Lipids in Health and Disease

RESEARCH

Open Access

Atherogenic index of plasma as a novel predictor for acute kidney injury and disease severity in acute pancreatitis: a retrospective cohort study

Wen Wu[1,2,3,4†], Yiming Li[1,2†], Yupei Zhang[3,4], Xing Chen[3,4], Chunzhen Zhang[3,4], Xingguang Qu[3,4], Zhaohui Zhang[3,4], Rong Zhang[3,4*] and Zhiyong Peng[1,2*]

Abstract

Background The atherogenic index of plasma (AIP) can be used to reveal atherosclerosis. This study evaluated the AIP's efficacy in predicting the prognosis of acute kidney injury (AKI) and severity of acute pancreatitis (AP).

Methods This retrospective cohort study recruited AP cases from the First College of Clinical Medical Science of China Three Gorges University between January 2019 and October 2023, including 1470 patients. AIP was computed using the formula: log10 [serum triglyceride (mmol/L)/serum high-density lipoprotein cholesterol (mmol/L)]. The AIP relationships with AKI occurrence and AP severity were validated using multivariable logistic regression models, subgroup and sensitivity analyses, and curve fitting.

Results Among the 1470 patients with AP, 250 (17%) developed AKI and 166 (11.3%) with severe AP. AIP was positively correlated with AKI and the severity of AP. Potential confounders were adjusted, consequently, AIP was positively linearly related to AKI (P for non-linearity: 0.731, OR 2.5, 95% CI 1.31–4.77,) and the severity of AP (P for non-linearity: 0.145, OR 3.1, 95% CI 1.53–6.27), respectively. The strength of the association between AIP and AKI, along with the severity of AP, was demonstrated through stratified analyses. Significant interactions were not observed in sex, age, hypertension, BMI, diabetes mellitus, SOFA score, BISAP score, and etiology of AP (all P for interaction > 0.05). The areas under the curves for AIP in predicting the incidence of AKI and severity of AP were 0.64 and 0.65, respectively.

†Wen Wu and Yiming Li are co-first authors.

†Rong Zhang and Zhiyong Peng are co-corresponding authors.

*Correspondence:
Rong Zhang
zhangrong20240304@163.com
Zhiyong Peng
zn001590@whu.edu.cn

Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Conclusions This is the first study to suggest that the AIP is critical for the assessment of AKI risk, recommending early screening of severity among AP cases. Due to the observational nature of the study, the potential for residual confounding, and the need for external validation in larger, independent cohorts.

Keywords Acute pancreatitis, Acute kidney injury, Atherogenic index of plasma, Insulin resistance, Lipid metabolism

Introduction

Acute pancreatitis (AP) indicates acute inflammatory conditions with localized pancreatic injury, affecting surrounding tissues or resulting in systemic inflammation by the activation of cytokine cascades [1]. More than 50% of AP cases have a minor, self-limiting process. However, severe acute pancreatitis (SAP) characterized by continuous organ dysfunction may develop fatal complications, with a mortality rate of up to 30% [2]. Moreover, acute kidney injury (AKI) related to AP demonstrates an incidence of 10–42% [3], contributing to multiple organ failure, which is a leading cause of death. Therefore, high-risk patients for AKI and SAP must be determined in a timely manner to assess the appropriate primary care level required for effective patient management.

Insulin resistance (IR) is the critical characteristic of type 2 diabetes mellitus (T2DM), significantly contributing to AKI [4]. IR induces the inflammatory process, dyslipidemia, and vascular endothelial dysfunction, as suggested by pathophysiological studies, probably driving the progression of SAP and AKI [4].

Atherogenic index of plasma (AIP), proposed in 2001 by Dobiásová and Frohlich [5]. a logarithmically transformed triglyceride (TG)-to-high-density lipoprotein cholesterol (HDL-C) ratio, is a novel and superior lipid marker that has recently emerged. Some articles recently have analyzed the relationship of AP with dyslipidemia. Metabolic syndrome and morbid obesity demonstrate an increased risk of moderately severe acute pancreatitis and SAP [6]. AIP, as the integrative lipid marker, is a reliable indicator of inflammation and disrupted lipid metabolism [7].

Therefore, this study investigates the relationship between AIP and the incidence of AKI and the severity of AP, offering insights for early risk assessment and management strategies in this population.

Materials and methods

Ethical statements

This observational, retrospective cohort study was conducted at the Yichang Central People's Hospital, the First College of Clinical Medical Science of China Three Gorges University. The study followed the Declaration of Helsinki guidelines and was authorized by the Ethics Committee of Yichang Central People's Hospital (ethical approval number: 2023-130-01). Informed consent was not required owing to the retrospective nature of the study.

Study population and eligibility criteria

Participants meeting the following criteria were enrolled: inpatients from the Yichang Central People's Hospital, First College of Clinical Medical Science of China Three Gorges University; and those with AP reporting to the hospital between January 2019 and October 2023. The exclusion criteria were as follows: patients with pre-existing AKI or SAP at the time of admission; those aged < 18 or > 80 years; women who were pregnant or breastfeeding; those with a hospital stay of ≤ 2 days; patients with chronic kidney disease; those with cancer; those who developed chronic pancreatitis; those who underwent nephrectomy or renal transplantation; and those lacking essential data required for our analysis, such as TG and HDL-C. Figure 1 illustrates the study design and review process.

Definitions and laboratory test results

Definition of AIP

The AIP was computed using the following formula: log10 (TG [mmol/L]/HDL-C [mmol/L]) [8].

AP diagnosis and severity classification

The AP diagnosis was made according to 2 or 3 characteristics below [9]: (1) specific abdominal pain, (2) serum amylase and/or lipase thrice the upper normal limit, and (3) radiological observations. AP severity could be categorized into mild (no organ failure and local/systemic complications), moderate (transient organ failure resolving in 48 h and local/systemic complications), and severe (continuous organ failure) according to revised Atlanta 2012 criteria [9].

AKI diagnosis and classification

AKI diagnosis was made according to the Kidney Disease: Improving Global Outcomes guidelines for clinical practice of AKI (2012) [10], including the following features: the elevated serum creatinine (CREA) content ≥ 0.3 mg/dL (≥ 26.5μmol/L) in 48 h, the elevated serum CREA content by ≥ 1.5 folds the baseline level in 7 days, or urine volume lasting more than 6 h and being less than 0.5 mg/kg/h. Additionally, basic serum CREA content was the minimum serum CREA content detected in 48 h before hospital admission. Serum CREA content during the initial detection in 48 h post-hospital admission was deemed as basic serum CREA content when serum CREA content was not detected.

