Journal of Inflammation Research

Dovepress
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ORIGINAL RESEARCH

Predictive Value of C-Reactive Protein/Albumin Ratio for Acute Kidney Injury in Patients with Acute Pancreatitis

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Purpose: This study aims to evaluate the predictive efficacy of the C-reactive protein/albumin ratio (CAR), a cost-effective, easily accessible, and reproducible biomarker obtained from standard blood tests, in forecasting acute kidney injury (AKI) among patients undergoing acute pancreatitis (AP). Considering that changes in the CAR are associated with AKI incidence in AP cases, this work aims to explore whether CAR can be used as the innovative, inflammation-based diagnostic marker for AKI in AP patients.

Methods: The current retrospective cohort study consecutively enrolled AP patients admitted to First College of Clinical Medical Science of China Three Gorges University during the period from January 2019 to October 2023. Data were extracted systematically in electronic medical records from these hospitalized individuals, including baseline demographic and clinical characteristics. To ascertain the association of the CAR level with the development of AKI, we carried out multivariate logistic regression, adjusting for potential confounders. These confounders were initially identified through univariate regression. Furthermore, the potential effect modifiers in the relationship between CAR and AKI occurrence were explored by stratified logistic regression.

Results: Totally, 1514 AP were recruited, including 257 (16.9%) with AKI. CAR was positively correlated with AKI. When adjusting for potential confounders, the AKI risk in patients in the upper CAR tertile (2.628–22.994) increased by 83% relative to those in lower tertile (0.05–0.289) (OR 1.83, 95% CI 1.13–2.96, P = 0.013). The AKI risk tended to increase according to the increasing CAR tertile (P for trend = 0.013). No significant interactions were observed among subgroups based on age, sex, BMI, admission to ICU, hypertension, DM, chronic obstructive pulmonary disease, severity of AP, etiology of AP, demand for CRRT, mechanical ventilation, and blood transfusion (all P > 0.05).

Conclusion: A higher CAR is significantly related to the higher AKI incidence in AP patients in the Chinese population.

Keywords: acute pancreatitis, acute kidney injury, CRP/albumin ratio, cohort study

Introduction

Acute pancreatitis (AP), the inflammatory exocrine pancreatic disorder, has been shown to be related to significant morbidity and mortality, particularly when systemic complications and local complications occur.[1,2] The global incidence of AP is reported between 20 and 40 cases per 100,000 individuals, with an increasing trend over recent decades.[3,4] Even though the general mortality rate of AP is below 5%, it can escalate to 30–50% in severe cases.[2,5]

Acute kidney injury (AKI), as a notable systemic complication, affects approximately 15% of AP patients,[6] with this figure increasing to 69% in severe AP cases.[7] AKI not only worsens the clinical status of AP patients but also significantly increases mortality risk and the likelihood of progressing to chronic kidney disease (CKD).[8] The challenge

Received: 20 June 2024
Accepted: 14 August 2024
Published: 16 August 2024

of early AKI identification and therapeutic strategy adjustment in individuals undergoing AP is vital for outcome improvement.

Evidence suggests C-reactive protein (CRP) and albumin (ALB) are vital for diagnosing, predicting, and assessing prognosis in AKI.[9–12] The C-reactive protein/albumin ratio (CAR), which is an emerging prognostic biomarker for inflammation, has been adopted for predicting adverse outcomes in various conditions.[13–16] Nevertheless, the correlation between this ratio and AKI in AP patients has been minimally investigated, with only one small-scale study presenting limited predictive accuracy.[17] Moreover, studies focusing on Chinese populations are lacking. Therefore, we have initiated a cohort study to investigate the correlation between the CAR and AKI in AP patients within the Chinese demographic.

Materials and Methods

Study Design

This is an observational, investigator-initiated, retrospective cohort study, which involved human participants were reviewed with the approval of the Hospital of Medicine Ethics Committee (ethical approval number: 2023–130-01). In addition, all the involved information was acquired from a retrospective chart of electronic medical records of patients undergoing AP at our institution between January 2019 and October 2023.

Inclusion and Exclusion Criteria

For the current retrospective study, the inclusion criteria included patients enrolled in the First College of Clinical Medical Science of China Three Gorges University, and those who suffered from AP. The exclusion criteria included patients whose age were less than 18, or older than 85 years; pregnant or breastfeeding women; the length of hospital stay ≤2 days; those undergoing CKD; patients undergoing malignant tumor; those undergoing chronic pancreatitis; patients receiving renal transplantation; and incomplete medical data. Figure 1 presented the patient who collected and reviewed the process.

Clinical Definitions and Laboratory Data

The Diagnosis of AP

AP was diagnosed based on symptoms, medical history, laboratory tests, physical examinations, as well as imaging examinations (including abdominal ultrasound, contrast-enhanced computed tomography, and magnetic resonance imaging). Finally, a restricted number of diagnosed AP patients were verified through exploratory laparotomy.[18]

