BMC Geriatrics

RESEARCH

Open Access

Albumin/fibrinogen ratio (AFR): a significant predictor of postoperative delirium in older patients undergoing non-neurosurgical and non-cardiac surgery

Jiang Huo[1,2†], Yuxiang Song[1†], Jing Lu[2], Guijin Dou[2], Huixian Chen[2], Weidong Mi[1,3*], Yingqun Yu[2*] and Yanhong Liu[1,3*]

Abstract

Objective The purpose of this research was to evaluate the prognostic significance of preoperative albumin to fibrinogen (AFR) for postoperative delirium (POD) in older patients with non-neurosurgical and non-cardiac surgery.

Method The retrospective cohort study included a group of patients aged 65 and above who underwent non-neurosurgical and non-cardiac surgery at the First Medical Center of Chinese PLA General Hospital from January 2014 to December 2021. AFR and POD correlation was evaluated through univariate and multivariable logistic regression analysis, as well as propensity score matching (PSM) and subgroup analysis.

Results In our study, the occurrence of POD was 2.9% (1566/53,609), with the AFR threshold identified as 10.625 based on the ROC curve. The study identified AFR ≤ 10.625 as a significant predictor of POD in both univariate and multivariable regression analyses, and the odds ratios (OR) were 2.65 (2.40–2.93), 1.98 (1.79–2.21), 1.51 (1.34–1.70), 1.27 (1.13–1.43) and 1.32 (1.14–1.53) in four models and the PSM model.

Conclusion AFR is a valuable predictor for predicting the development of POD in older patients receiving non-neurosurgical and non-cardiac procedures. This finding highlights the importance of preoperative assessment of AFR in these patients to better predict and manage the risk of POD.

Keywords Postoperative delirium, Albumin to Fibrinogen, Aged patients, Biomarker

Introduction

Postoperative delirium (POD) is a challenging clinical syndrome that occurs primarily in older patients after surgery [1]. Until today, there is still no effective pharmacological treatment for delirium [2]. The current mainstream approach remains non-pharmacological interventions. It is characterized by acute episodes of fluctuating cognitive impairment, attention disorders, and confusion [3, 4]. The prevalence of POD varies widely, with reports ranging from 2.5 to 70% for different types of surgery [5]. Delirium is influenced by various factors, including advanced age, cognitive deficits,

†Jiang Huo and Yuxiang Song contributed equally to this work.

*Correspondence:
Weidong Mi
wwdd1962@aliyun.com
Yingqun Yu
yuyingqun@sohu.com
Yanhong Liu
18618338301@163.com
[1]Department of Anaesthesiology, The First Medical Center of Chinese PLA General Hospital, Beijing 100853, China
[2]Department of Anaesthesiology, The Fifth Medical Center of Chinese PLA General Hospital, Beijing 100071, China
[3]National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing 100853, China

and chronic illnesses such as heart failure, cancer, and cerebrovascular disease. Other contributing factors are depression or anxiety, inflammation, a history of stroke, poor nutritional status, fluid and electrolyte balance disorders, and dependence on drugs or alcohol [6, 7]. The adverse effects of POD include longer hospital stays, increased health care costs, long-term cognitive decline, and higher mortality rates [8, 9]. In addition, POD often complicates the postoperative process in older patients, resulting in an overall reduction in quality of life and greater reliance on medical services.

The ratio of albumin to fibrinogen (AFR), is emerging as a novel prognostic immune biomarker. Albumin, a major plasma protein, is synthesized and secreted by the liver. It usually makes up more than 50% of the protein in the blood, and its concentration reflects nutritional status and systemic inflammation [10]. While fibrinogen, a glycoprotein synthesized by liver epithelial cells, plays a key role in regulating blood clotting. At the same time, when the body has inflammatory stimulation, its synthesis is greatly enhanced [11]. Alterations in the AFR could reflect a state of malnutrition, or an inflammatory response, all of which are also risk factors for the development of POD [12]. In the elderly, who are often subject to nutritional deficits and chronic inflammatory states, preoperative assessment of AFR may provide valuable insights into the risk of developing POD [13, 14]. Previous studies have shown the significance of AFR in predicting patient outcomes, particularly in various cancers such as non-small cell lung cancer (NSCLC), rectal cancer, gastric cancer, chronic lymphocytic leukemia, and breast cancer [15–17]. Moreover, AFR has also been identified as an independent predictor of POD after total joint arthroplasty [18]. However, existing studies are limited to specialty surgery, and few studies have revealed the relationship between AFR and POD in older patients with multiple surgical modalities.

In this study, we explored the potential of AFR as a predictive marker of POD in older patients. By establishing a large cohort that included 53,609 patients, our study aimed to assess the effectiveness of AFR in predicting POD risk in patients aged 65 and over undergoing surgery other than cardiac or neurosurgery.

Materials and methods

Patients

The study is a retrospective, observational cohort study. It was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the First Medical Center of the Chinese People's Liberation Army General Hospital (No. S2019-311-03). Informed consent was not required because the study was retrospective. To protect patient privacy, personally identifiable information was not extracted and only anonymous records were used.

Non-neurosurgical and non-cardiac procedures performed under anesthesia from January 2014 to December 2021 were considered eligible for inclusion. Exclusion criteria: (1) Endoscopy; (2) Emergency surgery; (3) American Society of Anesthesiologists (ASA) V; (4) Lack of exposure factor AFR.

Data collection

Baseline characteristics and demographic information of the patients were collected from hospital records. Additionally, perioperative data related to postoperative delirium was specifically gathered to facilitate a more comprehensive and precise analysis. The data collected included:

Demographic data: age, sex, body mass index (BMI), smoking, and drinking history.

Clinical data: ASA status, preoperative comorbidities including diabetes, hypertension, cardiovascular and cerebrovascular diseases, chronic obstructive pulmonary disease (COPD), anxiety, and depression, chronic kidney disease (CKD).