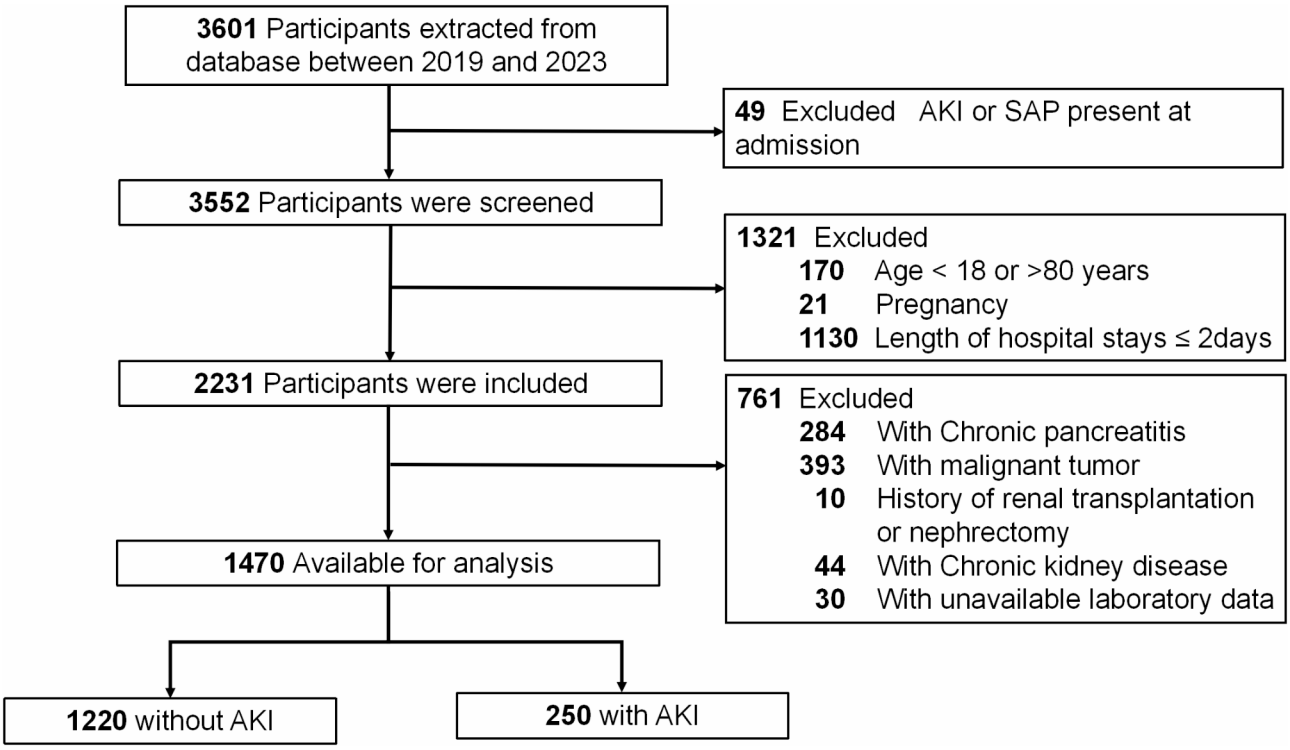

Fig. 1 Flowchart of the screening and enrollment of the study participants. AKI: acute kidney injury; SAP: severe acute pancreatitis

Data source

General data such as age; sex; body mass index (BMI); history of hypertension, diabetes mellitus (DM), and coronary heart disease (CHD); the length of hospital stays; heart rate (HR); respiratory rate (RR); pulse oxygen saturation (SpO_2); systolic blood pressure (SBP); the necessity of blood transfusion, mechanical ventilation, and continuous renal replacement treatment (CRRT); sequential organ failure assessment (SOFA) score; and Bedside Index of Severity in Acute Pancreatitis (BISAP) score in 24 h post-admission were extracted. Blood routine factors such as hemoglobin (HGB) level, hematocrit (HCT), and white blood cell count were also extracted. Biochemical factors such as fasting plasma glucose (FPG), albumin (ALB), serum CREA, calcium ion level (Ca^{2+}), sodium ion level (Na^{+}), C-reactive protein (CRP), aspartate aminotransferase, serum amylase (AMY), triglyceride (TG), and procalcitonin (PCT) were collected. The first blood sample collected within 4 h of hospital admission was used for laboratory analyses. The severity of AP was assessed using the BISAP score, harmless acute pancreatitis score (HAPS) [11], and SOFA score [12]. The endpoint was AP-induced AKI and AP severity during hospital stays.

Statistical analysis

The median and interquartile range (IQR), including 25th (Q25) and 75th (Q75) percentiles were used to represent continuous data. Normally distributed continuous data were examined using a one-way analysis of variance, while non-normally distributed data were explored using the Kruskal-Wallis H test. Additionally, categorical counterparts were specified by frequencies or percentages and compared using Chi-square and Fisher's exact tests.

Patients were classified according to AIP levels in tertiles ($AIP < 0.03$, $0.03 \le AIP < 1.05$, $AIP \ge 1.05$). Subsequently, the association of AIP levels with AKI and AP severity was assessed using smooth curve fitting and multivariablelogistic regression. The models that were not adjusted or adjusted for multiple variables were assessed simultaneously based on the Strengthening the Reporting of Observational Studies statement [13]. When the variables satisfied $P < 0.1$ using univariable regression, or if model covariable introduction or elimination modified the odds ratio (OR) by > 10%, covariable adjustment was performed. Three models including model 1 (with adjustment of sex, age, and BMI); model 2 (with adjustment of sex, age, BMI, hypertension, DM, CHD, chronic obstructive pulmonary disease (COPD), SBP, DBP, HR, temperature, RR, and SpO_2); and model 3 (with adjustment of WBC, CRP, PCT, AMY, Na^{+}, Ca^{2+}, CREA, CHOL, BISAP score, HAPS, SOFA score, and etiology based on model 2) were used. The baseline factors with clinical relevance or effect estimate change of > 10% were selected as confounders. A smooth curve using the restricted cubic spline method was created and subsequently adjusted

based on the covariable from model 3. Following this, the absent values were filled using a multiple imputation approach [14]. Descriptive analysis only reports the observed data, whereas regression models incorporate the estimated data. Subgroup homogeneity was assessed for further exploratory analysis using the stratified logistic regression model considering sex, age, BMI, diabetes, SOFA score, BISAP score and etiology of AP. Lastly, likelihood ratio tests were conducted to examine relations among AIP levels with AKI and AP severity of the subgroups. An ROC curve was plotted to evaluate the performance of AIP and other indicators like SOFA, BISAP, and HAPS in predicting AKI and the severity of AP. This evaluation was done by calculating the area under the curve and determining the optimal threshold.

Statistical analysis was performed using Free Statistics software (version 1.9), a statistical tool built on R (http://www.R-project.org, The R Foundation). Statistical significance was set at $P < 0.05$ (two-sided).

Results

Basic and clinical data of participants

A total of 1470 qualified patients were included. All patients had a median age of 53.0 (41.0, 65.0) years, consisting of 53.7% men and 46.3% women. Table 1 presents the basic patient features based on the AIP tertile. The patients of the Q3 group demonstrated an increased incidence of AKI and SAP; and greater BMI, FPG, TG, the demand for mechanical ventilation, CRRT, and transfusion levels.

This study comprised 1470 cases, including 250 (17.0%) with developing AKI. Those included AP cases were then classified into AKI ($n = 250$) or non-AKI group ($n = 1220$) based on whether they developed AKI or not. The AKI measurement was conducted during a follow-up period of up to 7 days, with a median follow-up time of 3.1 (1.1–5.2) days.