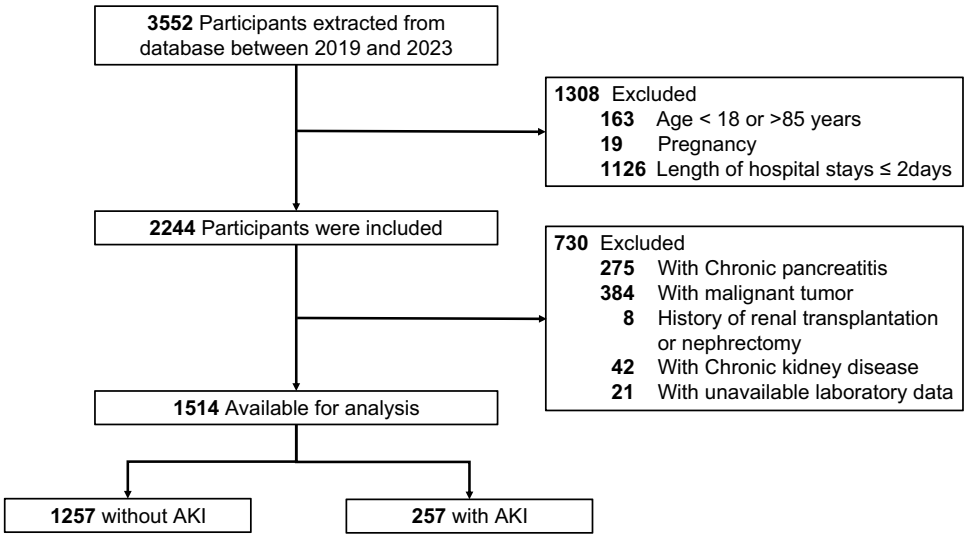

Figure 1 Flow diagram of the screening and enrollment of study participants.
Abbreviation: AKI, acute kidney injury.

The Severity of AP

The severity of AP was divided in line with the revised Atlanta classification. Mild AP was set as AP without any organ failure or local/systemic complications. Moderate AP was set as AP with transient organ failure (resolving within 2 days) and/or local or systemic complications without persistent organ failure. SAP was set as AP with persistent organ failure lasting over 48 hours (single or multiorgan failure).[19]

Diagnosis and Classification of AKI

In line with the criteria shown by the KIDGO guidelines (2012), diagnosis and classification of AKI were performed[20], where serum creatinine criteria was set as an elevated absolute value in serum creatinine level of ≥0.3 mg/dL (≥26.4 μmol/L) or a percentage elevation in serum creatinine level of ≥50% within 48 h. In addition, baseline serum creatinine level was set as the lowest serum creatinine level measured within 48 hours before admission to hospital. The serum creatinine level in the first measurement within 48 hours following admission to hospital could be regarded to be baseline serum creatinine level with no serum creatinine level being measured.

Data Collection

In this study, general information was gathered, which included sex, age, body mass index (BMI), the length of hospital stays, systolic blood pressure (SBP), demand for continuous renal replacement treatment (CRRT), blood transfusion, and mechanical ventilation (MV), sequential organ failure assessment (SOFA) score, and BISAP score within a day of admission. Blood routine parameters which contained white blood cell count, platelet count (PLT), hemoglobin (HGB) content, lymphocyte count, neutrophil count, and monocyte count were also gathered. Biochemical parameters included ALB, blood urea nitrogen (BUN), serum creatinine (CRE), total bilirubin (TB), direct bilirubin (DB), fasting plasma glucose (FPG), calcium ion concentration (Ca^{2+}), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), triglyceride (TG), CRP, and procalcitonin (PCT). The bedside Index of severity in acute pancreatitis (BISAP) score,[21] SOFA score,[22] and harmless acute pancreatitis score (HAPS)[23] were used to assess AP severity. The CRP/Alb ratio (CAR) was defined by dividing the CRP level by the ALB level. The defined endpoint event was AKI resulted from AP.

Statistical Analysis

Continuous variables can be indicated to be means with standard deviations, whereas categorical variables are suggested to be frequencies or percentages. In terms of continuous variables, statistical differences were identified with one-way ANOVA (for normally distributed data) or Kruskal–Wallis *H*-test (for skewed data), whereas the Chi-square or Fisher's exact test was adopted for categorical variables. Then, the subjects were grouped into tertiles by CRP/Alb ratio level. In order to investigate the association between CAR and AKI, multiple logistic regression analysis was carried out. Following the instructions in the Strengthening the Reporting of Observational Studies statement,[24] this study also explored both non-adjusted and multivariable-adjusted models. For variables satisfying $P < 0.1$ from univariate regression or when covariate addition or removal from the model changed ≥10% of odds ratio, adjustment for covariates was conducted. Three models were utilized: model 1 was adjusted for age, sex and BMI; model 2 was adjusted for age, sex, BMI, hypertension, diabetes mellitus (DM), coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), diastolic blood pressure (DBP), systolic blood pressure (SBP), heart rate (HR), body temperature, respiratory rate (RR), pulse oxygen saturation (SpO_2), severity, and etiology; model 3 was adjusted for age, sex, BMI, hypertension, DM, CHD, COPD, SBP, DBP, HR, body temperature, RR, SpO_2, severity, etiology, blood transfusion, CRRT, HGB, SOFA score, BISAP score, PCT, glycosylated hemoglobin A1c (HBA1c), prealbumin (PA), platelet (PLT), triglyceride (TG), calcium (Ca^{2+}), and amylase (AMY). Baseline variables that were regarded to be clinically associated or showed an alteration in effect estimate of >10% were selected to be confounders. Restricted cubic spline analysis was established and then adjusted in line with the covariables contained in model 3. Using logical regression, the linear relationship between CAR level and AKI was found. Additionally, subgroup analysis stratified by sex, age (≥ 65, < 65), BMI, ICU admission, hypertension, diabetes, CHD, COPD, Ventilation, transfusion, CRRT, SOFA (≥6 and <6), and severity and etiology of AP were performed, as previous description. In terms of the missing data, the predicted mean matching

method was used for filling in the missing values.[25] Table S1 presents the details of the missing value. Descriptive analyses report found data only, whereas regression models contain all the patients having multiple imputed data.

All the analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation) and Free Statistics software versions 1.9. A two-tailed test was performed and $p < 0.05$ was considered statistically significant.