Preoperative medication: benzodiazepines, opioids, anticholinergic drugs, antipsychotic, and nonsteroidal anti-inflammatory drugs (NSAIDs).

Laboratory tests: white blood cell (WBC), hemoglobin (Hb), platelets, glucose (Glu), thrombin time (TT), prothrombin time (PT), creatinine (Cre), fibrinogen, albumin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

Details related to surgery and treatment included surgical procedure type, anesthesia method, duration of surgery and anesthesia. Additional information gathered comprised urine output, blood loss, colloid and crystalloid volumes, blood transfusion, and intraoperative medications (such as anticholinergics, benzodiazepines, antipsychotics, opioids, and NSAIDs). Data also covered the duration of systolic blood pressure (SBP) above 140 mmHg, mean arterial pressure (MAP) below 60 mmHg, and diastolic blood pressure (DBP) above 90 mmHg.

Outcomes measurement

Patients were diagnosed with postoperative delirium using the Chart-based Delirium Identification Instrument (CHART-DEL) within a week of their surgery. The CHART-DEL is a validated method that can be used to review charts (medical records) to detect the presence of delirium [19]. Patients were excluded from the study if their preoperative medical records showed the diagnosis of delirium. Trained neurologists reviewed the medical records of patients who met the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) to make the final diagnosis [20].

Correlation between AFR and POD

The optimal threshold for AFR in predicting POD was determined to be 10.625 using the receiver operating characteristic (ROC) curve. Following this, AFR was divided into two categories using the specified threshold. Furthermore, AFR was segmented into four categories according to quartiles. Then we used logistic regression to explore the relationship between AFR and POD, treating AFR as a continuous, binary, and four-category variable.

Initially, unadjusted univariate logistic regression analysis was conducted. Based on these considerations, model 1 was constructed by adjusting for sex, age, BMI, and ASA status. Model 2 included additional variables such as smoking and alcohol use, diabetes, hypertension, cardiovascular disease, cerebrovascular disease, CKD, depression, preoperative drugs including anticholinergics, benzodiazepines, antipsychotics, opioids, and NSAIDs, WBC, Hb, platelet, Glu, TT, PT, Cre, AST. To enhance the analysis further, model 3 incorporated intraoperative data, encompassing the type and the length of surgery and anesthesia, urine output, blood loss, colloid and crystalloid volumes, blood transfusion, the use of NSAIDs, benzodiazepines, and dexmedetomidine, duration of MAP < 60 mmHg and SBP > 140 mmHg, while retaining the variables from previous models.

Propensity score-matching analysis

To reduce the potential impact of confounding factors, we utilized propensity score (PS) analysis and PSM to investigate the relationship between AFR and POD. In this study, we employed one-to-one matching using a greedy algorithm, setting a maximum caliper of 0.1, to pair patients with POD to those without POD who had similar PS. Patients without a suitable match within this range were excluded from the analysis. To ensure the comparability of matched patients, we used kernel density plots to compare the distribution of propensity scores before and after matching. We also calculated the standardized mean difference (SMD) for each baseline variable between the two groups, with a value of < 0.1 considered negligible.

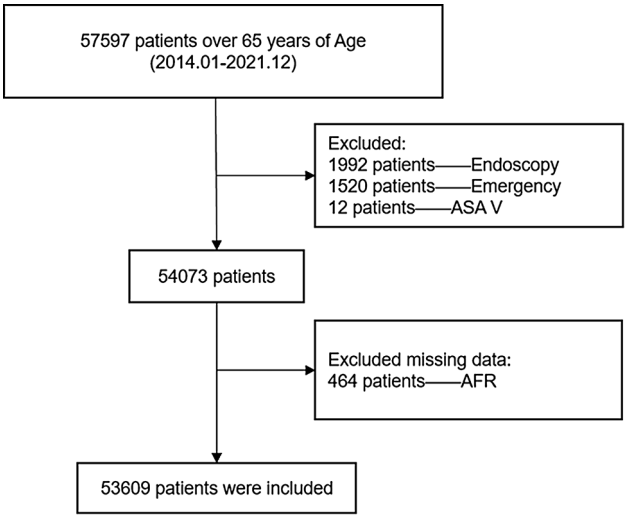

Fig. 1 Diagram of the enrollment process for the study

Subgroup analyses

To investigate potential sources of confounding factors in the influence of AFR on POD among different subgroups, our analysis was stratified based on age, sex, ASA status, hemoglobin level, surgical duration, and duration of MAP < 60 mmHg. The outcomes of our subgroup analyses are depicted through forest plots, which succinctly illustrate the predictive impact of AFR on POD within each subgroup.

Statistical analysis

In this study, continuous variables were presented as mean ± SD for normally distributed data, and as median with IQR for non-normally distributed data. Continuous variables were analyzed using the t test or Mann-Whitney U test. Categorical variables were reported as counts (percentages) and analyzed using either Fisher's exact test or the $\chi 2$ test. A two-tailed P-value of 0.05 was established as the threshold for statistical significance. All analyses were performed using R software version 4.1.3.

Results

Patient characteristics

We conducted a retrospective cohort of 57,597 patients aged over 65 who received non-neurosurgical and non-cardiac surgery between January 2014 and December 2021. After applying the above exclusion criteria, a final cohort of 53,609 patients was analyzed (Fig. 1). The cohort had a median age of 70 years (IQR: 67–74 years), with 48.2% of the participants being female. The incidence of POD was 2.9%.

By using the ROC curve, we determined the best threshold for preoperative AFR to predict POD in older patients as 10.625, with an AUC of 0.65 (0.63–0.66), shown in Additional file Fig. A1. We then divided patients into two groups based on this threshold: AFR ≤ 10.625 (n = 16,797) and AFR > 10.625 (n = 36,812).

There were statistically significant differences (P < 0.05) between the two groups in baseline characteristics, perioperative data, except for hypertension, anxiety, depression, preoperative use of NSAIDs, and duration of DBP > 90 mmHg. Compared with the other group, the group of AFR ≤ 10.625 had more women, older individuals, lower BMI, higher prevalence of smoking history, and a larger proportion of non-drinkers. This group also showed a higher incidence of comorbidities, including

diabetes, cardiovascular and cerebrovascular diseases, CKD, and COPD. Additionally, the duration of anesthesia and surgery was longer in this group (Table 1).