Among the enrolled population, 166 (11.3%) progressed to SAP. Based on severity, the population was divided into mild and moderate AP ($n = 1304$) and severe AP ($n = 166$), with a median follow-up time for severity assessment of 4.2 (2.0-6.4) days. There was no between-group difference in the history of DM, COPD, HGB, and HCT ($P > 0.05$). In contrast, the history of CHD, HR; the necessity of blood transfusion, mechanical ventilation, and CRRT; WBC; PCT; CRP; ALB; FPG; TG; and CREA exhibited significant differences ($P < 0.05$) (Table 2).

Multivariable analyses on the AIP level with AKI and the severity of AP

Using the multivariable logistic regression, relative to the AIP reference tertile (T1 < 0.03), the adjusted ORs for T2 (0.03–1.05) and T3 (≥ 1.05) were determined to be 1.27 (95% CI 0.71–2.25, $P = 0.419$) and 2.5 (95% CI 1.31–4.77, $P = 0.005$), respectively, after adjusting for covariables related to the higher incidence of AKI (Table 3).

Meanwhile, using the same method, relative to the AIP reference tertile (T1 < 0.03), the adjusted ORs for T2 (0.03–1.05) and T3 (≥ 1.05) were found to be 1.44 (95% CI 0.75–2.78, $P = 0.277$) and 3.1 (95% CI 1.53–6.27, $P = 0.002$), respectively, which were related to the higher severity of AP (Table 3). Mild and moderate acute pancreatitis are grouped into one category.

Dose-response relationship between AIP level with AKI and AP severity

The linear relations of AIP with AKI and AP severity were detected, when covariables from model 3 were adjusted, exhibiting a dose-response relationship in the restricted cubic spline (RCS) model (P for non-linearity = 0.731 and 0.145, respectively) (Fig. 2A + 2B).

Subgroup analysis

To evaluate whether the results were robust, this study conducted sensitivity analyses. We primarily focused on patients with BMI < 25 kg/m^2 (Table S1), and found that AIP was strongly correlated with the risk of AKI although the remaining variables were considered (OR 1.31, 95% CI 1.06–1.62). In addition, sensitivity analysis was conducted among non-DM patients. Consequently, AIP was still positively related to the incidence of AKI, though the remaining variables were adjusted (OR 1.33, 95% CI 1.08–1.64).

Simultaneously, after accounting for other variables, it was determined that AIP exhibited a strong relation to AP severity among participants with BMI < 25 kg/m^2 and non-diabetes using the same method (Table S1). Additionally, a sensitivity analysis was conducted on populations classified by different etiologies, and the results indicated that this study's findings remain robust.

Moreover, to determine the association of the unmeasured confounder with AKI incidence and AP severity the E-value was estimated using the results of model 3. The estimates of the E-value point were 1.63 for the positive association of AIP with the incidence of AKI and 2.56 for AP severity. Moreover, the unmeasured confounders might not have markedly influenced the finding strength compared to past research. The study findings remain robust after various sensitivity analyses.

Subgroup analyses were performed to explore the possible factors influencing the relation of AIP level with AKI and AP severity. Sex (female vs. male), age (< 65 vs. ≥65 years), BMI (< 25 vs. ≥25 kg/m^2), diabetes (yes vs. no), SOFA score (< 5 vs. ≥5), BISAP score (< 3 vs. ≥3) and etiology of AP [biliary vs. hyperlipidemic vs. other (alcoholic and others)] were selected to be the stratification variables. From Fig. 3, these confounders did not affect the relationship between AIP level with AKI (Fig. 3A) and

Table 1 Baseline characteristics of included patients grouped using tertile of AIP

Characteristics		AIP			*P* value
	Total (*N* = 1470)	**T1 (*N* = 490) < 0.03**	**T2 (*N* = 490) 0.03–1.05**	**T3 (*N* = 490) ≥ 1.05**	
Male	790 (53.7)	193 (39.2)	277 (56.5)	320 (65.3)	< 0.001
Age (years)	53.0 (41.0, 65.0)	59.0 (50.0, 69.0)	56.0 (44.0, 67.0)	46.0 (37.0, 55.0)	< 0.001
BMI (kg/m^2)	24.2 (21.7, 26.7)	23.0 (20.8, 25.6)	24.1 (21.6, 26.5)	25.4 (22.7, 28.3)	< 0.001
Death	23 (1.6)	3 (0.6)	8 (1.6)	12 (2.4)	0.068
ICU	240 (16.3)	44 (8.9)	73 (14.9)	123 (25.1)	< 0.001
LOS(d)	16.6 ± 12.7	15.9 ± 9.0	17.5 ± 14.5	16.6 ± 13.9	0.130
Hypertension	370 (25.2)	121 (24.7)	131 (26.7)	118(24.1)	0.535
DM	203 (13.8)	28 (5.7)	51 (10.5)	124 (25.3)	< 0.001
CHD	88 (6.0)	39 (8.0)	39 (8.0)	10 (2.0)	< 0.001
COPD	54 (3.7)	27 (5.5)	15 (3.1)	12 (2.5)	0.013
SBP (mmHg)	129.0 (117.0, 143.0)	126.0 (115.0, 140.0)	129.0 (116.8, 141.0)	131.0 (119.0, 148.0)	0.001
DBP (mmHg)	80.0 (72.0, 90.0)	79.0 (70.0, 86.0)	80.0 (71.0, 89.0)	84.0 (76.0, 97.0)	< 0.001
HR (bpm)	80.0 (72.0, 93.0)	78.0 (70.0, 87.0)	80.0 (72.0, 90.0)	86.0 (76.0, 103.0)	< 0.001
Temperature (degree C)	36.5 (36.4, 36.7)	36.5 (36.4, 36.6)	36.5 (36.4, 36.7)	36.5 (36.4, 36.7)	0.024
RR (bpm)	20.0 (19.0, 20.0)	20.0 (18.0, 20.0)	20.0 (19.0, 20.0)	20.0 (19.0, 21.0)	< 0.001
SpO_2 (%)	99.0 (97.0, 100.0)	99.0 (98.0, 100.0)	99.0 (97.0, 100.0)	99.0 (97.0, 100.0)	0.231
Mechanical ventilation	150 (10.4)	25 (5)	44 (8.9)	81 (16.5)	< 0.001
Transfusion	148 (10.0)	20(4.1)	42 (8.6)	86 (17.6)	< 0.001
CRRT	90 (6.1)	6 (1.2)	26 (5.4)	58 (12.0)	< 0.001
WBC (×10^9/L)	9.8 (6.6, 13.6)	8.4 (5.7, 12.1)	9.6 (6.6, 13.5)	11.2 (8.1, 14.7)	< 0.001
HGB (g/L)	129.0 (114.0, 145.0)	126.0 (113.0, 136.0)	127.0 (111.8, 143.0)	138.0 (118.0, 155.0)	< 0.001
HCT (%)	38.5 (34.5, 42.7)	37.8 (34.4, 40.9)	38.4 (34.0, 42.6)	40.1 (35.2, 44.0)	< 0.001
PCT (ng/ml)	0.2 (0.1, 0.9)	0.2 (0.1, 0.6)	0.2 (0.1, 0.8)	0.2 (0.1, 1.1)	0.145
CRP (mg/L)	37.1 (6.6, 134.7)	19.4 (5.0, 82.7)	42.2 (6.6, 140.3)	69.1 (10.3, 191.0)	< 0.001
AST (U/L)	41.0 (23.0, 139.5)	90.0 (29.0, 255.0)	40.0 (22.0, 136.2)	29.0 (21.0, 58.0)	< 0.001
ALT (U/L)	46.0 (22.0, 153.0)	113.0 (33.0, 271.0)	47.0 (22.0, 161.0)	28.5 (19.0, 54.0)	< 0.001
ALB (g/dl)	38.4 (33.6, 42.4)	38.9 (35.4, 41.8)	37.5 (32.7, 41.8)	39.4 (32.8, 43.5)	0.006
FPG (mmol/L)	6.7 (5.3, 9.1)	6.0 (5.0, 7.3)	6.4 (5.2, 8.1)	8.6 (6.2, 13.3)	< 0.001
AMY (U/L)	167.5 (67.0, 699.8)	348.0 (87.0, 1107.0)	134.0 (63.8, 617.0)	127.0 (61.0, 319.0)	< 0.001
TG (mmol/L)	1.5 (1.0, 3.6)	0.9 (0.7, 1.1)	1.6 (1.2, 2.1)	6.4 (3.2, 13.3)	< 0.001
HDL (mmol/L)	1.1 (0.8, 1.5)	1.5 (1.3, 1.8)	1.0 (0.8, 1.3)	0.8 (0.6, 1.1)	< 0.001
CHOL (mmol/L)	4.6 (3.7, 5.9)	4.3 (3.6, 5.1)	4.4 (3.5, 5.4)	5.8 (4.3, 8.5)	< 0.001
Na (mmol/L)	139.6 (136.7, 141.8)	140.5 (138.5, 142.4)	140.0 (137.6, 141.9)	137.3 (134.1, 140.3)	< 0.001
Ca (mmol/L)	2.2 (2.0, 2.4)	2.2 (2.1, 2.3)	2.2 (2.0, 2.3)	2.2 (2.0, 2.4)	0.141
CREA (μmol/L)	75.0 (61.1, 89.0)	71.0 (61.0, 85.0)	75.1 (61.0, 88.0)	78.0 (64.0, 93.0)	< 0.001
AKI	250 (17.0)	47 (9.5)	76 (15.5)	127 (25.9)	< 0.001
SOFA (score)	2.0 (1.0, 4.0)	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	0.237
Etiology					< 0.001
biliary	988 (67.2)	463 (94.7)	374 (76.4)	151 (30.9)	
hyperlipidemic	344 (23.4)	8 (1.6)	67 (13.7)	269 (54.9)	
alcoholic	50 (3.4)	5 (1)	18 (3.6)	27(5.5)	
others	88 (6.0)	14 (2.8)	31 (6.3)	43 (8.7)	
Severity	nan	nan	nan	nan	< 0.001
mild and moderate	1304 (88.7)	464 (94.7)	444 (90.7)	396 (80.8)	
severe	166 (11.3)	26 (5.3)	46 (9.3)	94 (19.2)	

