance hemodialysis; ICH, intracerebral hemorrhage.

(Use of hypoglycemic agents/insulin or fasting plasma glucose (FPG) ≥7.0 mmol/L or HbA1c ≥6.5% at enrollment),[18] smoking status, alcohol consumption and end-stage kidney disease (ESKD) etiology. Laboratory tests included hemoglobin (HB), white blood cell count (WBC), platelet count (PLT), red blood cell distribution width (RDW), fasting glucose (FPG), albumin (ALB), alanine aminotransferase (ALT), serum creatinine (SCR), serum uric acid (SUA), fibrinogen (FIB), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), parathyroid hormone (PTH), and calcium (Ca). For the ICH group, these measurements were obtained after the onset of ICH but prior to initiating specific interventions for ICH. For the Non-ICH group, blood samples were collected immediately prior to the mid-week hemodialysis session (ie, after a 2-day interdialytic interval) to standardize metabolic conditions and minimize acute effects of dialysis on fibrinogen and albumin levels. All the above laboratory tests were conducted within 24 hours of admission. FAR was calculated as FIB (mg/dL) x 100%/ALB (g/L). Brain computed tomography (CT) scans were analyzed by two independent neuroradiologists blinded to clinical data. ICH diagnosis and characterization adhered to the SMASH-U criteria, with hematoma volume quantified using the ABC/2 method. Intraventricular extension was graded via the Graeb Score. Discrepancies were resolved through consensus or third-party adjudication. For the ICH group, imaging confirmed spontaneous intracerebral hemorrhage. For the Non-ICH group, baseline CT ruled out acute ICH, and follow-up imaging was conducted only if new neurological symptoms emerged during dialysis or hospitalization.

Statistical Analysis

The SPSS 27.0 and R language 4.1.3 software were used to conduct all statistical analyses and to generate plots. Quantitative data conforming to a normal distribution were expressed as mean ± standard deviation, and intergroup

comparisons were conducted using an independent sample *t*-test; Non-normally distributed data were represented by median values (P25, P75), and intergroup comparisons were tested using rank sum test. The count data were expressed as frequency (%), and intergroup comparisons were tested using the chi-square test. Firstly, chi square test and independent sample *t*-test were used to compare the differences in categorical and continuous variable characteristics between the non-ICH and ICH groups. FAR was divided into quartiles, and logistic regression analysis was used to further evaluate the correlation between FAR and ICH risk. The results of adjusting for confounding factors across several models were displayed as odds ratios (OR) with 95% confidence intervals (CI). Among them, covariates were not adjusted in the coarse model; Age and gender were adjusted in model 1; history of hypertension and diabetes were included in model 2 on the basis of model 1 adjustment. FIB and RDW were incorporated into model 3 building on the adjustment made in model 2. The non-linear relationship between FAR and ICH was determined using restricted cubic splines (RCSs). The hierarchical logistic regression model was used to study the interactions between several subgroups at a hierarchical level. Receiver operating characteristic (ROC) curves were used to analyze and plot diagnostic performance graphs related to FIB, ALB, FAR, and ICH. The diagnostic value was evaluated by calculating the area under the curve (AUC) of the ROC curve. To statistically compare the diagnostic performance of FAR, FIB, and ALB, we performed pairwise comparisons of the areas under the ROC curves using DeLong's non-parametric method. A significance level of $p<0.05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 536 MHD patients were admitted, including 254 female patients and 282 male patients. Table 1 presents the baseline characteristics of MHD patients with or without ICH. No significant differences were observed in age, sex, BMI, HB, PLT, ALB, SCR, SUA, TG, TC, LDL-C, HDL-C, Ca, PTH, history of smoking, alcohol consumption and ESKD etiology between groups. ($p>0.05$). ICH group patients' WBC, RDW, ALT, FIB, and FAR both increased, while FPG

Table 1 Baseline Characteristics of MHD Patients in Two Groups

Variables	Non-ICH Group (n = 329)	ICH Group (n = 207)	*P value*
Age (years)	68.00 (60.00, 75.00)	68.00 (61.00, 76.00)	0.606
BMI (kg/m^2)	23.50 (20.80, 26.30)	23.50 (21.00, 25.51)	0.538
Sex, n(%)			0.655
Male	171 (51.98)	111 (53.62)	
Female	158 (48.02)	96 (46.38)	
Smoking status, n(%)			0.255
No	133 (40.43)	94 (45.41)	
Yes	196 (59.57)	113 (54.59)	
Alcohol consumption, n(%)			0.396
No	184 (55.93)	108 (52.17)	
Yes	145 (44.07)	99 (47.83)	
Hypertension, n(%)			**<0.001**
No	55 (16.72)	11 (5.31)	
Yes	274 (83.28)	196 (94.69)	
Diabetes, n(%)			**0.025**
No	158 (48.02)	79 (38.16)	
Yes	171 (51.98)	128 (61.84)	
ESKD Etiology, n(%)			0.815
Diabetic nephropathy	133 (40.43)	79 (38.16)	
Chronic glomerulonephritis	62 (18.84)	38 (18.36)	

(*Continued*)

Table 1 (Continued).