Results

Patients' Baseline and Clinical Data

In accordance with occurrence of AKI, the involved AP patients were categorized as AKI group (n = 257) and non-AKI group (n = 1257). There existed no obvious difference in patients' BMI and SBP between the two groups (P > 0.05), while there exhibited obvious differences in sex, age, SOFA score, the length of hospital stays, demand for MV, blood transfusion and CRRT, ALB, CRE, WBC, PLT, PCT, CRP, TG, FPG, as well as CAR (P < 0.001) (Table 1).

Totally, 1514 patients were recruited and 257 (16.9%) developed AKI. Table 2 presents the baseline demographic characteristics of the study population, stratified by CAR level tertiles. Relative to patients in the lowest serum CAR

Table 1 Baseline Characteristics of Included Patients Grouped by the Occurrence of AKI

Characteristics	No-AKI (n = 1257)	AKI (n = 257)	P value
Male	642 (51.1)	170 (66.1)	< 0.001
Age(years)	53.0 (41.0, 64.0)	56.0 (44.0, 69.0)	0.002
Death	5 (0.4)	18 (7)	< 0.001
LOS (days)	13.0 (10.0, 18.0)	16.0 (10.0, 26.0)	< 0.001
ICU	115 (9.1)	132 (51.4)	< 0.001
Hypertension	304 (24.2)	88 (34.2)	< 0.001
DM	177 (14.1)	48 (18.7)	0.059
CHD	77 (6.1)	26 (10.1)	0.021
COPD	48 (3.8)	16 (6.2)	0.081
Weight (kg)	64.0 (56.0, 75.0)	65.0 (55.0, 75.0)	0.704
Height(cm)	163.0 (158.0, 170.0)	167.0 (158.0, 172.0)	0.001
BMI (kg/m2)	24.1 (21.8, 26.7)	24.2 (20.8, 26.9)	0.437
SBP (mmHg)	130.0 (119.0, 143.0)	123.0 (110.0, 140.0)	< 0.001
DBP (mmHg)	80.0 (74.0, 90.0)	80.0 (66.0, 89.0)	< 0.001
HR (bpm)	78.0 (72.0, 90.0)	90.0 (76.0, 110.0)	< 0.001
Temperature (degree C)	36.5 (36.4, 36.6)	36.5 (36.4, 36.8)	0.013
RR (bpm)	20.0 (19.0, 20.0)	20.0 (19.0, 21.0)	0.009
SpO2(%)	99.0 (98.0, 100.0)	98.0 (96.0, 100.0)	< 0.001
Ventilation	73 (5.8)	85 (33.1)	< 0.001
Transfusion	70 (5.6)	98 (38.1)	< 0.001
CRRT	21 (1.7)	71 (27.6)	< 0.001
PLT(×109/L)	181.0 (139.0, 234.0)	172.0 (110.0, 227.0)	0.004
PCT(×109/L)	0.1 (0.0, 0.6)	1.1 (0.2, 6.5)	< 0.001
CRP (mg/L)	31.4 (5.9, 119.0)	88.7 (16.9, 200.2)	< 0.001
ALB (g/L)	39.1 (34.9, 42.7)	34.8 (28.6, 39.7)	< 0.001
AMY (U/L)	163.0 (64.5, 716.0)	202.0 (92.0, 607.0)	0.065
PA (mg/L)	162.3 (111.0, 210.0)	144.8 (92.0, 230.0)	0.625
HBA1c (%)	5.9 (5.4, 7.0)	5.9 (5.4, 7.5)	0.381
TG (mmol/L)	1.5 (1.0, 3.4)	1.8 (1.2, 6.4)	< 0.001
Ca^{2+} (mmol/L)	2.2 (2.1, 2.4)	2.1 (1.9, 2.3)	< 0.001
SOFA (score)	2.0 (1.0, 3.0)	5.0 (2.0, 7.0)	< 0.001

(*Continued*)

Table 1 (Continued).

Characteristics	No-AKI (n = 1257)	AKI (n = 257)	P value
BISAP (score)	1.2 ± 1.1	2.0 ± 1.3	< 0.001
HAPS (score)	0.0 (0.0, 1.0)	1.0 (0.0, 1.0)	< 0.001
Severity of AP			< 0.001
Mild and moderate	1181 (94)	162 (63)	
Severe	76 (6)	95 (37)	
Etiology of AP			< 0.001
Biliary	887 (70.6)	132 (51.4)	
Hyperlipidemic	289 (23)	65 (25.3)	
Alcoholic	42 (3.3)	9 (3.5)	
Others	39 (3.1)	51 (19.8)	
CAR	0.8 (0.1, 3.3)	2.5 (0.4, 6.6)	< 0.001

Notes: Values are expressed as mean ± SD or median (IQR) for continuous variables and percentage for categorical variables.

Abbreviations: LOS, Length of hospital stay; y, years; DM, diabetes mellitus; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate; SpO_2, pulse oxygen saturation; Ventilation, noninvasive or invasive mechanical ventilation; Transfusion, blood transfusion; CRRT, continuous renal replacement treatment; HGB, hemoglobin; PLT, platelet count; PCT, procalcitonin; CRP, C-reactive protein; ALB, albumin; AMY, amylase; PA, prealbumin; HBA1c, glycosylated hemoglobin A1c; TG, triglyceride; Ca^{2+}, Calcium; CRE, creatinine; SOFA, sequential organ failure assessment score; BISAP, Bedside Index of Severity in Acute Pancreatitis score; HAPS, harmless acute pancreatitis score; AKI, Acute kidney injury; CAR, CRP to ALB ratio; IQR, interquartile range; $p < 0.05$ was considered statistically significant.