Table 1 (continued)

Characteristics		AIP			*P* value
	Total (*N* = 1470)	**T1 (*N* = 490) < 0.03**	**T2 (*N* = 490) 0.03–1.05**	**T3 (*N* = 490) ≥ 1.05**	
BISAP (score)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	0.352
HAPS	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	1.0 (0.0, 1.0)	< 0.001

Data are numbers (N) and percentages (%), or mean (SD), medians (IQR, 25th-75th percentile)

BMI: body mass index; LOS: length of hospital stay; d: days; DM: diabetes mellitus; CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; RR: respiratory rate; SpO_2: pulse oxygen saturation; Mechanical ventilation: noninvasive or invasive mechanical ventilation; Transfusion: blood transfusion; CRRT: continuous renal replacement treatment; WBC: white blood cell count; HGB: hemoglobin; HCT: hematocrit; PCT: procalcitonin; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALB: albumin; FPG: fasting plasma glucose; AMY: serum amylase; TG: triglyceride; HDL: high-density lipoprotein; CHOL: total cholesterol; Na: sodium; Ca: calcium; CREA: creatinine; AKI: Acute kidney injury; SOFA: sequential organ failure assessment score; BISAP: Bedside Index of Severity in Acute Pancreatitis score; HAPS: harmless acute pancreatitis score; AIP: atherogenic index of plasma; IQR: interquartile range; $P < 0.05$ was considered statistically significant

AP severity (Fig. 3B) (all $P > 0.05$). The resulting strength was verified using subgroup analyses.

ROC analysis

ROC analysis (Table S2 and Fig. 4) assessed AIP's potential for predicting AKI, resulting in an AUC of 0.64 (95% CI 0.60–0.67), with sensitivity and specificity of 54.26% and 69.65%, respectively. In comparison, the AUCs for SOFA, BISAP, and HAPS were 0.75, 0.69, and 0.69, respectively.

Similarly, to evaluate AIP's ability to predict AP severity, another ROC curve was plotted (Table S2 and Fig. 4), yielding an AUC of 0.65 (95% CI 0.61–0.70), with sensitivity and specificity of 60.82% and 66.34%, respectively. The AUCs for SOFA, BISAP, and HAPS were 0.81, 0.73, and 0.71, respectively.

Additionally, ROC curve analyses were performed for the biliary and hyperlipidemic pancreatitis cohorts (Table S3, Fig. S1 and Fig. S2). The AUC for predicting AKI and the severity of AP in the biliary pancreatitis group were 0.63 and 0.65, respectively. In contrast, the AUC values for the hyperlipidemic pancreatitis group were 0.60 for AKI prediction and 0.59 for AP severity.

Discussion

This study analyzed 1,470 patients with AP to explore the relationship of AIP with the incidence of AKI and the severity of AP among the Chinese population. Consequently, AIP independently predicted the risk, exhibiting linear dose-response relationships with both AKI and AP severity. The robustness of these associations was further supported by the comprehensive sensitivity and subgroup analyses, consistently highlighting the positive association between AIP and the occurrence of AKI and the severity of AP. While the AUCs may appear modest, the high sensitivity and operational simplicity of AIP make it particularly suitable for early triage in resource-constrained settings. AIP is a promising noninvasive predictive tool to evaluate the risk of AKI and AP severity, proposing potential clinical utility for early risk stratification and management.