Variables	Non-ICH Group (n = 329)	ICH Group (n = 207)	*P value*
Other causes	134 (40.73)	90 (43.48)	
HB (g/L)	89.00 (76.00, 101.00)	85.00 (69.50, 104.50)	0.219
WBC ($\times 10^9$/L)	6.17 (5.21, 7.50)	6.69 (5.21, 8.28)	**0.026**
PLT ($\times 10^9$/L)	189.00 (145.00, 237.00)	184.00 (139.50, 236.50)	0.424
RDW (%)	47.80 (44.40, 50.60)	49.00 (45.70, 53.30)	**<0.001**
FPG (mmol/L)	9.78 (7.47, 12.12)	9.06 (6.38, 12.16)	**0.033**
ALB (g/L)	34.28 (21.05, 47.47)	35.37 (23.04, 44.56)	0.777
ALT (U/L)	9.80 (5.70, 13.80)	12.10 (7.70, 18.00)	**<0.001**
SCR (μmol/L)	619.00 (465.00, 804.00)	597.60 (448.00, 826.25)	0.601
FIB (mg/dL)	8.34 (4.48, 13.07)	12.14 (7.36, 16.69)	**<0.001**
SUA (μmol/L)	346.20 (250.50, 429.60)	352.22 (275.00, 463.00)	0.095
TG (mmol/L)	1.34 (0.94, 1.73)	1.44 (1.06, 1.75)	0.068
TC (mmol/L)	4.77 (3.34, 6.10)	4.95 (3.50, 6.28)	0.242
LDL-C (mmol/L)	2.79 (2.19, 3.26)	2.73 (2.10, 3.24)	0.777
HDL-C (mmol/L)	2.30 (1.39, 3.21)	2.33 (1.55, 3.31)	0.235
PTH (pg/mL)	270.00 (156.00, 434.00)	257.00 (156.00, 384.50)	0.242
Ca (mmol/L)	2.26 (1.58, 2.93)	2.13 (1.79, 2.50)	0.133
FAR	9.63 (7.21, 12.54)	14.05 (9.60, 19.10)	**<0.001**

Note: The *P values* in bold are defined as statistical significance.
Abbreviations: MHD, maintenance hemodialysis; BMI, body mass index; ESKD, end-stage kidney disease; HB, hemoglobin; WBC, white blood cell count; PLT, platelet count; RDW, red blood cell distribution width; FPG, fasting glucose; ALB, albumin; ALT, alanine aminotransferase; SCR, serum creatinine; SUA, serum uric acid; FIB, fibrinogen; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PTH, parathyroid hormone; Ca, calcium; FAR, fibrinogen to albumin ratio.

decreased ($p<0.05$). Moreover, there was a significant difference in the history of hypertension, diabetes between MHD patients with and without ICH ($p<0.05$).

Logistic Regression Analysis of Univariate and Multivariate

The univariate logistic regression model showed that hypertension, HB, RDW, ALT, ALB, FIB, TG, HDL-C, PTH, and FAR were significantly correlated with the occurrence of ICH ($p<0.05$). Multivariate analysis identified FAR (OR=1.07, 95% CI: 1.03–1.10), hypertension (OR=2.98, 95% CI: 1.43–6.20), RDW (OR=1.08, 95% CI: 1.04–1.13), and FIB (OR=1.13, 95% CI: 1.09–1.18) as independent ICH predictors ($p<0.05$) (Table 2).

Association Between FAR and the Risk of ICH in Various Models

Further multivariate regression analysis was conducted to verify the relationship between FAR and ICH (Table 3). In Model 0, without adjustments, high FAR levels were significantly associated with the occurrence of ICH (medium FAR, OR 9.62, 95% CI 4.37–21.18; high FAR, OR 24.54, 95% CI 11.37–52.96). In Model 1, after adjusting for age and gender, a significant association was still observed between high FAR levels and ICH risk (mid FAR, OR 9.62, 95% CI 4.37–21.18; high FAR, OR 24.66, 95% CI 11.42–53.23). In model 2, confounding factors such as blood pressure and diabetes were further adjusted for. A significant correlation was still observed between higher FAR levels and ICH risk (mid FAR, OR 9.16, 95% CI 4.16–20.18; high FAR, OR 24.05, 95% CI 11.14–51.95). Add FIB and RDW to the model based to model 2. There is still a significant association between higher FAR levels and ICH risk (mid FAR, OR 6.55, 95% CI 2.87–14.92; high-FAR, OR 12.21, 95% CI 4.87–30.60) (all $p < 0.001$).

Table 2 Univariate and Multivariate Logistic Regression Analysis of Risk Factors for ICH in MHD Patients

Variables	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P value*	OR (95% CI)	*P value*
Sex, n(%)	0.94 (0.66 ~ 1.33)	0.710		
Smoking status, n(%)	0.82 (0.57 ~ 1.16)	0.256		
Alcohol consumption, n(%)	1.16 (0.82 ~ 1.65)	0.396		
Hypertension, n(%)	3.58 (1.83 ~ 7.01)	**<0.001**	2.98 (1.43 ~ 6.20)	**0.004**
Diabetes, n(%)	1.50 (1.05 ~ 2.13)	**0.026**	1.35 (0.89 ~ 2.05)	0.152
ESKD Etiology, n(%)				
Diabetic nephropathy	1.00			
Chronic glomerulonephritis	1.03 (0.63 ~ 1.69)	0.900		
Other causes	1.13 (0.77 ~ 1.66)	0.533		
Age (years)	1.01 (0.99 ~ 1.03)	0.379		
BMI (kg/m^2)	0.99 (0.94 ~ 1.04)	0.641		
HB (g/L)	1.00 (0.99 ~ 1.01)	0.427		
WBC ($\times10^9$/L)	1.00 (0.99 ~ 1.01)	0.610		
PLT ($\times10^9$/L)	1.00 (1.00 ~ 1.00)	0.193		
RDW (%)	1.08(1.04 ~ 1.12)	**<0.001**	1.08(1.04 ~ 1.13)	**<0.001**
FPG (mmol/L)	0.98 (0.94 ~ 1.02)	0.358		
ALB (g/L)	1.00 (0.99 ~ 1.01)	0.780		
ALT (U/L)	0.99 (0.99 ~ 0.99)	**0.026**	1.00 (0.99 ~ 1.00)	0.167
SCR (μmol/L)	1.00 (1.00 ~ 1.00)	0.381		
FIB (mg/dL)	1.14 (1.10 ~ 1.18)	**<0.001**	1.13 (1.09 ~ 1.18)	**<0.001**
SUA (μmol/L)	1.00 (1.00 ~ 1.00)	0.578		
TG (mmol/L)	1.35 (0.98 ~ 1.86)	0.068		
TC (mmol/L)	1.05 (0.96 ~ 1.14)	0.291		
LDL-C (mmol/L)	0.98 (0.84 ~ 1.15)	0.824		
HDL-C (mmol/L)	1.10 (0.94 ~ 1.29)	0.227		
PTH (pg/mL)	1.00 (1.00 ~ 1.00)	0.170		
Ca (mmol/L)	0.81 (0.62 ~ 1.05)	0.112		
FAR	1.05 (1.02 ~ 1.08)	**<0.001**	1.07 (1.03 ~ 1.10)	**<0.001**

Note: The *P values* in bold are defined as statistical significance.(P<0.05).