Correlation between the AFR and POD

We employed four models to investigate the association between AFR and POD. In the analysis of AFR as a continuous variable, univariate logistic regression showed a significant correlation, with an OR of 0.86 (95% CI: 0.85–0.87, $P<0.001$). Lower AFR was found to be linked to a higher risk of POD in the multivariate logistic regression models, with adjusted odds ratios of 0.90, 0.94, and 0.97, respectively ($P<0.001$, Additional file Table A1).

Furthermore, we identified the optimal threshold value for AFR to be 10.625 and classified the cases into two groups based on this criterion. In the univariate analysis, the OR for the group with AFR ≤ 10.625 was 2.65 (95% CI: 2.40–2.93, $P<0.001$). The correlation was consistently strong in all multivariable logistic regression models, with ORs ranging from 1.13 to 2.21 ($P<0.001$, Table 2).

Then we categorized patients into four groups based on quartiles of AFR: AFR ≤ 9.95, 9.95 < AFR ≤ 12.27, 12.27 < AFR ≤ 14.50, and AFR > 14.50. Our univariate analysis showed that patients in the AFR ≤ 9.95 and 9.95 < AFR ≤ 12.27 groups had a significantly higher risk of developing POD compared to those in the AFR > 14.50 group ($P<0.001$). This trend persisted even after conducting multivariate regression analysis, confirming that lower AFR is a consistent predictor of increased POD risk. After adjusting for various variables, the AFR ≤ 9.95 group still had a significantly higher risk of POD compared to the AFR > 14.50 group (OR = 1.27, $P<0.01$) in Model 3 (Additional file Table A2).

In addition, the decision curve analysis (DCA) conducted for AFR demonstrated that considering AFR could lead to favorable net benefits for patients (Fig. 2A). Additionally, the calibration curve displayed reliable performance (Fig. 2B).

Analysis and adjustment using propensity score matching

To control for potential confounding variables, we employed PSM in our cohort study, with a 1:1 ratio between the AFR > 10.625 group and the AFR ≤ 10.625 group. We successfully matched 12,200 patients in each group by considering 28 variables, including sex, age, BMI, smoking history, CKD, preoperative use of opioid and psychotropic drugs, Hb, WBC, platelet count, Glu, TT, PT, AST, type and length of surgery and anesthesia, ASA status, urine output, blood loss, colloid and crystalloid volumes, blood transfusion, the use of NSAIDs and benzodiazepines, duration of SBP > 140 mmHg and the duration MAP < 60 mmHg. The propensity score distribution both before and after performing PSM was illustrated in Fig. 3A and B.

After matching, the baseline characteristics between the two groups were well-balanced, with all covariates exhibiting SMD < 0.1. Following PSM, AFR continued to independently predict POD in the multivariable logistic regression analysis. The OR for AFR ≤ 10.625 was 1.32 (95% CI: 1.14–1.53, $P<0.001$), as shown in Table 2. Additional multivariable logistic regression analysis outcomes can be found in Table A3.

Subgroup analyses

Subgroup analysis revealed that AFR ≤ 10.625 was statistically significant across subgroups defined by gender, age, ASA status, Hb, and duration of surgery ($P<0.05$), as shown in Fig. 4. Based on the OR values in each subgroup, it was found that AFR had a stronger association with POD in specific patient subgroup, which included female patients, aged ≤ 70 years, with ASA status ≥ III, duration of surgery ≤ 120 min, Hb > 130 g/L, and duration of MAP ≤ 60 mmHg for ≤ 10 min.

Discussion

This study aimed to investigate the predictive effect of AFR on POD in older patients. Previous studies have identified low postoperative AFR as a risk factor for POD in older patients, but were limited by small sample sizes and narrow focus on specific surgeries. To address these limitations, we conducted a large retrospective cohort study with 53,609 patients undergoing various procedures. Rigorous statistical methods, including univariate and multivariate logistic regression, PSM, DCA, and calibration curves, were employed. Our results showed that preoperative AFR remained a reliable predictor of POD across different surgical procedures.

Our study provides strong evidence supporting AFR as a significant predictor of postoperative delirium (POD) in surgical patients. Lower AFR values were associated with a higher incidence of POD ($P<0.001$) when considering AFR as a continuous variable. Using a binary variable with a cutoff of 10.625, AFR ≤ 10.625 was identified as a risk factor for POD in both univariate and multivariable logistic regression analyses ($P<0.001$). Further analysis, dividing AFR into four groups, confirmed the association between AFR ≤ 9.95 and increased odds of POD. After adjusting for 28 variables and performing 1:1 propensity score matching, with each group consisting of 12,200 patients, the influence of other variables was eliminated (SMD < 0.1). Multivariable logistic regression analysis of the PSM matched cohort revealed that a decrease in AFR remained a predictive factor for POD ($P<0.001$). These findings were consistent across different subgroups, including various age groups, ASA status, genders, hemoglobin, and surgical durations. Patients with AFR ≤ 10.625 had an increased risk of developing POD in the subgroup with a duration of MAP < 60 mmHg ≤ 10 min.