The pathophysiology of AKI during AP is still inadequately explored. However, a critical pathophysiologic course is related to the premature activation of pancreatic enzymes in the acinar cells. It results in autodigestion of the pancreas and nearby tissues, thus promoting the development of AKI. The activated proteases and enzymes are released in the systemic circulation, leading to damage to the endothelium, resulting in the extravasation of fluid out of vascular space, hypotension, hypovolemia, increased abdominal pressure, hypercoagulability, intense vasoconstriction of kidneys, and deposition of glomerular fibrin [3]. A significant relationship between AP-AKI and inflammation has been established [15]. Accumulating evidence suggests that IR exerts an important effect on the occurrence and progression of AP-related AKI. For the assessment of IR, the hyperinsulinemic-euglycemic glucose clamp approach has been deemed the gold standard [16]; however, it is generally impractical owing to its demands for significant time, labor, expense, and technical expertise. Consequently, alternative indices such as AIP have emerged as practical, effective, and reliable methods for the assessment of IR [17–20]. Significant associations with various health outcomes have been revealed through AIP studies. Previous study indicates that AIP is related to the incidence of undiagnosed diabetes among acute coronary syndrome cases, particularly for patients with normal weight and low-density lipoprotein cholesterol content ≥ 1.8 mmol/L [21]. In addition, the J-shaped relationship was observed in the baseline AIP levels with all-cause mortality among American adults [22]. Yin et al. found that the AIP demonstrates the inverse L-shaped and J-shaped relationship with IR and T2DM, respectively, suggesting that AIP reduction to an optimal level could be crucial in preventing IR and T2DM [23]. Moreover, Qu et al. highlighted that the elevation of basic AIP contents markedly correlates with an increased incidence of stroke among middle-aged and elderly individuals, demonstrating different

Table 2 Baseline characteristics of included patients grouped using AKI and severity

Variables	Total (*N* = 1470)	Non-AKI (*N* = 1220)	AKI (*n* = 250)	*P* value	Mild and moderate AP (*N* = 1304)	Severe AP (*N* = 166)	*P* value
Male	790 (53.7)	623 (51.1)	167 (66.8)	< 0.001	691 (53)	97 (58.5)	0.177
Age (years)	53.0 (41.0, 65.0)	53.0 (41.0, 64.0)	56.0 (44.0, 69.0)	0.002	53.0 (41.0, 64.5)	56.0 (43.0, 69.0)	0.092
BMI (kg/m^2)	24.2 (21.7, 26.7)	24.1 (21.8, 26.7)	24.2 (20.8, 26.9)	0.437	24.2 (21.9, 26.7)	23.4 (20.2, 27.0)	0.038
Death	23 (1.6)	6 (0.5)	17 (6.8)	< 0.001	5 (0.4)	18(10.5)	< 0.001
ICU	240 (16.3)	111 (9.1)	129 (51.6)	< 0.001	75(5.8)	165 (99.4)	< 0.001
LOS (d)	16.6 ± 12.7	15.8 ± 11.6	20.8 ± 16.5	< 0.001	15.5 ± 10.4	25.3 ± 22.4	< 0.001
Hypertension	370 (25.2)	296 (24.2)	74 (29.6)	< 0.001	339 (25.2)	52 (31.3)	0.106
DM	203 (13.8)	155 (12.7)	48 (19.2)	0.059	173 (13.3)	30 (18.1)	0.295
CHD	88 (6.0)	75 (6.1)	13(10.0)	0.021	71(6.3)	17 (10.5)	0.04
COPD	54 (3.7)	39 (3.2)	15 (5.2)	0.081	44 (3.4)	10 (6.0)	0.263
SBP (mmHg)	129.0 (117.0, 143.0)	130.0 (119.0, 143.0)	123.0 (110.0, 140.0)	< 0.001	129.0 (117.0, 142.0)	128.0 (110.0, 147.5)	0.561
DBP (mmHg)	80.0 (72.0, 90.0)	80.0 (74.0, 90.0)	80.0 (66.0, 89.0)	< 0.001	80.0 (72.0, 90.0)	80.0 (70.0, 90.0)	0.400
HR (bpm)	80.0 (72.0, 93.0)	78.0 (72.0, 90.0)	90.0 (76.0, 110.0)	< 0.001	78.0 (72.0, 90.0)	100.0 (81.5, 118.0)	< 0.001
Temperature (degree C)	36.5 (36.4, 36.7)	36.5 (36.4, 36.6)	36.5 (36.4, 36.8)	0.013	36.5 (36.4, 36.7)	36.6 (36.4, 36.7)	0.006
RR (bpm)	20.0 (19.0, 20.0)	20.0 (19.0, 20.0)	20.0 (19.0, 21.0)	0.009	20.0 (19.0, 20.0)	20.0 (19.0, 25.0)	< 0.001
SpO_2 (%)	99.0 (97.0, 100.0)	99.0 (98.0, 100.0)	98.0 (96.0, 100.0)	< 0.001	99.0 (98.0, 100.0)	97.0 (94.0, 99.0)	< 0.001
Mechanical ventilation	150 (10.4)	70 (5.8)	80 (32.0)	< 0.001	47 (3.6)	103 (62.0)	< 0.001
Transfusion	148 (10.0)	63(5.2)	95 (38.0)	< 0.001	68(5.2)	80 (48.2)	< 0.001
CRRT	90 (6.1)	20 (1.7)	70 (27.6)	< 0.001	31(2.3)	59 (35.5)	< 0.001
WBC (×10^9/L)	9.8 (6.6, 13.6)	9.6 (6.4, 13.2)	11.1 (7.8, 15.8)	< 0.001	9.6 (6.5, 13.2)	12.2 (8.9, 16.8)	< 0.001
HGB (g/L)	129.0 (114.0, 145.0)	129.0 (116.0, 144.0)	128.0 (106.0, 151.0)	0.266	129.0 (115.0, 144.0)	130.0 (103.5, 149.5)	0.668
HCT (%)	38.5 (34.5, 42.7)	38.7 (34.9, 42.3)	37.6 (32.1, 43.5)	0.061	38.5 (34.7, 42.3)	39.4 (30.7, 44.6)	0.877
PCT (ng/ml)	0.2 (0.1, 0.9)	0.1 (0.0, 0.6)	1.1 (0.2, 6.5)	< 0.001	0.1 (0.0, 0.6)	1.9 (0.6, 20.6)	< 0.001
CRP (mg/L)	37.1 (6.6, 134.7)	31.4 (5.9, 119.0)	88.7 (16.9, 200.2)	< 0.001	32.0 (6.0, 121.6)	113.3 (16.4, 216.5)	< 0.001
AST (U/L)	41.0 (23.0, 139.5)	41.0 (23.0, 143.0)	45.0 (25.9, 132.0)	0.356	39.0 (22.0, 137.0)	54.0 (31.0, 176.5)	0.002
ALT (U/L)	46.0 (22.0, 153.0)	48.0 (23.0, 163.0)	35.0 (20.0, 81.0)	< 0.001	46.0 (22.0, 153.5)	45.0 (22.0, 115.5)	0.697
ALB (g/dl)	38.4 (33.6, 42.4)	39.1 (34.9, 42.7)	34.8 (28.6, 39.7)	< 0.001	38.9 (34.8, 42.7)	32.7 (27.8, 38.8)	< 0.001
FPG (mmol/L)	6.7 (5.3, 9.1)	6.6 (5.3, 8.9)	7.5 (5.7, 11.2)	< 0.001	6.6 (5.3, 8.9)	8.3 (6.3, 11.2)	< 0.001
AMY (U/L)	167.5 (67.0, 699.8)	163.0 (64.5, 716.0)	202.0 (92.0, 607.0)	0.065	163.0 (66.0, 666.0)	247.0 (87.0, 934.0)	0.017
TG (mmol/L)	1.5 (1.0, 3.6)	1.5 (1.0, 3.4)	1.8 (1.2, 6.4)	< 0.001	1.5 (1.0, 3.4)	1.9 (1.1, 5.4)	0.003
HDL (mmol/L)	1.1 (0.8, 1.5)	1.2 (0.9, 1.5)	0.9 (0.5, 1.3)	< 0.001	1.2 (0.9, 1.5)	0.7 (0.4, 1.3)	< 0.001
CHOL (mmol/L)	4.6 (3.7, 5.9)	4.6 (3.7, 5.8)	4.8 (3.4, 7.4)	0.259	4.6 (3.7, 5.8)	4.9 (3.1, 13.7)	0.022
Na (mmol/L)	139.6 (136.7, 141.8)	139.7 (137.1, 141.8)	137.9 (135.1, 141.0)	< 0.001	139.6 (136.9, 141.7)	138.9 (135.4, 142.1)	0.328
Ca (mmol/L)	2.2 (2.0, 2.4)	2.2 (2.1, 2.4)	2.1 (1.9, 2.3)	< 0.001	2.2 (2.1, 2.4)	2.0 (1.8, 2.2)	< 0.001
CREA (μmol/L)	75.0 (61.1, 89.0)	71.0 (59.0, 83.0)	95.5 (84.0, 193.0)	< 0.001	73.0 (60.9, 87.0)	87.0 (75.2, 99.0)	< 0.001
AKI	250 (17.0)	0 (0)	250 (100)	< 0.001	158(12.1)	92 (55.4)	< 0.001
SOFA (score)	2.0 (1.0, 4.0)	2.0 (1.0, 3.0)	5.0 (2.0, 7.0)	< 0.001	2.0 (1.0, 3.0)	5.0 (3.0, 7.5)	< 0.001
Etiology				< 0.001			< 0.001
biliary	988 (67.3)	861 (70.6)	128(51.2)		918 (70.3)	70 (42.2)	
hyperlipidemic	344 (23.4)	281 (23)	63 (25.2)		306 (23.5)	38 (22.9)	
alcoholic	50 (3.4)	40 (3.3)	10 (4.0)		40 (3.1)	10 (6.0)	
others	88 (5.9)	38 (3.1)	49(19.6)		40 (3.1)	48 (28.9)	
Severity				< 0.001			< 0.001
mild and moderate	1304 (88.7)	1147 (94)	157 (62.8)		1304 (100)	0 (0)	