Abbreviations: ICH, intracerebral hemorrhage; MHD, maintenance hemodialysis; ESKD, end-stage kidney disease; BMI, body mass index; HB, hemoglobin; WBC, white blood cell count; PLT, platelet count; RDW, red blood cell distribution width; FPG, fasting glucose; ALB, albumin; ALT, alanine aminotransferase; SCR, serum creatinine; SUA, serum uric acid; FIB, fibrinogen; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PTH, parathyroid hormone; Ca, calcium; FAR, fibrinogen to albumin ratio.

Table 3 Multivariate Logistic Analysis of the Association Between FAR (per-1 SD Increase) and the Presence of ICH

Variables	Model 0		Model 1		Model 2		Model 3	
	OR (95% CI)	*P value*	OR (95% CI)	*P value*	OR (95% CI)	*P value*	OR (95% CI)	*P value*
FAR<7.6	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
7.6≦FAR≦11.1	9.62 (4.37 ~ 21.18)	**<0.001**	9.62 (4.37 ~ 21.18)	**<0.001**	9.16 (4.16 ~ 20.18)	**<0.001**	6.55 (2.87 ~ 14.92)	**<0.001**
FAR>11.1	24.54 (11.37 ~ 52.96)	**<0.001**	24.66 (11.42 ~ 53.23)	**<0.001**	24.05 (11.14 ~ 51.95)	**<0.001**	12.21 (4.87 ~ 30.60)	**<0.001**

Notes: Model 0: unadjusted. Model 1: Model 0 + age and sex. Model 2: Model 1 + hypertension and diabetes. Model 3: Model 2 + RDW and FIB. ORs reflected the associations between FAR (per 1SD increase) and different indicators of ICH. The *P values* in bold are defined as statistical significance.

Abbreviations: ICH, intracerebral hemorrhage; RDW, red blood cell distribution width; FIB, fibrinogen; FAR, fibrinogen to albumin ratio.

RCSs for Analyzing the Relationship Between FAR and the Risk of ICH

To further validate the association between FAR and ICH in MHD patients, we employed restricted cubic spline (RCS) analysis. The results showed that, There is a non-linear correlation between FAR and ICH risk in MHD patients (*p for*

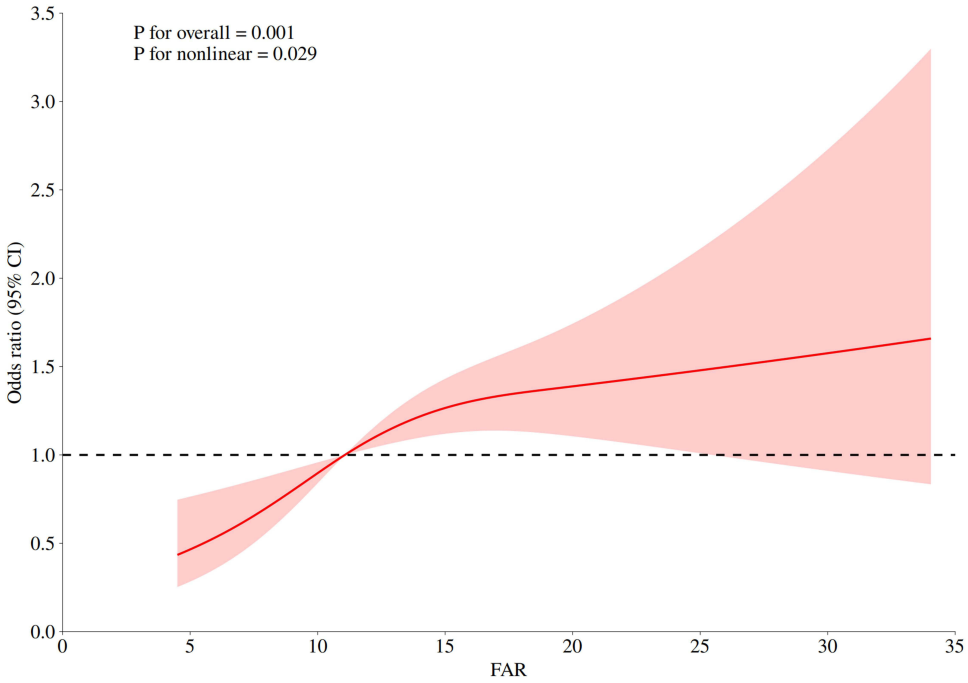

Figure 2 Restricted cubic spline analysis of the relationship between FAR and ICH risk.
Abbreviations: FAR, fibrinogen to albumin ratio; ICH, intracerebral hemorrhage.

non-linear=0.029; Figure 2). Noteworthy, above the threshold of 12, higher FAR levels were associated with an increased risk of ICH, suggesting a potential link between FAR levels and the occurrence of ICH.

Exploration of Subgroup Analysis

This study evaluated the interaction terms of important variables that may alter ICH risk to confirm the association between FAR and ICH risk. According to age, gender, smoking, alcohol consumption, hypertension, diabetes, BMI and enrollment subgroup analysis. The results are shown in Figure 3. The results showed that all factors had no interactive effect on ICH risk. This means that FAR alone is a factor that increases the risk of developing ICH in MHD patients.