Table 2 Basic Characteristics in Enrolled Patients Classified According to the CAR Tertile

Characteristics	T1 (n = 505) CAR:0.05–0.289	T2 (n = 504) CAR:0.292–2.624	T3 (n = 505) CAR:2.628–22.994	P value
Male	239 (47.3)	280 (55.6)	293 (58)	0.002
Age(years)	54.0 (43.0, 64.0)	54.0 (42.8, 66.0)	52.0 (40.0, 65.0)	0.488
Death	7 (1.4)	7 (1.4)	9 (1.8)	0.839
LOS (days)	12.0 (10.0, 17.0)	13.0 (10.0, 18.0)	14.0 (10.0, 22.0)	< 0.001
ICU	56 (11.1)	65 (12.9)	126 (25)	< 0.001
Hypertension	115 (22.8)	125 (24.8)	152 (30.1)	0.023
DM	61 (12.1)	80 (15.9)	84 (16.6)	0.093
CHD	32 (6.3)	35 (6.9)	36 (7.1)	0.872
COPD	15 (3)	19 (3.8)	30 (5.9)	0.053
Weight (kg)	61.5 (55.0, 72.0)	64.0 (55.0, 74.0)	65.0 (56.0, 78.0)	< 0.001
Height(cm)	163.0(158.0, 170.0)	164.0(158.0, 170.0)	165.0(158.0, 170.0)	0.122
BMI (kg/m^2)	23.4 (21.5, 26.1)	24.2 (21.7, 26.7)	24.6 (22.0, 27.6)	< 0.001
SBP (mmHg)	127.0 (117.0, 142.0)	128.0 (117.0, 143.0)	130.0(116.0, 144.0)	0.537
DBP (mmHg)	80.0 (72.0, 89.0)	80.0 (72.8, 90.2)	80.0 (72.0, 90.0)	0.182
HR (bpm)	76.0 (70.0, 85.0)	80.0 (72.0, 90.0)	88.0 (76.0, 104.0)	< 0.001
Temperature (degree C)	36.5 (36.3, 36.6)	36.5 (36.4, 36.7)	36.6 (36.4, 36.7)	< 0.001
RR (bpm)	20.0 (18.0, 20.0)	20.0 (19.0, 20.0)	20.0 (19.0, 21.0)	< 0.001
SpO_2(%)	99.0 (98.0, 100.0)	99.0 (97.0, 100.0)	98.0 (96.0, 100.0)	< 0.001
Ventilation	33 (6.5)	38 (7.5)	87 (17.2)	< 0.001
Transfusion	40 (7.9)	46 (9.1)	82 (16.2)	< 0.001
CRRT	16 (3.2)	24 (4.8)	52 (10.3)	< 0.001
WBC ($\times 10^9$/L)	8.0 (5.3, 11.9)	9.3 (6.6, 13.1)	11.7 (8.9, 15.8)	< 0.001
HGB (g/L)	130.0 (118.0, 145.0)	130.5 (112.8, 148.0)	126.0 (110.0, 142.0)	0.006
PLT($\times 10^9$/L)	183.0 (143.0, 225.0)	185.0 (143.8, 245.0)	166.0 (124.0, 224.0)	0.001

(*Continued*)

Table 2 (Continued).

Characteristics	T1 (n = 505) CAR:0.05–0.289	T2 (n = 504) CAR:0.292–2.624	T3 (n = 505) CAR:2.628–22.994	P value
PCT (ng/m/L)	0.1 (0.0, 0.2)	0.2 (0.1, 0.5)	0.6 (0.2, 2.8)	< 0.001
CRP (mg/L)	3.7 (1.9, 6.6)	37.1 (20.9, 63.5)	185.4 (134.7, 249.1)	< 0.001
ALB (g/L)	41.2 (38.0, 44.3)	39.0 (35.1, 42.2)	33.5 (29.2, 38.6)	< 0.001
FPG (mmol/L)	6.2 (5.0, 8.4)	6.6 (5.3, 9.0)	7.3 (5.8, 10.0)	< 0.001
AMY (U/L)	225.0 (76.0, 976.0)	175.0 (72.0, 769.5)	130.0 (56.0, 411.0)	< 0.001
PA (mg/L)	194.9 (155.5, 239.0)	159.1 (115.0, 210.0)	117.0 (81.0, 171.0)	< 0.001
HBA1c (%)	5.9 (5.3, 6.6)	5.9 (5.4, 7.0)	6.1 (5.4, 7.7)	< 0.001
TG (mmol/L)	1.4 (1.0, 2.5)	1.4 (0.9, 3.6)	1.8 (1.1, 4.4)	< 0.001
Ca^{2+} (mmol/L)	2.3 (2.1, 2.4)	2.2 (2.1, 2.4)	2.1 (1.9, 2.2)	< 0.001
CRE (μmol/L)	65.0 (53.5, 78.1)	69.9 (57.0, 84.0)	70.6 (55.0, 98.0)	< 0.001
SOFA (score)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	3.0 (1.0, 4.0)	< 0.001
BISAP (score)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	2.0 (0.0, 2.0)	< 0.001
HAPS (score)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	< 0.001
Severity of AP				< 0.001
Mild and moderate	469 (92.9)	466 (92.5)	408 (80.8)	
Severe	36 (7.1)	38 (7.5)	97 (19.2)	
Etiology of AP				< 0.001
Biliary	380 (75.2)	342 (67.9)	297 (58.8)	
Hyperlipidemic	85 (16.8)	121 (24)	148 (29.3)	
Alcoholic	13 (2.6)	14 (2.8)	24 (4.8)	
Others	27 (5.3)	27 (5.4)	36 (7.1)	
CAR	0.1 (0.0, 0.2)	1.0 (0.5, 1.7)	5.5 (3.9, 7.6)	< 0.001
AKI	53 (10.5)	76 (15.1)	128 (25.3)	< 0.001