Table 2 (continued)

Variables	Total (*N* = 1470)	Non-AKI (*N* = 1220)	AKI (*n* = 250)	*P* value	Mild and moderate AP (*N* = 1304)	Severe AP (*N* = 166)	*P* value
severe	166 (11.3)	73 (6)	93 (37.2)		0 (0)	166 (100)	
BISAP (score)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	< 0.001	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	< 0.001
HAPS (score)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	1.0 (0.0, 1.0)	< 0.001	0.0 (0.0, 1.0)	1.0 (1.0, 2.0)	< 0.001

Data are numbers (N) and percentages (%), or mean (SD), medians (IQR, 25th-75th percentile)

BMI: body mass index; LOS: length of hospital stay; d, days; DM: diabetes mellitus; CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; RR: respiratory rate; SpO_2: pulse oxygen saturation; Mechanical ventilation: noninvasive or invasive mechanical ventilation; Transfusion: blood transfusion; CRRT: continuous renal replacement treatment; WBC: white blood cell count; HGB: hemoglobin; HCT: hematocrit; PCT: procalcitonin; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALB: albumin; FPG: fasting plasma glucose; AMY: serum amylase; TG: triglyceride; HDL: high-density lipoprotein; CHOL: total cholesterol; Na: sodium; Ca: calcium; CREA: creatinine; AKI: Acute kidney injury; SOFA: sequential organ failure assessment score; BISAP: Bedside Index of Severity in Acute Pancreatitis score; HAPS: harmless acute pancreatitis score; AIP: atherogenic index of plasma; IQR: interquartile range; $P < 0.05$ was considered statistically significant

Table 3 Multiple logistic regression analysis for AIP with AKI and severity in the acute pancreatitis (AP) population

	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
AKI				
AIP	1.44 (1.29 ~ 1.61), < 0.001	1.71 (1.5 ~ 1.94), < 0.001	1.62 (1.4 ~ 1.87), < 0.001	1.45 (1.15 ~ 1.82), 0.001
AIP, tertiles				
T1	Reference	Reference	Reference	Reference
T2	1.74 (1.19 ~ 2.56), 0.004	1.83 (1.23 ~ 2.71), 0.003	1.7 (1.13 ~ 2.56), 0.011	1.27 (0.71 ~ 2.25), 0.419
T3	3.33 (2.33 ~ 4.77), < 0.001	4.61 (3.11 ~ 6.84), < 0.001	3.74 (2.45 ~ 5.71), < 0.001	2.5 (1.31 ~ 4.77), 0.005
P - trend	< 0.001	< 0.001	< 0.001	0.005
Severity				
AIP	1.54 (1.35 ~ 1.75), < 0.001	1.83 (1.57 ~ 2.12), < 0.001	1.68 (1.4 ~ 2.02), < 0.001	1.66 (1.3 ~ 2.12), < 0.001
AIP, tertiles				
T1	Reference	Reference	Reference	Reference
T2	1.82 (1.12 ~ 2.97), 0.017	2.01 (1.22 ~ 3.3), 0.006	1.74 (1 ~ 3.03), 0.05	1.44 (0.75 ~ 2.78), 0.277
T3	4.21 (2.69 ~ 6.58), < 0.001	6.04 (3.74 ~ 9.75), < 0.001	4.06 (2.35 ~ 7.01), < 0.001	3.1 (1.53 ~ 6.27), 0.002
P - trend	< 0.001	< 0.001	< 0.001	0.001

Results for each model are presented as OR (95% CI), *P* value

AKI: acute kidney injury; AIP: atherogenic index of plasma; T: tertile; OR: odds ratio; 95%CI: 95% confidence interval

AIP of Tertile 1: < 0.03; Tertile 2: 0.03–1.05; Tertile 3: ≥ 1.05

Model 1: Sex + Age + BMI

Model 2: Sex + Age + BMI + Hypertension + DM + CHD + COPD + SBP + DBP + HR + Temperature + RR + SpO_2

Model 3: Sex + Age + BMI + Hypertension + DM + CHD + COPD + SBP + DBP + HR + Temperature + RR + SpO_2 + HGB + WBC + CRP + PCT + AMY + Na + Ca + CREA + CHOL + BISAP + HAPS + SOFA + Etiology

features according to their status of glucose metabolism [24]. However, to date, no study has analyzed the relationship of the AIP with AKI in patients with AP.