Predictive Value of FIB, ALB and FAR for the Risk of ICH

ROC analysis revealed FAR's superior predictive accuracy (AUC=0.75) compared to FIB (AUC=0.67) and ALB (AUC=0.49) (Figure 4 and Table 4). The optimal FAR cutoff was 12.2 (sensitivity=0.73, specificity=0.60). Formal statistical comparisons using DeLong's test revealed that FAR exhibited significantly superior discriminatory accuracy compared to both FIB ($Z = 2.15$, $p = 0.032$) and ALB ($Z = -7.72$, $p < 0.001$). Conversely, ALB demonstrated significantly lower predictive value than FIB ($Z = -5.20$, $p < 0.001$). (Table 5).

Discussion

This study primarily investigates the correlation between FAR and ICH risk in MHD patients through retrospective analysis. We found that the combination of hypertension, RDW, FIB, and FAR are significant risk factors for developing ICH in MHD patients. In addition, there is a non-linear correlation between FAR and ICH insurance. FAR >12.2 is significantly correlated with increased ICH risk. Among them, FIB, ALB, and FAR are all indicators reflecting the state of microinflammation and are important predictors of ICH in MHD patients, indicating the presence of malnutrition and micro inflammation in ICH patients. In recent years, studies have shown that MHD patients generally have a mild inflammatory state, with an incidence rate of 26% to 35%. High levels of pro-inflammatory cytokines are closely related to the occurrence of ICH in MHD patients.[19,20]

Variables	n (%)	FAR<12.2	FAR ≥ 12.2	OR (95%CI)	P	P for interaction
All patients	536 (100.00)	109/316	98/220	1.53 (1.07 ~ 2.17)	0.019	
Sex						0.285
0	282 (52.61)	61/165	50/117	1.27 (0.78 ~ 2.06)	0.329	
1	254 (47.39)	48/151	48/103	1.87 (1.12 ~ 3.14)	0.017	
Smoke						0.213
0	227 (42.35)	50/126	44/101	1.17 (0.69 ~ 2.00)	0.555	
1	309 (57.65)	59/190	54/119	1.84 (1.15 ~ 2.96)	0.011	
Drink						0.439
0	292 (54.48)	64/185	44/107	1.32 (0.81 ~ 2.16)	0.266	
1	244 (45.52)	45/131	54/113	1.75 (1.04 ~ 2.93)	0.034	
HTN						0.644
0	66 (12.31)	6/38	5/28	1.16 (0.32 ~ 4.26)	0.824	
1	470 (87.69)	103/278	93/192	1.60 (1.10 ~ 2.32)	0.014	
DM						0.217
0	237 (44.22)	39/143	40/94	1.98 (1.14 ~ 3.42)	0.015	
1	299 (55.78)	70/173	58/126	1.26 (0.79 ~ 2.00)	0.337	
Age custom						0.982
1	2 (0.37)	0/2	0/0	NA	NA	
2	534 (99.63)	109/314	98/220	1.51 (1.06 ~ 2.15)	0.022	
BMI custom						0.573
1	286 (53.36)	57/166	56/120	1.67 (1.03 ~ 2.71)	0.036	
2	250 (46.64)	52/150	42/100	1.36 (0.81 ~ 2.30)	0.242	

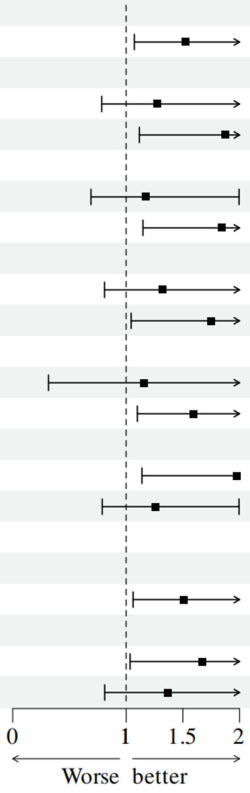

Figure 3 Subgroup analysis of association between FAR and ICH risk.
Abbreviations: FAR, fibrinogen to albumin ratio; ICH, intracerebral hemorrhage; HTN, hypertension; DM, diabetes; BMI, body mass index.