Notes: Values are expressed as mean ± SD or median (IQR) for continuous variables and percentage for categorical variables.
Abbreviations: LOS, Length of hospital stay; y, years; DM, diabetes mellitus; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate; SpO_2, pulse oxygen saturation; Ventilation, noninvasive or invasive mechanical ventilation; Transfusion, blood transfusion; CRRT, continuous renal replacement treatment; WBC, white blood cell count; HGB, hemoglobin; PLT, platelet count; PCT, procalcitonin; CRP, C-reactive protein; ALB, albumin; FPG, fasting plasma glucose; AMY, amylase; PA, prealbumin; HBA1c, glycosylated hemoglobin A1c; TG, triglyceride; Ca^{2+}, Calcium; CRE, creatinine; SOFA, sequential organ failure assessment score; BISAP, Bedside Index of Severity in Acute Pancreatitis score; HAPS, harmless acute pancreatitis score; AKI, Acute kidney injury; CAR, CRP to ALB ratio; IQR, interquartile range; $p < 0.05$ was considered statistically significant.

tertile (T1), patients with intermediate (T2) and high (T3) CAR ratio level were higher on demand for mechanical ventilation, blood transfusion and RRT, higher SOFA score and BISAP score on admission, higher BMI, higher TG level, higher FPG level, and longer hospitalization. AKI incidence was also shown to be higher in patients with high CAR levels ($P < 0.001$).

Univariate and Multivariate Analyses of CAR and AKI

According to univariate analysis, age, sex, hypertension, DM, coronary heart disease, systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, SpO_2, severity, etiology, blood transfusion, MV, CRRT, SOFA score, BISAP score, PCT, HBA1C, PA, TG, Ca^{2+}, and AMY were shown to be significant confounding factors which influenced AKI incidence ($P < 0.001$) (Table S2). Based on multiple logistic regression analysis, CAR showed a positive correlation with AKI when it was considered to be a continuous variable (OR 1.16, 95% CI 1.12–1.21, $P < 0.001$, Table 3). The positive correlation was of significance following adjusting confounding variables (OR 1.07, 95% CI 1.01–1.13, $P = 0.024$). With CAR levels being divided into tertiles, the OR of AKI was 1.51 for T2 and 2.90 for T3 relative to T1 without adjustment (Table 3). Following multivariate adjustment, T3 still showed a notably higher risk of AKI than T1 in both the minimally adjusted model (model 1, OR 2.84, 95% CI 2.00–4.05, $P < 0.001$) and fully adjusted model (model 3, OR 1.83, 95% CI 1.13–2.96, $P = 0.013$), whereas T2 was no longer notably different from T1. In addition, the risk of AKI obviously increased stepwise across CAR-level tertiles (P for trend = 0.013).

Table 3 Multiple Logistic Regression Analysis Between CAR and AKI

	Non-Adjusted Model	Adjusted Model 1	Adjusted Model 2	Adjusted Model 3
	OR (95%CI), P value	OR (95% CI), P value	OR (95% CI), P value	OR (95% CI), P value
CAR	1.16(1.12~1.21), <0.001	1.16(1.12~1.21), <0.001	1.08 (1.03~1.13), 0.003	1.07(1.01~1.13), 0.024
CAR, tertiles				
T1	Reference	Reference	Reference	Reference
T2	1.51 (1.04~2.2), 0.03	1.45 (0.99~2.12), 0.054	1.37 (0.9~2.08), 0.139	1.37(0.87~2.17), 0.173
T3	2.9(2.04~4.1), <0.001	2.84 (2~4.05), <0.001	1.8 (1.19~2.71), 0.005	1.83(1.13~2.96), 0.013
P for trend	<0.001	<0.001	0.005	0.013

Notes: Results for each model are presented as OR (95% CI), P value. Model 1: adjusted for age, sex and BMI. Model 2: adjusted for age, sex, BMI, Hypertension, DM, CHD, COPD, SBP, DBP, HR, Temperature, RR, SpO_2, severity and etiology. Model 3: adjusted for age, sex, BMI, Hypertension, DM, CHD, COPD, SBP, DBP, HR, Temperature, RR, SpO_2, severity, etiology, transfusion, CRRT, BISAP, SOFA, PCT, HGB, PLT, HBA1c, PA, TG, Ca^{2+} and AMY.

Abbreviations: AKI, acute kidney injury; CAR, CRP to ALB ratio; T, tertile; OR, odds ratio; 95% CI, 95% confidence interval.

Dose–Response Relationship Between CAR Level and AKI

From Figure 2, with increasing CAR level, adjusted ORs for AKI also dose-responsively elevated. This correlation persists across varying severities (mild and moderate vs severe) of AP, revealing a consistent trend between CAR and AKI, as presented in Figure S1.

ROC Curves for Comparison of Biomarkers to Predict AKI

From Figure 3, we compared the predictive value of various inflammation-related indicators for acute kidney injury (AKI) in patients with acute pancreatitis. Among these, the area under the ROC curve (AUC) for the C-reactive protein-to-albumin ratio (CAR) was 59.48% (95% CI: 54.63–64.32%), which was higher than the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), but lower than the SOFA score, BISAP score, and HAPS score. The details were seen in Table S3.

Subgroup Analysis

Subgroup analyses were carried out to investigate potential correlations between CAR (considered as a continuous variable) and AKI (Figure 4).

The association between CAR and AKI could be coordinated in following subgroups: age (<65 vs ≥65 years; P-interaction = 0.597), sex (female vs male; P-interaction = 0.523), BMI (<28 kg/m^2 vs ≥28 kg/m^2; P-interaction = 0.423), admission to ICU (yes vs no; P-interaction = 0.565), hypertension (yes vs no; P-interaction = 0.804), DM (yes vs no; P-interaction = 0.083), chronic obstructive pulmonary disease (yes vs no; P-interaction = 0.346), severity of AP (mild and moderate vs severe; P-interaction = 0.682), etiology of AP (Biliary vs Hyperlipidemic vs Alcoholic vs Others; P-interaction = 0.181), demand for RRT (yes vs no; P-interaction = 0.241), mechanical ventilation (yes vs no; P-interaction = 0.325), and blood transfusion (yes vs no; P-interaction = 0.406).