AIP is strongly associated with cardiovascular diseases [25, 26] and demonstrates significant ability in predicting various metabolic disorders, particularly type 2 diabetes and non-alcoholic fatty liver disease (NAFLD) [27],T2DM, along with metabolic syndrome, dyslipidemia, and NAFLD, are well-established risk factors for AP [28, 29]. A strong theoretical foundation is observed for investigating the relationship between these indices and the severity of AP. The association between AIP and the severity of pancreatitis has been minimally explored. A single-center study comprising 323 participants

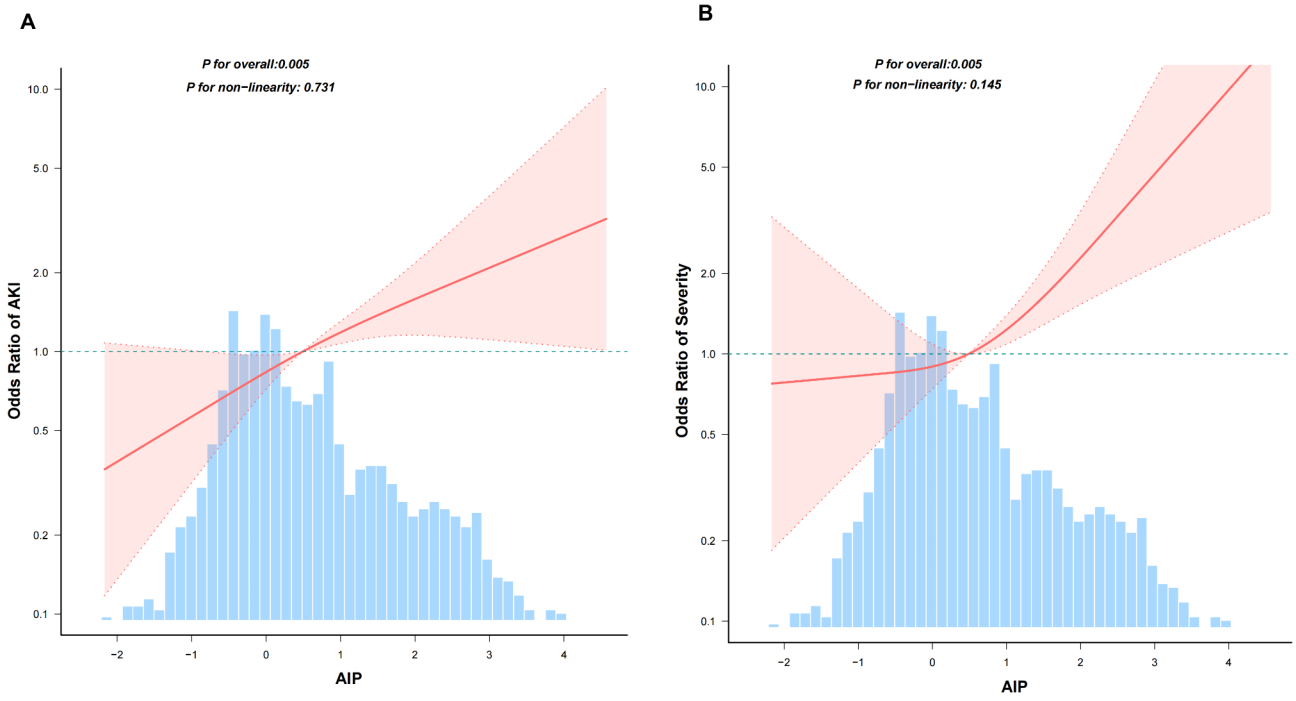

Fig. 2 Association between the AIP with AKI (**A**) and AP severity (**B**) in RCS. Adjusted for all covariables as model 3. Solid lines indicate the odds ratio of AKI or the severity of AP and dotted lines represent the corresponding 95% CI. OR = 1 was set as the reference line. AIP: atherogenic index of plasma; AKI: acute kidney injury; AP: acute pancreatitis; RCS: restricted cubic spline

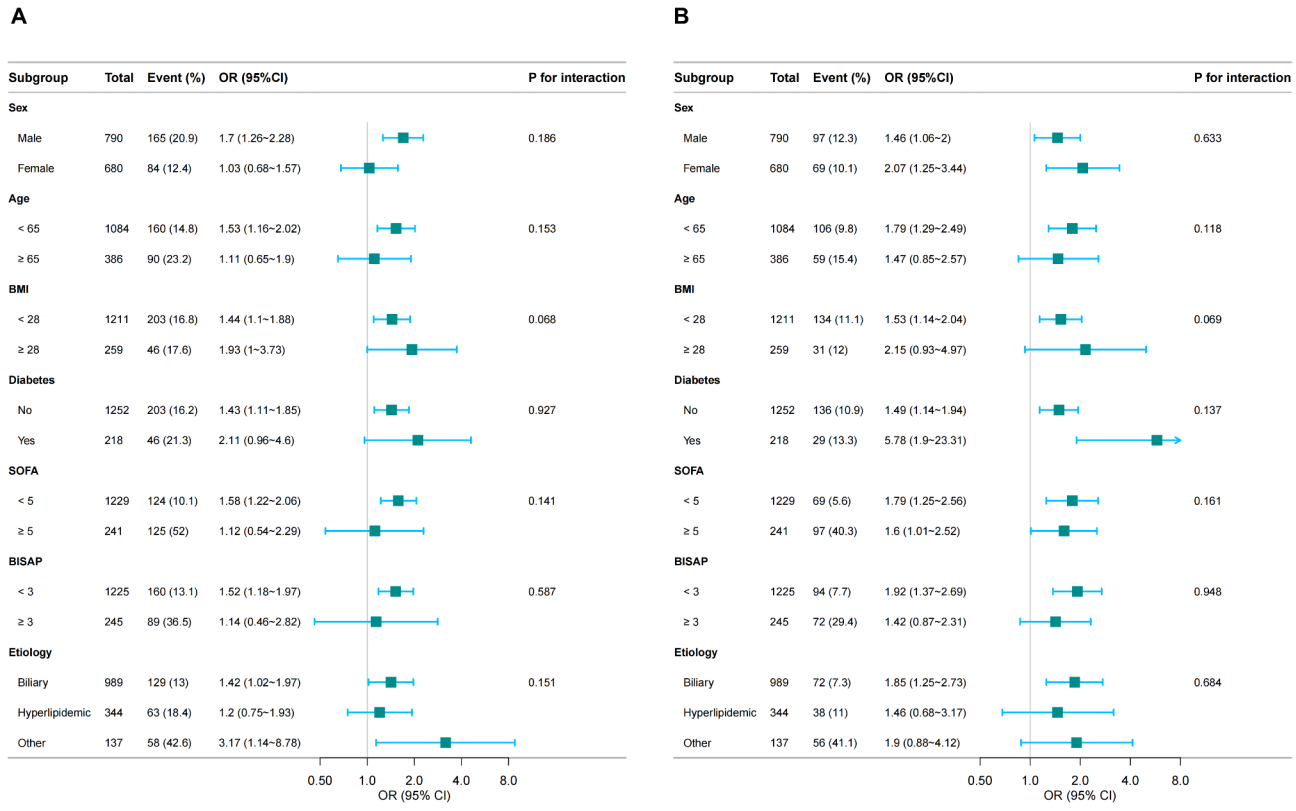

Fig. 3 The relationship between AIP with AKI **(A)** and **AP** severity **(B)** according **to** the basic features. Except for the stratification component itself, each stratification factor was adjusted for all covariables as model 3