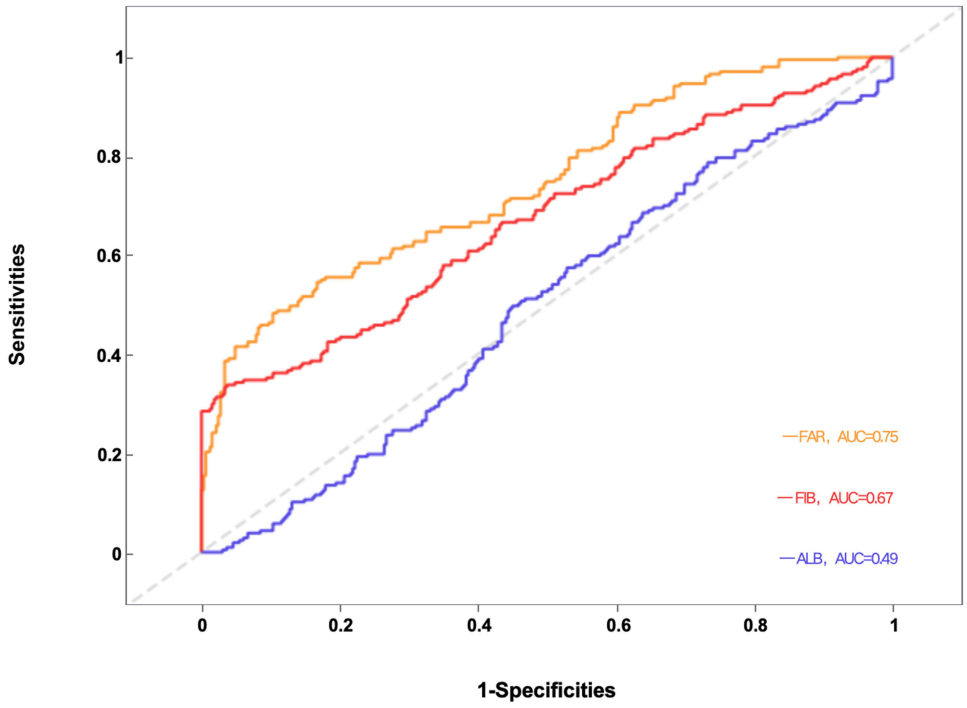

Figure 4 Receiver operating characteristic curves of FIB, ALB and FAR associated with ICH in MHD patients.
Abbreviations: FIB, fibrinogen; ALB, albumin; FAR, fibrinogen to albumin ratio; ICH, intracerebral hemorrhage; MHD, maintenance hemodialysis.

Table 4 Predictive Value of FAR, ALB and FAR for ICH Risk

Variables	AUC(95% CI)	Sensitivity(95% CI)	Specificity(95% CI)	Cut off value
ALB	0.49 (0.44 ~0.54)	0.55 (0.50 ~0.60)	0.50 (0.43 ~0.57)	35.7
FIB	0.67 (0.63 ~0.72)	0.65 (0.60 ~0.70)	0.58 (0.51 ~0.65)	344.5
FAR	0.75 (0.70 ~0.70)	0.73 (0.68 ~0.77)	0.60 (0.54 ~0.67)	12.2

Abbreviations: AUC, area under curve; ALB, albumin; FIB, fibrinogen; FAR, fibrinogen to albumin ratio; ICH, intracerebral hemorrhage; MHD, maintenance hemodialysis.

Table 5 DeLong's Test Results for Pairwise Comparison of AUCs

Comparison	Z-statistic	*P value*
ALB vs FIB	−5.20	**<0.001**
FAR vs FIB	2.15	**0.032**
ALB vs FAR	−7.72	**<0.001**

Note: The *P values* in bold are defined as statistical significance. (P<0.05).
Abbreviations: AUC, area under curve; ALB, albumin; FIB, fibrinogen; FAR, fibrinogen to albumin ratio.

FIB is the final product of the cascade of glycoproteins and coagulation synthesized in the liver, which rapidly increases in the presence of injury, infection, or inflammation. It is often used as an inflammation indicator and a risk predictor for thrombosis.[21] A high FIB level of is closely related to coronary artery disease and cerebrovascular accidents. A meta-analysis of a prospective observational study involving 92174 individuals found that fibrinogen level is a strong independent predictor of myocardial infarction and stroke.[22] During the ICH process, fibrinogen not only participates in coagulation, but also in the post fermentation process, which can consume a large amount of fibrinogen.[23] In the following period, a large amount of inflammatory cytokines, including IL-6, will be released, which can increase the permeability of the blood-brain barrier and is related to the release of fibrinogen. Therefore, the level of fibrinogen may increase due to inflammatory reactions.[24] Besides, high levels of FIB increase the risk of stroke and lead to early deterioration of neurological function in primary cerebral infarction.[25] The multivariate logistic regression in this study showed that FIB is the sole risk factor for ICH. (p<0.001), And in the ROC curve, the AUC is 0.67, which has good predictive value for the occurrence of ICH.

ALB not only reflects nutritional status, but also participates in the inflammatory response in the body. Inflammation can lead to malnutrition, which can trigger inflammatory reactions.[26] Studies have demonstrated that low ALB concentrations are significantly associated with poor prognosis in ischemic stroke patients.[27] Patients with ICH accompanied by leukopenia have poor neurological function and poor prognosis. In animal models, albumin treatment can significantly reduce infarct volume and cerebral edema.[28] In addition, ALB can maintain the integrity of the brain barrier, reduce oxidative stress-related neuronal death, and improve neurological function after ICH. Therefore, patients with low ALB levels who lack protein protection are more likely to develop ICH.[29] However, in the multivariate logistic model, we did not find a significant negative correlation between ALB and poor prognosis. One possible explanation is that in MHD patients, the occurrence of cerebral hemorrhage is influenced by multiple factors, such as the use of anticoagulants during dialysis, which may increase the risk of hemorrhage. Additionally, patients often experience mild inflammation and malnutrition. Inflammatory reactions can promote the synthesis of acute phase protein in the liver, leading to changes in protein distribution, while malnutrition can cause the loss of protein synthesis materials, further reducing protein levels. These complex interactions make it difficult for a single protein level to accurately reflect the risk of cerebral hemorrhage.[30]

FIB and ALB are indicators of microinflammatory status in MHD patients. However, their specificity is limited when analyzed independently due to confounding factors. FAR, as the ratio of FIB and ALB, is a novel clinical inflammatory marker proposed in recent years, and has been proven to be positively correlated with micro inflammation in multiple previous studies. Furthermore, FAR has been identified as a predictor of adverse outcomes in patients with cardiovascular

diseases, cancer, sepsis, and stroke.[10,31] It has been used to determine medical conditions including malnutrition, coagulation system, systemic inflammation, and liver dysfunction.[32] Compared to traditional micro inflammatory markers such as CRP, IL-6, TNF - α, and other factors, FAR has advantages such as convenience, affordability, and easy accessibility.

This is the first study on the predictive value of FAR for ICH in MHD patients. Multiple logistic regression in this study showed that FAR was the sole risk factor for ICH ($p<0.001$), and the ROC curve result showed an AUC of 0.75, which had excellent predictive value for the occurrence of ICH. Therefore, a higher FAR is a new independent predictor of ICH in MHD patients. This discovery may help assist in clinical evaluation of patient prognosis. This helps clinical doctors identify and monitor the early risk of ICH in MHD patients, preventing the deterioration of their condition.