Table 1 Baseline patient characteristics between the groups

Characteristic	Unadjusted sample ($n=53609$)			PSM adjusted (1:1) ($n=24400$)		
	AFR > 10.625 ($n=36812$)	AFR ≤ 10.625 ($n=16797$)	SMD	AFR > 10.625 ($n=12200$)	AFR ≤ 10.625 ($n=12200$)	SMD
Sex (male) (%)†	19,273 (52.4)	8466 (50.4)	0.039	6116 (50.1)	6153 (50.4)	0.006
Age, years†	69.00 [67.00, 73.00]	71.00 [67.00, 76.00]	0.35	71.00 [67.00, 75.00]	70.00 [67.00, 75.00]	0.024
BMI, kg/m^{2}†	24.00 [22.00, 27.00]	23.00 [21.00, 26.00]	0.108	24.00 [22.00, 26.00]	24.00 [21.00, 26.00]	0.014
Smoke (%)†			0.045			0.006
Smoking	4678 (12.7)	2013 (12.0)		1502 (12.3)	1483 (12.2)	
Cessation	4118 (11.2)	2109 (12.6)		1498 (12.3)	1486 (12.2)	
Alcohol (%)			0.028			0.03
Drinking	2500 (6.8)	1238 (7.4)		822 (6.7)	915 (7.5)	
Dry out	6013 (16.3)	2627 (15.6)		1923 (15.8)	1907 (15.6)	
Hypertension (%)	17,425 (47.3)	8010 (47.7)	0.007	6149 (50.4)	5705 (46.8)	0.073
Diabetes (%)	8013 (21.8)	4296 (25.6)	0.09	3059 (25.1)	2990 (24.5)	0.013
Cardiovascular disease (%)	4858 (13.2)	2483 (14.8)	0.046	1795 (14.7)	1728 (14.2)	0.016
Cerebrovascular disease (%)	2982 (8.1)	1681 (10.0)	0.066	1073 (8.8)	1142 (9.4)	0.02
Depression (%)	146 (0.4)	86 (0.5)	0.017	56 (0.5)	48 (0.4)	0.01
Anxiety (%)	32 (0.1)	18 (0.1)	0.006	32 (0.1)	18 (0.1)	0.006
CKD (%)†	514 (1.4)	480 (2.9)	0.101	281 (2.3)	282 (2.3)	0.001
COPD (%)	773 (2.1)	498 (3.0)	0.055	278 (2.3)	326 (2.7)	0.025
Preoperative medication (%)						
Anticholinergic drug	16,171 (43.9)	6749 (40.2)	0.076	5314 (43.6)	5232 (42.9)	0.014
Benzodiazepines	9112 (24.8)	3549 (21.1)	0.086	2729 (22.4)	2599 (21.3)	0.026
NSAIDs	3020 (8.2)	1388 (8.3)	0.002	1143 (9.4)	1047 (8.6)	0.028
Opium†	610 (1.7)	958 (5.7)	0.216	428 (3.5)	427 (3.5)	< 0.001
Antipsychotic drugs†	63 (0.2)	165 (1.0)	0.107	45 (0.4)	40 (0.3)	0.007
Hemoglobin, g/L†	133.00 [123.00, 143.00]	122.00 [109.00, 133.00]	0.701	127.00 [116.00, 137.00]	126.00 [115.00, 137.00]	0.002
WBC count, *10^{9}/L†	5.65 [4.75, 6.69]	6.45 [5.31, 7.87]	0.424	6.11 [5.09, 7.35]	6.19 [5.15, 7.46]	0.02
Platelet, *10^{9}/L†	201.00 [167.00, 239.00]	233.00 [189.00, 284.00]	0.535	221.00 [182.00, 266.00]	221.00 [182.00, 265.00]	0.007
Glu, mmol/L†	5.15 [4.70, 5.86]	5.31 [4.76, 6.28]	0.187	5.22 [4.73, 6.09]	5.23 [4.72, 6.10]	0.003
TT, s†	16.50 [15.80, 17.20]	16.00 [15.30, 16.80]	0.203	16.20 [15.60, 16.90]	16.10 [15.40, 16.80]	0.037
PT, s†	13.10 [12.50, 13.60]	13.30 [12.70, 13.90]	0.244	13.20 [12.70, 13.80]	13.20 [12.70, 13.80]	0.028
Cre, μmol/L	71.70 [61.60, 83.10]	70.10 [58.90, 83.60]	0.036	71.00 [60.70, 83.30]	70.40 [59.50, 83.50]	0.049
AST, U/L†	19.32 (24.36)	28.39 (47.75)	0.239	14.40 [10.70, 20.90]	14.00 [10.00, 22.00]	0.048
ALT, U/L	16.70 [14.20, 20.50]	16.70 [13.40, 23.70]	0.239	16.70 [13.90, 20.80]	16.40 [13.30, 21.83]	0.035
Type of surgery (%)†			0.413			0.046
E.N.T	3823 (10.4)	1261 (7.5)		1041 (8.5)	1095 (9.0)	
Thoracic surgery	4113 (11.2)	943 (5.6)		818 (6.7)	865 (7.1)	
Gynecological surgery	1323 (3.6)	397 (2.4)		329 (2.7)	331 (2.7)	
Orthopedic surgery	9556 (26.0)	5087 (30.3)		3700 (30.3)	3672 (30.1)	
Urinary surgery	4266 (11.6)	1155 (6.9)		935 (7.7)	996 (8.2)	
Gastrointestinal surgery	5052 (13.7)	3266 (19.4)		2310 (18.9)	2128 (17.4)	
Hepatobiliary and pancreatic surgery	5202 (14.1)	3792 (22.6)		2320 (19.0)	2339 (19.2)	
Others	3477 (9.4)	896 (5.3)		747 (6.1)	774 (6.3)	
Duration of surgery, min†	125.00 [80.00, 185.00]	145.00 [95.00, 214.00]	0.248	140.00 [90.00, 205.00]	136.00 [90.00, 200.00]	0.024
Duration of anesthesia, min†	175.00 [125.00, 237.00]	195.00 [145.00, 270.00]	0.268	190.00 [140.00, 260.00]	190.00 [140.00, 255.00]	0.025
ASA (%)†			0.292			0.018
I	438 (1.2)	129 (0.8)		103 (0.8)	109 (0.9)	
II	30,615 (83.2)	12,109 (72.1)		9256 (75.9)	9326 (76.4)	
III	5668 (15.4)	4362 (26.0)		2769 (22.7)	2686 (22.0)	
IV	91 (0.2)	197 (1.2)		72 (0.6)	79 (0.6)	

Table 1 (continued)