Discussion

This study examined the association of CAR with AKI among AP patients. This study found that CAR was positively related to AKI, and that risk of AKI elevated with stepwise across CAR-level tertiles through a dose-dependent way following adjustment for confounders. Stratified logistic regression analysis also indicated stable relationship between CAR and AKI in subgroups.

Among the different markers of inflammation, serum CRP refers to a positive acute phase reactant synthesized by the liver and its level in the blood elevates within hours as a response to inflammation and infection.[26] Usually, it can be applied in infection and inflammation follow-up owing to the short half-life, easy measurement, as well as the close

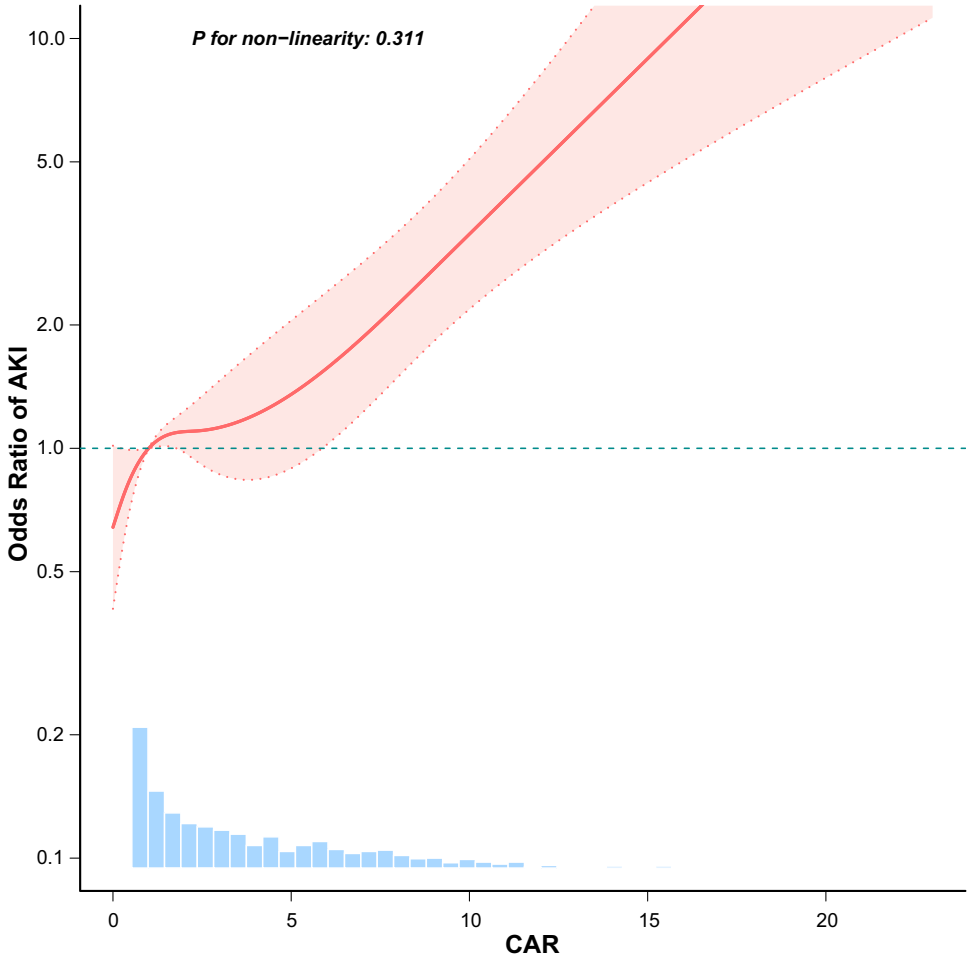

Figure 2 Adjusted dose-response association between CAR values and AKI. Solid lines represent the odds ratio of AKI and dotted lines represent the corresponding 95% CI. ORs were adjusted for variates with model 2. OR = 1 was set as the reference line.
Abbreviations: AKI, acute kidney injury; CAR, CRP-to-ALB ratio; OR, odds ratio; 95% CI, 95% confidence interval.

association with prognosis of the disease.[27,28] It is adopted for diagnosing, treating, and predicting mortality in inflammatory patients.[11,29] ALB represents the negative acute phase reactant generated in the liver, with its blood level declining in inflammation. It is previously suggested to be the mechanism of amino acid sparing during systemic inflammation; however, it is increasingly synthesized at an acute phase.[30,31] In several studies, ALB is related to inflammation severity, patient outcome, and mortality.[9,32] The reason refers to the close association between inflammation and malnutrition. Under pathological circumstances, there are intimate and complicated interactions between inflammation and malnutrition. For instance, inflammation may lead to malnutrition, while malnutrition can thus play a role of the detrimental factor for managing inflammation. Therefore, a single marker (inflammation or malnutrition) can hardly offer a robust risk prediction for diseases, including AKI.

The CRP/Alb, as a novel inflammation-based prognostic indicator, is related to the severity of inflammation[7] and mortality.[33] Elevated CAR is primarily adopted for predicting the patient poor outcomes in many diseases, such as colorectal cancer,[15] brain metastases in solid cancers,[13] and sepsis.[14,16] The elevated levels of CAR have been primarily found to be associated with dismal prognostic outcome of patients with sepsis.[33] Moreover, Chen et al found CAR to be the risk factor for mortality of sepsis-induced AKI cases,[14] and that the values of CAR were significantly higher in the non-survival group compared to the survival group. However, there are limited studies on its effectiveness in predicting the AP-induced AKI risk, especially in the Chinese population.