Compared to traditional inflammatory markers like CRP or IL-6, FAR offers distinct advantages. While CRP solely reflects systemic inflammation, FAR encapsulates both inflammatory and nutritional imbalances, which are pivotal in MHD patients. For example, Celebi et al found FAR to be a stronger predictor of coronary artery disease severity than CRP, as CRP levels may fluctuate with transient infections unrelated to chronic vascular pathology.[13] Compared to previous studies, similar views have also been reported. Researchers found a significant positive correlation between FAR and C-reactive protein (r=0.527, $p<0.001$), further confirming that FAR is an inflammation related indicator.[33] The study by Ruan showed that high FAR is independently associated with increased risk of hemorrhagic conversion. (OR=5.027, 95% CI=5.027 (2.309–10.942), $p<0.001$). FAR can help clinical doctors make preliminary judgments on the risk of hemorrhagic transformation in stroke patients.[31,34] Previous studies have shown that inflammatory response plays an important role in tumor enlargement. It can damage the blood-brain barrier (BBB), further leading to sustained damage to the ducts around the initial site of the tumor and delayed exit time, and affecting coagulation function. Previous studies have shown that high FAR is associated with increased swelling in patients with ICH.[35] In addition, research has found that FAR is associated with the spontaneous transformation of cerebral infarction. Elevated FAR is associated with poor prognosis and the presence of adverse events in patients with cardiovascular disease, cancer, venous arterial extracorporeal membrane oxygenation, and stroke.[11]

In this study, to evaluate the predictive value of FIB, ALB, and FAR for the occurrence of ICH, ROC curve analysis shows that the AUC of FAR (0.75) is surpassed both FIB (0.67) and ALB (0.49). The DeLong's test results further validate the clinical utility of FAR as a composite biomarker. Its significantly higher AUC compared to both FIB and ALB underscores its ability to integrate complementary prognostic information from FIB and ALB. FAR is more effective than FIB and ALB in predicting the occurrence of ICH. It has been confirmed that FAR can serve as a laboratory indicator reflecting the inflammatory status, nutritional status, and hemodynamics of the body. Its predictive value is higher than that of FIB, ALB, and CRP, and it is easy to obtain for monitoring. It may be one of the new biomarkers for ICH in MHD patients.

In the multi-model correction results of this study: the attenuation of FAR associations in model 3 (including RDW and FIB) suggests that FAR partially overlaps with these variables in capturing inflammatory and coagulation pathways. FIB, a component of FAR, is directly associated with hypercoagulable states and endothelial activation, whereas RDW reflects systemic inflammation and oxidative stress.[22] This is consistent with previous studies in which composite biomarkers (eg, FAR) showed reduced independence when adjusted for their components.[14] Nonetheless, FAR had significant predictive value in Model 3 (OR=12.21), emphasizing its utility as a holistic marker integrating fibrinogen-driven inflammation and albumin-mediated vascular integrity.

Based on interquartile analyses (eg, OR > 12), although these values reflect the strong correlation between FAR and ICH risk, they may be influenced by the synergistic effects of fibrinogen-driven hypercoagulability and hypoalbuminemia-induced endothelial dysfunction.[30] Besides, retrospective studies are inherently susceptible to residual confounding, such as unmeasured variables like vascular calcification or uremic toxin accumulation, which may lead to inflated effect estimates.

In addition, the multiple logistic regression model of this study also showed that the combination of hypertension and RDW were the sole risk factors for developing ICH. Among MHD patients with basic diseases, abnormal blood pressure, abnormal blood lipid and diabetes are the most common, and the combination of these diseases is a risk factor for the occurrence of ICH. During dialysis treatment, changes in hemodynamics, the precipitation of antihypertensive drugs, and the application of erythropoietin can cause cerebrovascular diseases when the blood pressure exceeds the load that the tube wall can withstand. Under the mediation of high blood pressure, it can promote tumor enlargement and increase the risk of brain hemorrhage,

affecting the prognosis.[36] Previous studies have shown that RDW is related to heart failure, myocardial infarction coronary, atherosclerosis, carotid atherosclerosis and central atherosclerosis. Some studies have found that RDW is related to the risk of carotid atherosclerosis, and the early stage of carotid atherosclerosis is related to the risk of moderate carotid atherosclerosis.[37] Studies have analyzed that the RDW is positively correlated with cardiovascular events in MHD patients ($r=0.439$, $p<0.05$). Additionally, many research results suggest that the RDW is the sole risk factor for cardiovascular events in MHD patients, and the two are positively correlated.[38] And these previous research conclusions are largely consistent with the results of this study.

Compared to previous similar studies, The strength of this study lies in our validation that FAR is a significant risk factor for the onset of ICH in MHD patients. In addition, this is the first study to investigate the prediction value of FAR for ICH in patients on MHD.

However, this study also has some limitations. Firstly, due to its design as a single center cross-sectional study with a relatively small sample size, the results cannot be used to establish causal relationships, which may lead to variation. Secondly, calcium-phosphorus product and serum phosphate levels, which are closely linked to vascular calcification in dialysis patients, were not analyzed due to incomplete retrospective data. This omission may affect the generalizability of FAR's predictive role in populations with advanced mineral bone disease. Thirdly, as this was a retrospective study, dynamic measurements (eg, HbA1c trends or ambulatory blood pressure monitoring) were unavailable. In addition, this study only analyzes the baseline FAR. The dynamic changes of the FAR during hospitalization are unavailable. FAR values in the ICH group were measured post-ICH onset, which may reflect acute inflammatory responses triggered by the hemorrhage. Fourthly, the study did not compare the predictive efficacy of FAR with traditional inflammatory indicators (such as CRP and IL-6), which limits the demonstration of its clinical specificity. Fifth, while anticoagulation protocols were standardized, residual heparin effects or individual variations in drug metabolism may confound bleeding risk. Prospective monitoring of anticoagulant levels and bleeding diaries would strengthen future analyses. Notably, the exclusion of patients with prior cerebral infarction may introduce selection bias. However, this exclusion was necessary to ensure that observed associations between FAR and ICH were not confounded by residual effects of prior infarctions. Finally, these results are not applicable to all types of ICH as they exclude brain injury, aneurysms, vascular malformations, Moyamoya disease, malignant tumors, fluid diseases, and the use of anticoagulants or antiplatelet drugs in violation of medical advice.