Characteristic	Unadjusted sample ($n=53609$)			PSM adjusted (1:1) ($n=24400$)		
	AFR > 10.625 ($n=36812$)	AFR ≤ 10.625 ($n=16797$)	SMD	AFR > 10.625 ($n=12200$)	AFR ≤ 10.625 ($n=12200$)	SMD
Type of Anesthesia (%)†			0.194			0.012
Local anesthesia	74 (0.2)	63 (0.4)		44 (0.4)	44 (0.4)	
Basal and local anesthesia	421 (1.1)	257 (1.5)		180 (1.5)	174 (1.4)	
Intravenous anesthesia	358 (1.0)	121 (0.7)		86 (0.7)	94 (0.8)	
Nerve blocks	1394 (3.8)	1269 (7.6)		751 (6.2)	755 (6.2)	
Intraspinal anesthesia	1112 (3.0)	662 (3.9)		417 (3.4)	423 (3.5)	
General anesthesia	32,403 (88.0)	13,789 (82.1)		10,255 (84.1)	10,263 (84.1)	
General anesthesia combined with other anesthesia	1050 (2.9)	636 (3.8)		467 (3.8)	447 (3.7)	
Urine, ml†	200.00 [100.00, 500.00]	300.00 [100.00, 500.00]	0.061	250.00 [100.00, 500.00]	200.00 [100.00, 500.00]	< 0.001
Blood loss, ml†	50.00 [20.00, 200.00]	100.00 [50.00, 200.00]	0.18	100.00 [50.00, 200.00]	100.00 [50.00, 200.00]	0.001
Crystalloid, ml†	1200.00 [1100.00, 1800.00]	1600.00 [1100.00, 2100.00]	0.233	1600.00 [1100.00, 2100.00]	1600.00 [1100.00, 2100.00]	0.03
Colloid, ml†	500.00 [0.00, 500.00]	500.00 [0.00, 500.00]	0.269	500.00 [0.00, 500.00]	500.00 [0.00, 500.00]	0.021
Blood transfusion (%)†	3477 (9.4)	3159 (18.8)	0.271	1816 (14.9)	1806 (14.8)	0.002
Intraoperative medication (%)						
Droperidol	3316 (9.0)	1682 (10.0)	0.034	1176 (9.6)	1196 (9.8)	0.006
Glucocorticoid	22,988 (62.4)	10,218 (60.8)	0.033	7543 (61.8)	7454 (61.1)	0.015
NSAIDs†	18,807 (51.1)	7707 (45.9)	0.104	5801 (47.5)	5838 (47.9)	0.006
Benzodiazepine†	7828 (21.3)	2590 (15.4)	0.151	1960 (16.1)	1963 (16.1)	0.001
Dexmedetomidine	4209 (11.4)	2131 (12.7)	0.038	1506 (12.3)	1453 (11.9)	0.013
Duration of SBP > 140 mmHg, min†	5.00 [0.00, 20.00]	10.00 [0.00, 30.00]	0.215	10.00 [0.00, 30.00]	10.00 [0.00, 25.00]	0.029
Duration of DBP > 90 mmHg, min	0.00 [0.00, 5.00]	0.00 [0.00, 5.00]	0.002	0.00 [0.00, 0.00]	0.00 [0.00, 5.00]	0.016
Duration of MAP < 60 mmHg, min†	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.174	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.007
POD (%)	721 (2.0)	845 (5.0)	0.168	366 (3.0)	445 (3.6)	0.036

The data are shown as the median (interquartile range), n (%), or mean ± SD

†Variables included in the propensity score

Abbreviations: AFR Alb/Fib ratio, SMD Standardized mean difference, PSM Propensity Score Matching, BMI Body mass index, COPD Chronic obstructive pulmonary disease, CKD Chronic kidney disease, ASA American Society of Anesthesiologists physical status classification system, E.N.T Otolaryngology, ophthalmology, stomatology, SBP Systolic blood pressure, DBP Diastolic blood pressure, MAP Mean arterial pressure, WBC White blood cell, Glu Glucose, Cre Creatinine, AST Aspartate aminotransferase, ALT Alanine aminotransferase, NSAIDs Non-steroidal anti-inflammatory drugs, TT Thrombin Time, PT Prothrombin Time

Table 2 Association between AFR and POD with logistic regression models and PSM analysis

Model	OR[a]	95%CI	*P*
Unadjusted model	2.65	2.40–2.93	< 0.001
Model 1 [b]	1.98	1.79–2.21	< 0.001
Model 2 [c]	1.51	1.34–1.70	< 0.001
Model 3 [d]	1.27	1.13–1.43	< 0.001
Model PSM [e]	1.32	1.14–1.53	< 0.001

AFR Alb/Fib ratio, POD Postoperative delirium, OR Odds ratio, CI Confidence interval, PSM Propensity score matching

[a] The ORs of AFR ≤ 10.625

[b] Model 1 adjusted for age, sex, BMI, ASA

[c] Model 2 adjusted for smoking, and drinking history, diabetes, hypertension, cardiovascular disease, cerebrovascular disease, depression, CKD, preoperative medication including anticholinergic drugs, antipsychotic drugs, benzodiazepines, opium, and NSAIDs, Hb, WBC, Platelet, Glu, TT, PT, Cre, AST as well as variables from the previous model 1

[d] Model 3 adjusted for model 1 plus model 2, as well as intraoperative data including type of surgery, duration of surgery and anesthesia, urine, blood loss, crystalloid, colloid, blood transfusion, the use of NSAIDs, benzodiazepines, and dexmedetomidine, duration of SBP > 140 mmHg and MAP < 60 mmHg