AKI is the major complication secondary to AP. It is associated with a dismal prognostic outcome, particularly when renal replacement is needed. Although its underlying pathophysiology is still unknown, it may be related to hypovolemia

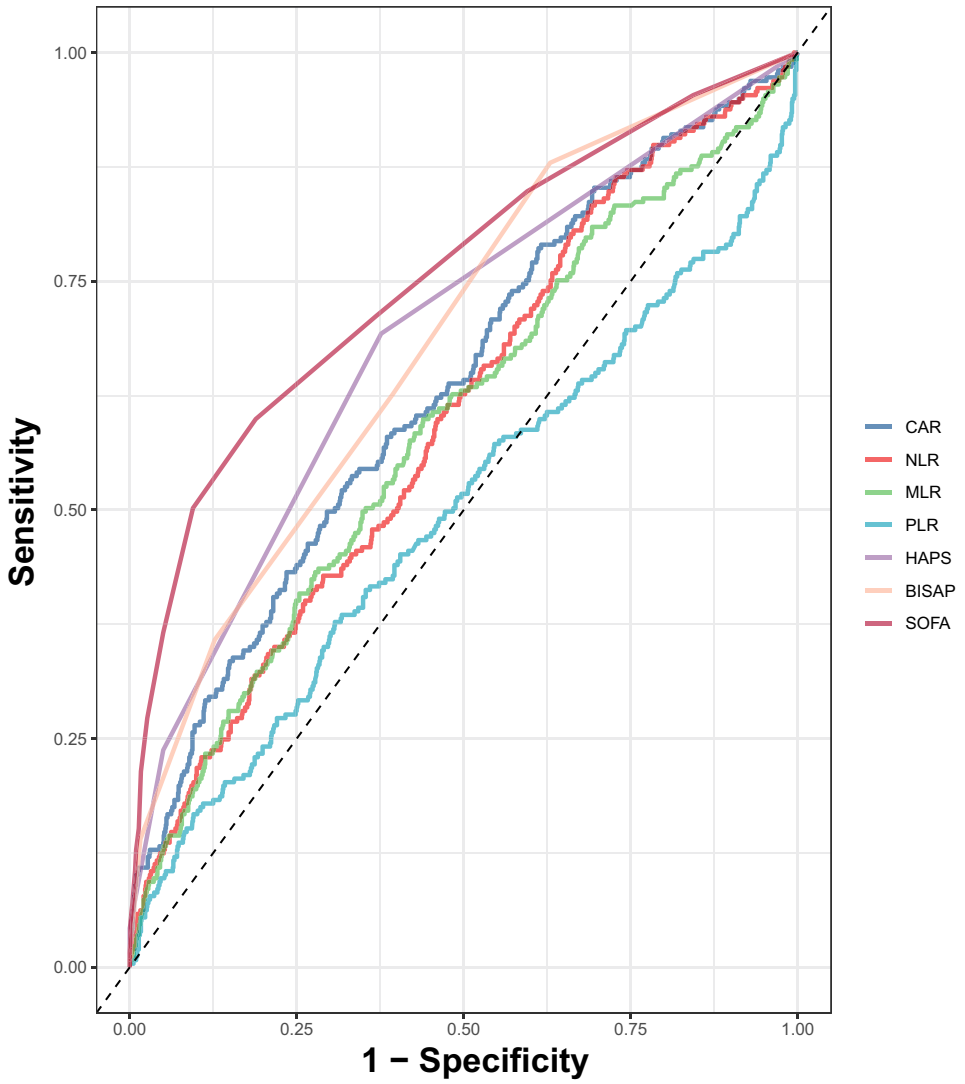

Figure 3 ROC curves for comparison of biomarkers to predict AKI.
Abbreviations: CAR, C-reactive protein-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; HAPS, harmless acute pancreatitis score; BISAP, Bedside Index of Severity in Acute Pancreatitis score; SOFA, sequential organ failure assessment score.

and the complicated interactions among vascular, inflammatory and humoral factors.[34] Studies indicate that inflammatory markers like NLR, PLR, and MLR predict poor outcomes in acute pancreatitis.[35–38] Nevertheless, the sample size is small in these studies, and the accuracy of the predictive models is lacking[39,40]. Our research reveals that CAR has a higher AUC, underscoring its greater value in predicting AKI in these patients. Currently, many scores have been utilized for assessing AP prognoses, including APACHE II score, Ranson, modified computed tomography severity index (MCTSI), SOFA score, and BISAP score. However, numerous parameters and complicated algorithms are needed to calculate these scores, which can therefore limit their clinical application. CAR level is only calculated by two laboratory parameters. Meanwhile, thus, it is the easy, efficient, cost-effective, and routinely determined biomarker for AP patients, among the traditional inflammation markers. The findings that CAR is the highly potential biological marker used to predict AKI caused by AP.