In future research, the sample size can be further expanded, and multi center prospective studies can be conducted to deeply explore the long-term application value of FAR in predicting ICH risk in MHD patients, and further clarify the specific molecular mechanism of its impact on ICH development. At the same time, the effectiveness of targeted measures to reduce ICH risk in MHD patients can be explored.

Conclusions

This study confirms that FAR serves as an independent predictor of ICH in MHD patients, with a significantly elevated ICH risk when FAR exceeds 12.2. Compared to fibrinogen or albumin alone, FAR demonstrated superior predictive accuracy (AUC=0.75). Additionally, hypertension, RDW, and fibrinogen were identified as critical risk factors for ICH. These findings suggest that FAR may act as a potential biomarker for early identification of high-risk MHD patients, however, its clinical utility needs to be validated by multicenter prospective studies combining FAR with established predictors, such as ambulatory blood pressure trends and neuroimaging markers. Such advancements will enhance precision in risk prediction and prevention of ICH in this vulnerable population, ultimately improving clinical outcomes and advancing nephrology and cerebrovascular research.

Data Sharing Statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Baoding No. 1 Central Hospital. (approval number:2024178). Informed consent was obtained from all participants prior to the enrollment. The study complies with the Declaration of Helsinki.

Consent for Publication

Written informed consent was obtained from the patients for publication of this study.

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Author Contributions

All authors made significant contributions to the work reported, including conception, study design, execution, data acquisition, analysis, and interpretation. Xiaojie He drafted the manuscript. Yaqing Wang and Yuqing Wang performed statistical analysis and data curation. Xiaodong Li supervised the study, reviewed the literature, and revised the manuscript critically. All authors approved the final version to be published, agreed on the journal for submission, and take accountability for all aspects of the work.

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Disclosure

The authors declare no competing interests.

References

1. de Oliveira Manoel AL. Surgery for spontaneous intracerebral hemorrhage. *Crit Care*. 2020;24(1):45. doi:10.1186/s13054-020-2749-2
2. Feigin VL, Roth GA, Naghavi M, et al. Global Burden of Diseases, Injuries and Risk Factors Study 2013 and Stroke Experts Writing Group. Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol*. 2016;15(9):913–924. doi:10.1016/S1474-4422(16)30073-4.
3. Zhang M, Zhang L, Hu Y, et al. Sarcopenia and echocardiographic parameters for prediction of cardiovascular events and mortality in patients undergoing maintenance hemodialysis. *PeerJ*. 2022;10:e14429. doi:10.7717/peerj.14429
4. Wang HH, Hung SY, Sung JM, Hung KY, Wang JD. Risk of stroke in long-term dialysis patients compared with the general population. *Am J Kidney Dis*. 2014;63(4):604–611. doi:10.1053/j.ajkd.2013.10.013
5. Wyld M, Webster AC. Chronic kidney disease is a risk factor for stroke. *J Stroke Cerebrovasc Dis*. 2021;30(9):105730. doi:10.1016/j.jstrokecerebrovasdis.2021.105730
6. Reilly RF, Jain N. Warfarin in nonvalvular atrial fibrillation-Time for a change? *Semin Dial*. 2019;32(6):520–526. doi:10.1111/sdi.12829
7. Steward C. Dialysis disequilibrium syndrome in the neurointensive care unit: a case study. *Nephrol Nurs J*. 2019;46(6):597–603.
8. Sá Martins V, Aguiar L, Dias C, et al. Predictors of nutritional and inflammation risk in hemodialysis patients. *Clin Nutr*. 2020;39(6):1878–1884. doi:10.1016/j.clnu.2019.07.029
9. Bihl JC, Zhang C, Zhao Y, et al. Angiotensin-(1-7) counteracts the effects of Ang II on vascular smooth muscle cells, vascular remodeling and hemorrhagic stroke: role of the NFκB inflammatory pathway. *Vascul Pharmacol*. 2015;73:115–123. doi:10.1016/j.vph.2015.08.007
10. Fonseca S, Costa F, Seabra M, et al. Systemic inflammation status at admission affects the outcome of intracerebral hemorrhage by increasing perihematomal edema but not the hematoma growth. *Acta Neurol Belg*. 2021;121(3):649–659. doi:10.1007/s13760-019-01269-2
11. Tai H, Zhu Z, Mei H, Sun W, Zhang W. Albumin-to-fibrinogen ratio independently predicts 28-day mortality in patients with peritonitis-induced sepsis. *Mediat. Inflamm*. 2020;2020:7280708. doi:10.1155/2020/7280708
12. Ding Y, Xue L. The potential value of fibrinogen to albumin ratio (FAR) in the assessment of inflammation in spondyloarthritis. *BMC Musculoskelet Disord*. 2022;23(1):864. doi:10.1186/s12891-022-05797-6
13. Celebi S, Ozcan Celebi O, Berkalp B, Amasyali B. The association between the fibrinogen-to-albumin ratio and coronary artery disease severity in patients with stable coronary artery disease. *Coron Artery Dis*. 2020;31(6):512–517.
14. Zheng L, Wang Z, Liu J, et al. Association between admission blood fibrinogen-to-albumin ratio and clinical outcomes after acute lacunar stroke. *Biomark Med*. 2021;15(2):87–96. doi:10.2217/bmm-2019-0537
15. Zhang L, Wang Z, Xiao J, et al. Prognostic value of fibrinogen-to-albumin ratio in patients with gastric cancer receiving first-line chemotherapy. *Oncol Lett*. 2020;20(4):10. doi:10.3892/ol.2020.11871
16. Williams B, Mancia G, Spiering W, et al. ESC Scientific Document Group. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2019;40(5):475. PMID: 30165516. doi:10.1093/eurheartj/ehy686
17. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44(9):2182. doi:10.2337/dc21-ad09.
18. Kalantar-Zadeh K, Jafar TH, Nitsch D, et al. Chronic kidney disease. *Lancet*. 2021;398(10302):786–802. doi:10.1016/S0140-6736(21)00519-5
19. Watanabe Y, Suzuki K, Inoue T, Kurita H, Okada H. Functional prognosis following spontaneous intracerebral hemorrhage in patients on hemodialysis: a retrospective study of 100 consecutive cases. *Renal Replacement Therapy*. 2024;10(1):44. doi:10.1186/s41100-024-00528-0