[e] Model PSM was a multivariable logistic regression

Albumin, an abundant plasma protein in the human body, is considered a marker of weakness, nutrition, inflammation, and functional capacity [21, 22]. Several cross-sectional studies have suggested a positive correlation between serum albumin levels and MMSE scores in hip fracture and AD patients [23, 24] Previous research has indicated that abnormal albumin is a risk factor for POD in cardiac surgery patients, and low albumin levels are also associated with delirium prediction in non-cardiac surgery [25, 26]. In our previous study, we also found that the albumin-related Prognostic Nutritional Index (PNI) can be used to predict postoperative delirium [27]. The reason for this association may be that low albumin suggests malnutrition, inflammation, and lower levels of function in the elderly, all of which are known risk factors for POD. Additionally, a study by Jee et al. found a negative correlation between serum albumin and amyloid-beta (Aβ) deposition, suggesting that albumin may play a role in regulating Aβ levels [24, 28]. Recent research

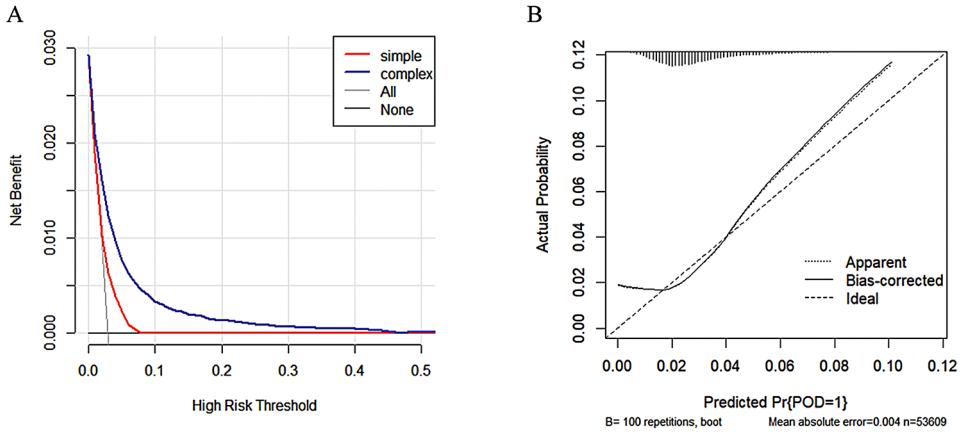

Fig. 2 (**A**) The Decision Curve Analysis of AFR for POD. (**B**) The Calibration curve of AFR for POD. Abbreviations: simple model = unjusted model; complex model = model 3

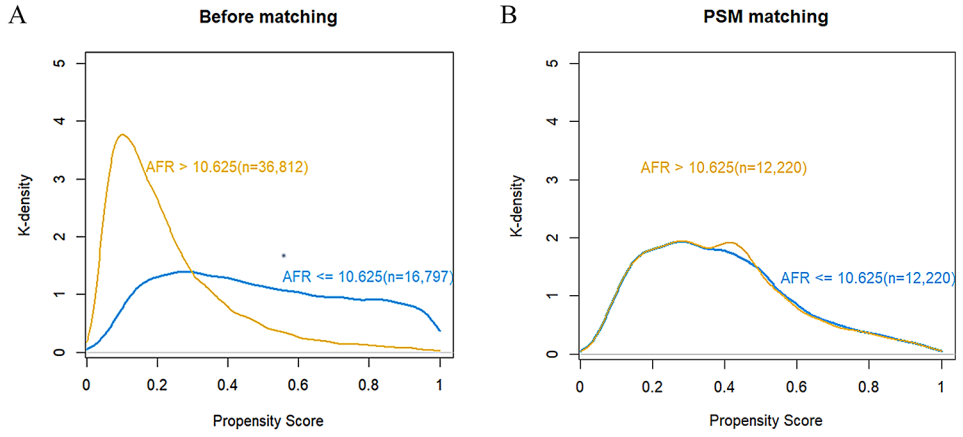

Fig. 3 Distribution of propensity scores in patients with AFR > 10.625 and AFR ≤ 10.625. (**A**) Before matching. (**B**) PSM matching. Abbreviations: AFR Alb/Fib ratio

has also shown a correlation between Aβ deposition and the severity of perioperative delirium [29, 30]. Fibrinogen is a multifunctional protein that circulates in the blood as a soluble dimer [31]. Recent studies have found that fibrinogen has multiple effects on central nervous system inflammation activation, induction of brain hemorrhage formation, promotion of cognitive decline, and inhibition of repair [32]. The mechanism involves leakage of fibrinogen into the brain when the blood-brain barrier is disrupted, leading to glial cell activation, axonal injury, inhibition of oligodendrocyte progenitor cell (OPC) differentiation and myelin regeneration, binding to Aβ, opening the blood-brain barrier by direct interaction with brain endothelial cells, inducing astrocytic scar formation, and inhibiting neural dendrite growth [33, 34]. Previous research evaluating the proteome of cerebrospinal fluid in patients with delirium identified 16 abnormal proteins, including fibrinogen, providing evidence for the relationship between fibrinogen and delirium [35]. AFR, as the ratio of these two biomarkers, is currently widely used for predicting the prognosis of tumors and has predictive value in acute pancreatitis and rheumatoid arthritis [27, 36, 37]. Additionally, Gao et al. found that Fibrinogen/Albumin Ratio (FAR) is an effective indicator for predicting the prognosis of triple negative breast cancer (TNBC), and its mechanism may be related to chronic inflammation promoting tumor progression, while malnutrition aggravates cancer cachexia [38]. Kim KS et al. demonstrated that FAR is a feasible and useful marker for predicting one-year mortality in critically ill patients in the intensive care unit, and its potential factors are still related to inflammation, immunity, and nutritional status [39, 40]. This further confirmed the association between AFR and inflammation and nutritional status, explaining the predictive effect of AFR on POD.