This study has the following strengths. Firstly, this study is currently the largest sample study on AP-related AKI in the Chinese population, and adjusted for as many confounding variables as possible. Secondly, subgroup analysis is used to reinforce our conclusion that there is a positive correlation of CAR with AKI of AP patients. Thirdly, stratified analysis of etiology indicates that CAR has a high predictive value for cholelithiasis and hyperlipidemic pancreatitis, CAR

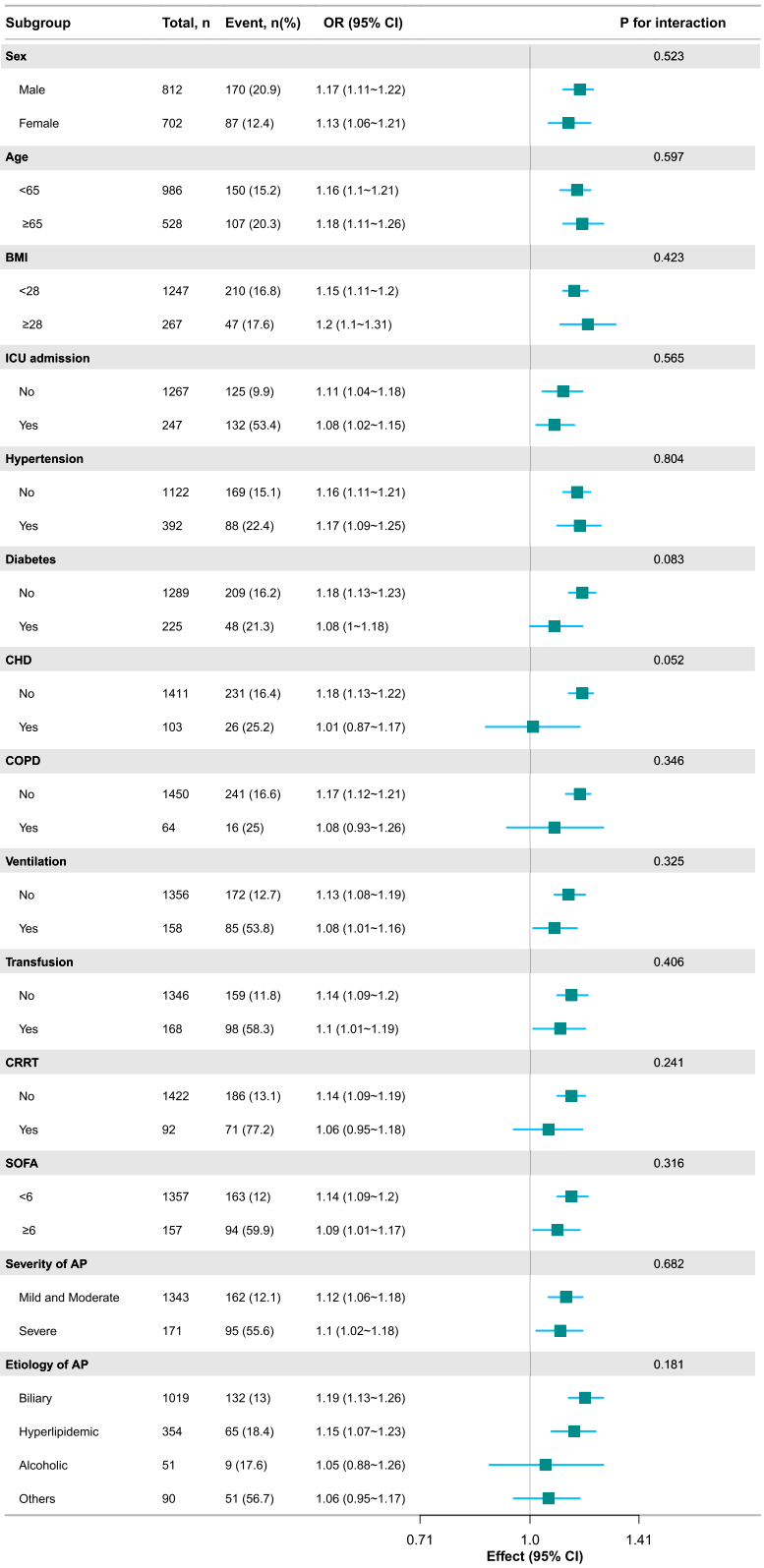

Figure 4 Stratified logistic regression analysis to identify variables that modify the correlation between CAR values and AKI. Adjusted factors included sex, age, BMI, ICU admission, hypertension, diabetes, CHD, COPD, ventilation, transfusion, CRRT, SOFA, and severity and etiology of AP.

Abbreviations: AKI, acute kidney injury; CAR, CRP-to-ALB ratio; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; BMI, body mass index; CRRT, continuous renal replacement treatment; SOFA, sequential organ failure assessment score; AP, CRP-to-ALB ratio; OR, odds ratio; 95% CI, 95% confidence interval.

exhibits a predictive trend although there was no statistical difference for alcoholic pancreatitis and other causes, which may be associated with the low number of cases of alcoholic pancreatitis and other causes.

However, our study also presents the following limitations. At first, the retrospective data collection at a single academic center could have caused selection bias. Secondly, we did not include CT imaging features, which we intend to incorporate in our future study. Thirdly, regardless of the potential association of CAR with AKI, this study did not provide the causality due to its observational design. In future studies, more prospective studies need to be performed to verify the association.

Conclusion

To conclude, CAR is consistently and strongly linked to the increased AKI incidence among Chinese AP patients. Monitoring CAR levels could contribute to identifying high AKI risk patients. More research should be conducted to demonstrate our results and understand the CAR-AKI association mechanism.

Data Sharing Statement

Data is available from the corresponding author on reasonable request.

Ethical Statement

The current retrospective study was approved by the Ethics Committee of the First College of Clinical Medical Science of China Three Gorges University (ethical approval number: 2023-130-01), which waived consent from study participants as it was not required due to the retrospective nature of the study. All patient data was anonymized during processing. This study was performed following the Declaration of Helsinki.

Acknowledgments

Wen Wu and Yu-Pei Zhang are co-first authors for this study. We extend our gratitude to Ming-Zi Tao and Tao Wu for contribution to the structured data extraction. We thank Dr. Liu Jie (People's Liberation Army of China General Hospital, Beijing, China) for helping in this revision.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

All authors have declared that they have no conflicts of interest in this work.

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