20. Cohen SD, Phillips TM, Khetpal P, Kimmel PL. Cytokine patterns and survival in haemodialysis patients. *Nephrol Dial Transplant*. 2010;25(4):1239–1243. doi:10.1093/ndt/gfp625
21. Wang Y, Gao L. Inflammation and cardiovascular disease associated with hemodialysis for end-stage renal disease. *Front Pharmacol*. 2022;13:800950. doi:10.3389/fphar.2022.800950
22. Ernst E, Resch KL. Fibrinogen as a cardiovascular risk factor: a meta-analysis and review of the literature. *Ann Intern Med*. 1993;118(12):956–963. doi:10.7326/0003-4819-118-12-199306150-00008
23. Wang G, Zhang J. Hematoma expansion: clinical and molecular predictors and corresponding pharmacologi- cal treatment. *Curr Drug Targets*. 2017;18(12):1367–1376. doi:10.2174/1389450117666160712092224
24. Lim-Hing K, Rincon F. Secondary hematoma expansion and perihemorrhagic edema after intracerebral hemorrhage: from bench work to practical aspects. *Front Neurol*. 2017;8:74. doi:10.3389/fneur.2017.00074
25. Zhang L, Zhao MH, Zuo L, et al. CK-NET Work Group. China kidney disease network (CK-NET) 2015 annual data report. *Kidney Int Suppl*. 2019;9(1):e1–e81. doi:10.1016/j.kisu.2018.11.001.
26. Wen Y, Yang J, Han X. Fibrinogen-to-albumin ratio is associated with all-cause mortality in cancer patients. *Int J Gen Med*. 2021;14:4867–4875. doi:10.2147/IJGM.S322735
27. Cho YM, Choi IS, Bian RX, Kim JH, Han JY, Lee SG. Serum albumin at admission for prediction of functional outcome in ischaemic stroke patients. *Neurol Sci*. 2008;29(6):445–449. doi:10.1007/s10072-008-1024-0
28. De La Mata NL, Alfaro-Ramirez M, Kelly PJ, Masson P, Al-Shahi Salman R, Webster AC. Absolute risk and risk factors for stroke mortality in patients with end-stage kidney disease (ESKD): population-based cohort study using data linkage. *BMJ Open*. 2019;9(2):e026263. doi:10.1136/bmjopen-2018-026263
29. Gardner AW, Montgomery PS, Casanegra AI, Silva-Palacios F, Ungvari Z, Csiszar A. Association between gait characteristics and endothelial oxidative stress and inflammation in patients with symptomatic peripheral artery disease. *Age*. 2016;38(3):64. doi:10.1007/s11357-016-9925-y
30. Li J, Zhou X, Xiang Y, et al. Clinical significance of preoperative fibrinogen to albumin ratio in patients with glioblastoma: a singe center experience. *Cancer Manag Res*. 2021;13:3259–3269. doi:10.2147/CMAR.S305025
31. Wang Y, Li J, Chang S, Zhou K, Che G. Low albumin to fibrinogen ratio predicts poor overall survival in esophageal small cell carcinoma patients: a retrospective study. *Cancer Manag Res*. 2020;12:2675–2683. doi:10.2147/CMAR.S250293
32. Chen T, Sun JL, Zhang J. The relationship between fibrinogen-to-albumin ratio and in-stent restenosis in patients with coronary artery disease undergoing drug-eluting stenting. *Coron Artery Dis*. 2020;31(7):586–589. doi:10.1097/MCA.0000000000000890
33. Xiao L, Jia Y, Wang X, Huang H. The impact of preoperative fibrinogen-albumin ratio on mortality in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Clin Chim Acta*. 2019;493:8–13. doi:10.1016/j.cca.2019.02.018
34. Ruan Y, Yuan C, Liu Y, et al. High fibrinogen-to-albumin ratio is associated with hemorrhagic transformation in acute ischemic stroke patients. *Brain Behav*. 2021;11(1):e01855. doi:10.1002/brb3.1855
35. Li Z, You M, Long C, et al. Hematoma expansion in intracerebral hemorrhage: an update on prediction and treatment. *Front Neurol*. 2020;11:702. doi:10.3389/fneur.2020.00702
36. Yu-Huan S, Guang-Yan C, Yue-Fei X. Risk factors for intracerebral hemorrhage in patients undergoing maintenance hemodialysis. *Front Neurol*. 2023;14:1111865. doi:10.3389/fneur.2023.1111865
37. Strömberg S, Nordanstig A, Bentzel T, Österberg K, Bergström GM. Risk of early recurrent stroke in symptomatic carotid stenosis. *Eur J Vasc Endovasc Surg*. 2017;54(6):793. doi:10.1016/j.ejvs.2017.09.017
38. Li N, Zhou H, Tang Q. Red blood cell distribution width: a novel predictive indicator for cardiovascular and cerebrovascular diseases. *Dis Markers*. 2017;2017:7089493. doi:10.1155/2017/7089493