Our study has some limitations that deserve consideration. Firstly, the retrospective nature of the study may have contributed to a relatively low incidence of POD, despite the inclusion of many patients. This may be due to low activity-delirium being difficult to diagnose [41]. Secondly, our study only focused on preoperative experiments and examined the predictive value of preoperative

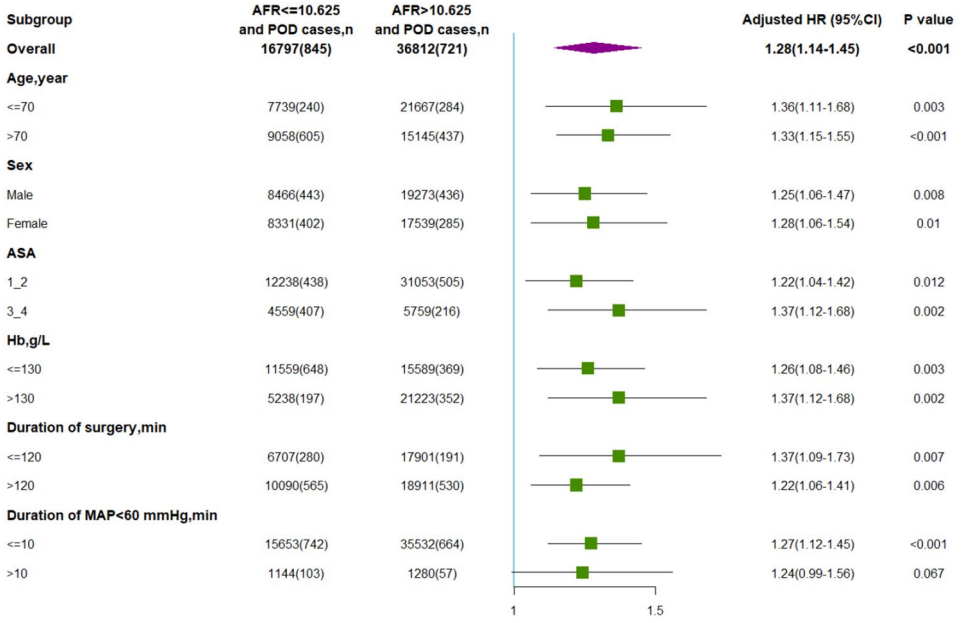

Fig. 4 Subgroup analyses of the association between AFR and postoperative delirium. Abbreviations: AFR Alb/Fib ratio; POD, postoperative delirium; OR, odds ratio; CI, Confidence interval; ASA, American Society of Anesthesiologists classification; Hb, hemoglobin; MAP, mean arterial pressure

AFR for POD. The changes in AFR before and after surgery may have a better predictive value for POD. Moreover, it remains unclear whether targeted interventions for patients with low preoperative AFR can effectively reduce the occurrence of POD, which requires further exploration in future studies.

Conclusion

To summarize, the preoperative AFR demonstrates predictive value for POD in non-neurosurgical and non-cardiac patients. AFR serves as an easily obtainable indicator. Considering AFR in preoperative evaluations can be a valuable risk stratification strategy for POD, potentially leading to a reduction in its incidence among these patient populations.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-025-05714-1.

Supplementary Material 1

Acknowledgements

We would like to thank Tong-Yan Sun and Wei Wei of Hangzhou Le9 Healthcare Technology Co., Ltd., for help in the clinical data collection of this study.

Author contributions

J.H, Y.X.S and Y.H.L conceptualized and designed the study. W.D.M obtained funding. Y.X.S, J.L and G.J.D collected the data. J.H, Y.Q.Y and H.X.C analysed data, prepared and reviewed figures. Y.X.S contributed for statistical analysis. J.H drafted the manuscript. Y.H.L and W.D.M critically revised the manuscript. All authors gave the approval of final version of paper.

Funding

This work was supported by the National Key Research and Development Program of China [No.2018YFC2001901, No.2024YFA1012102].

Data availability

All the data shown in this study is available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This study has been approved by the Ethics Committee of the First Medical Center of the Chinese People's Liberation Army General Hospital (No. S2019-311-03), which exempted the requirement for informed consent due to their retrospective nature.

Consent for publication

Not applicable.

Clinical trial number

Not applicable.

Report on or involve the use of any animal or human data or tissue

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 25 August 2024 / Accepted: 17 January 2025
Published online: 03 March 2025

References

1. Ho MH, Nealon J, Igwe E, et al. Postoperative delirium in older patients: a systematic review of Assessment and incidence of postoperative delirium. Worldviews Evid Based Nurs. 2021;18(5):290–301.
2. Igwe EO, Nealon J, Mohammed M, et al. Multi-disciplinary and pharmacological interventions to reduce post-operative delirium in elderly patients: a systematic review and meta-analysis. J Clin Anesth. 2020;67:110004.
3. Keenan CR, Jain S, Delirium. Med Clin North Am. 2022;106(3):459–69.

4. Wilson JE, Mart MF, Cunningham C, et al. Delirium Nat Rev Dis Primers. 2020;12(1):90.
5. Jin Z, Hu J, Ma D. Postoperative delirium: perioperative assessment, risk reduction, and management. Br J Anaesth. 2020;125(4):492–504.
6. Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. J Am Geriatr Soc. 2006;54(10):1578–89.
7. Elie M, Cole MG, Primeau FJ, Bellavance F. Delirium risk factors in elderly hospitalized patients. J Gen Intern Med. 1998;13(3):204–12.
8. Qureshi O, Arthur ME. Recent advances in predicting, preventing, and managing postoperative delirium. Fac Rev. 2023;12:19.
9. Bramley P, McArthur K, Blayney A, McCullagh I. Risk factors for postoperative delirium: an umbrella review of systematic reviews. Int J Surg. 2021;93:106063.
10. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Semin Dial. 2004;17(6):432–7.
11. Herrick S, Blanc-Brude O, Gray A, Laurent G, Fibrinogen. Int J Biochem Cell Biol. 1999;31(7):741–6.
12. Onoprienko A, Hofstetter G, Dorittke T et al. The prognostic value of the fibrinogen-albumin-ratio index (FARI) in patients with advanced vulvar cancer. J Pers Med. 2022;12(11).
13. Edfors E, Westergren A. Home-Living Elderly people's views on Food and meals. J Aging Res. 2012;2012:761291.
14. Alberro A, Iribarren-Lopez A, Sáenz-Cuesta M, Matheu A, Vergara I, Otaegui D. Inflammaging markers characteristic of advanced age show similar levels with frailty and dependency. Sci Rep. 2021;23(1):4358.
15. Yu W, Ye Z, Fang X, Jiang X, Jiang Y. Preoperative albumin-to-fibrinogen ratio predicts chemotherapy resistance and prognosis in patients with advanced epithelial ovarian cancer. J Ovarian Res. 2019;18(1):88.
16. You X, Zhou Q, Song J, Gan L, Chen J, Shen H. Preoperative albumin-to-fibrinogen ratio predicts severe postoperative complications in elderly gastric cancer subjects after radical laparoscopic gastrectomy. BMC Cancer. 2019;18(1):931.
17. Li H, Wang H, Shao S, Gu Y, Yao J, Huang J. Pretreatment albumin-to-fibrinogen ratio independently predicts Chemotherapy Response and Prognosis in patients with locally advanced rectal Cancer undergoing total Mesorectal Excision after Neoadjuvant Chemoradiotherapy. OncoTargets Therapy. 2020;13:13121–30.
18. Jiang L, Lei G. Albumin/fibrinogen ratio, an independent risk factor for postoperative delirium after total joint arthroplasty. Geriatr Gerontol Int. 2022;22(5):412–7.
19. Kaushik R, McAvay GJ, Murphy TE, et al. In-Hospital delirium and disability and cognitive impairment after COVID-19 hospitalization. JAMA Netw Open. 2024;1(7):e2419640.
20. Leonard MM, Nekolaichuk C, Meagher DJ, et al. Practical assessment of delirium in palliative care. J pain Symptom Manage. 2014;48(2):176–90.
21. Picca A, Coelho-Junior HJ, Calvani R, Marzetti E, Vetrano DL. Biomarkers shared by frailty and sarcopenia in older adults: a systematic review and meta-analysis. Ageing Res Rev. 2022;73:101530.
22. Eckart A, Struja T, Kutz A, et al. Relationship of nutritional status, inflammation, and serum albumin levels during Acute illness: a prospective study. Am J Med. 2020;133(6):713–e7227.
23. Min JY, Ha SW, Yang SH et al. Chronic status of serum albumin and cognitive function: a retrospective cohort study. J Clin Med. 2022;11(3).
24. Kim JW, Byun MS, Lee JH, et al. Serum albumin and beta-amyloid deposition in the human brain. Neurol. 2020;18(7):e815–26.
25. Rudolph JL, Jones RN, Levkoff SE, et al. Derivation and validation of a preoperative prediction rule for delirium after cardiac surgery. Circulation. 2009;20(2):229–36.
26. Marcantonio ER, Goldman L, Mangione CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. Jama. 1994;12(2):134–9.
27. Song Y-X, Wang Q, Ma Y-L, et al. Preoperative prognostic nutritional index predicts postoperative delirium in aged patients after surgery: a matched cohort study. Gen Hosp Psychiatry. 2024;86:58–66.
28. Boada M, Ortiz P, Anaya F et al. Amyloid-targeted therapeutics in Alzheimer's disease: use of human albumin in plasma exchange as a novel approach for Abeta mobilization. Drug News Perspect. 2009;22(6):325 – 39.
29. Torres-Velázquez M, Parker M, Bo A, et al. Amyloid deposition on positron emission tomography correlates with severity of perioperative delirium: a case-control pilot study. Br J Anaesth. 2022;128(3):e226–8.
30. Cunningham EL, McGuinness B, McAuley DF, et al. CSF Beta-amyloid 1–42 concentration predicts Delirium following elective arthroplasty surgery in an Observational Cohort Study. Ann Surg. 2019;269(6):1200–5.
31. Gaule TG, Ajjan RA. Fibrin(ogen) as a therapeutic target: opportunities and challenges. Int J Mol Sci. 2021;22(13).
32. Stefanadi E, Tousoulis D, Papageorgiou N, Briasoulis A, Stefanadis C. Inflammatory biomarkers predicting events in atherosclerosis. Curr Med Chem. 2010;17(16):1690–707.
33. Fang C, Lau WL, Sun J, et al. Chronic kidney disease promotes cerebral microhemorrhage formation. J Neuroinflammation. 2023;25(1):51.
34. Ahn HJ, Glickman JF, Poon KL, et al. A novel Aβ-fibrinogen interaction inhibitor rescues altered thrombosis and cognitive decline in Alzheimer's disease mice. J Experimental Med. 2014;211(6):1049–62.
35. Poljak A, Hill M, Hall RJ, et al. Quantitative proteomics of delirium cerebrospinal fluid. Translational Psychiatry. 2014;4(11):e477.
36. Zou YX, Qiao J, Zhu HY, et al. Albumin-to-fibrinogen ratio as an independent Prognostic parameter in untreated chronic lymphocytic leukemia: a retrospective study of 191 cases. Cancer Res Treat. 2019;51(2):664–71.
37. Yue W, Liu Y, Ding W, et al. The predictive value of the prealbumin-to-fibrinogen ratio in patients with acute pancreatitis. Int J Clin Pract. 2015;69(10):1121–8.
38. Gao W, Li M, Zhang Y. Fibrinogen/Albumin ratio (FAR) in patients with Triple negative breast Cancer and its relationship with epidermal growth factor receptor expression. OncoTargets Therapy. 2021;14:5403–15.
39. Kim KS, Oh AR, Park J, Ryu JA. Association between Fibrinogen-to-albumin ratio and prognosis in patients admitted to an Intensive Care Unit. J Clin Med. 2023;12(4).
40. Wen Y, Yang J, Han X. Fibrinogen-to-albumin ratio is Associated with all-cause mortality in Cancer patients. Int J Gen Med. 2021;14:4867–75.
41. Teale EA, Siddiqi N, Clegg A, Todd OM, Young J. Non-pharmacological interventions for managing delirium in hospitalised patients. Cochrane Database Syst Rev. 2017.

Publisher's note