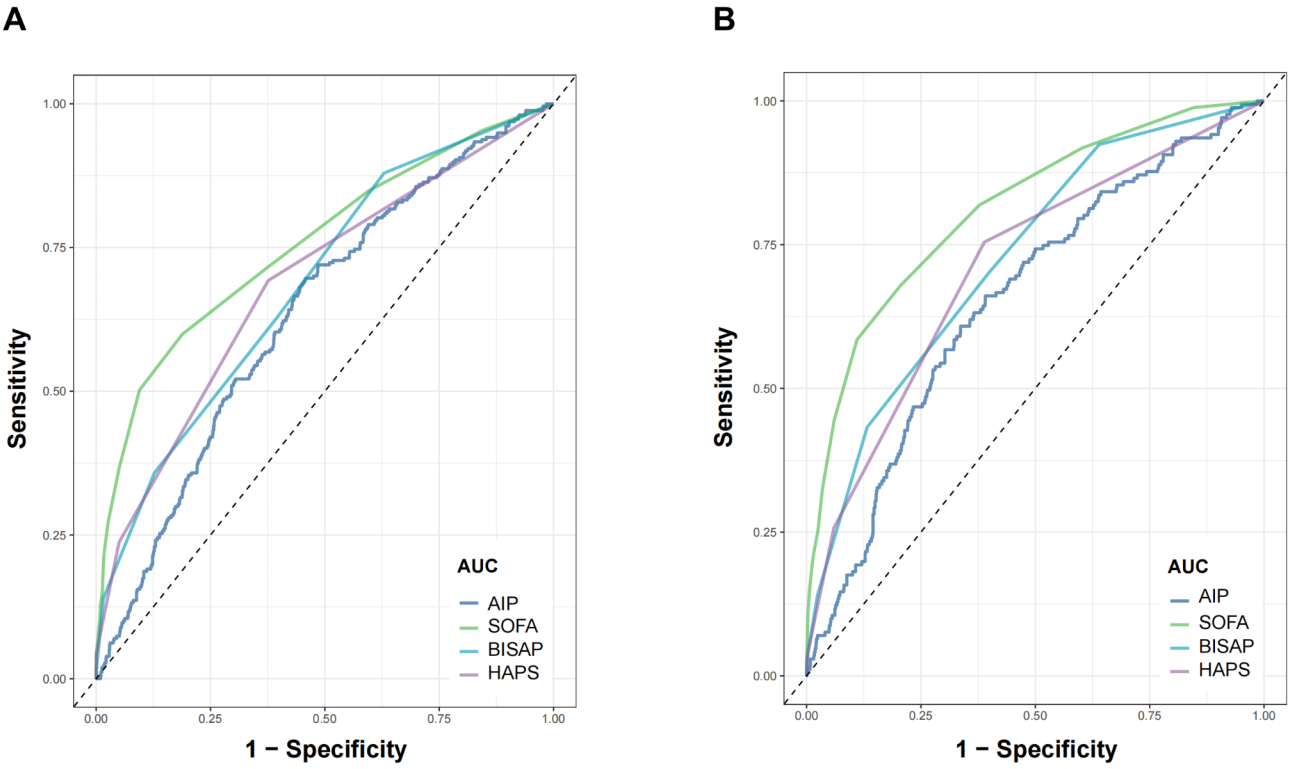

Fig. 4 ROC curves for AIP to predict AKI risk (**A**) and AP severity (**B**) in all participants. AUC: area under the curve; ROC: receiver operating characteristic; AIP: atherogenic index of plasma; AKI: acute kidney injury; AP: acute pancreatitis; SOFA: sequential organ failure assessment score; BISAP: Bedside Index of Severity in Acute Pancreatitis score; HAPS: harmless acute pancreatitis score

demonstrated significantly elevated AIP levels among patients with SAP versus those having mild disease ($P < 0.001$) [30]. The study by Cho et al. reported that the AUC was 0.709 for AIP in forecasting SAP. While this study's findings are in accordance with these results, a slightly lower AUC of 0.64 was observed. This was potentially associated with the different sample characteristics and study populations, particularly with a higher proportion of alcohol-induced pancreatitis in their cohort compared to our predominantly Chinese population.

This study conducted thorough sensitivity analyses to mitigate bias and enhance our result strength across multiple stratified subgroups, including patients with high versus normal BMI, presence versus absence of DM, alcoholic versus nonalcoholic pancreatitis, and hyperlipidemic versus non-hyperlipidemic pancreatitis. Our findings show strong predictive capabilities of AIP for AKI and SAP across these diverse subgroups, thus corroborating and extending the limited existing evidence. This consistency across various etiologies of AP and comorbidities underscores the potential utility of these indices as valuable prognostic tools in the management of AP. In biliary pancreatitis, systemic inflammation [31, 32] and biliary obstruction can alter AIP levels. While in hyperlipidemic pancreatitis, elevated AIP may signal a different pathological mechanism due to the toxic effects of triglycerides on the pancreas, indicating unique lipoprotein changes. This implies that AIP could serve as a valuable biomarker for identifying patients at risk of pancreatitis.

Contemporary studies have determined the robust association of IR with both the prognosis and severity of AP [33]. This relationship warrants a detailed assessment of the underlying pathophysiological mechanisms. IR is the decreased sensitivity or compromised target tissue or organ response to insulin, affecting the absorption and use of glucose. However, this metabolic dysfunction has several important implications. First, IR plays a critical role in chronic metabolic disorders and their complications [33]. Second, the condition presents as a chronic, low-grade inflammatory state, possibly worsening inflammatory cascades in AP [34]. Third, a complex pathway of kidney injury is initiated by IR, primarily by the sympathetic nervous system activation, which triggers increased activity of the renin-angiotensin system and elevation of glomerular capillary pressure. These hemodynamic alterations subsequently disturb renal cell metabolism and induce structural changes, including mesangial hyperplasia and renal hypertrophy, ultimately leading to endothelial cell proliferation and progressive kidney damage.

Both AKI and AP are characterized by inflammatory responses, which may be influenced by altered lipid profiles associated with AIP. Elevated levels of pro-inflammatory cytokines (such as TNF-α and IL-6) can be triggered by the accumulation of atherogenic lipoproteins [35, 36]. This inflammatory milieu can lead to further complications, including endothelial dysfunction and microvascular injury in the kidneys and pancreas [37, 38], exacerbating the severity of both conditions.

This study offers vital insights into the mechanistic relationship between IR and AP. Comprehending these pathophysiological pathways may assist in the development of targeted therapeutic interventions and allow for more precise prognostic assessments in AP management. This understanding potentially paves the way for innovative therapeutic strategies centered on IR modulation in the treatment of AP.

Strengths and limitations

This study has several strengths. To the best of our knowledge, this is the first study to successfully establish that one IR factor linked to AKI is independently and positively related to the severity of AP in the population. Secondly, the statistical methodology used in this study reduced the residual confounders by rigorous adjustments. Thirdly, various sensitivity analyses were performed to evaluate the reliability of the results, like converting AIP to a categorical factor; assessing the relationship of AIP with AKI and AP severity by excluding patients with BMI ≥ 25 kg/m², DM, alcoholic pancreatitis, and hyperlipidemic pancreatitis; performing subgroup analyses; and computation of E-values for exploring the possible unmeasured variables.

However, several limitations warrant consideration. Firstly, although this was the largest investigation to date comparing IR indices in patients with AP, the retrospective study design poses certain constraints. Secondly, as there was a lack of longitudinal data on glucose and lipid parameters, a dynamic evaluation of IR indices on outcomes could not be performed. Finally, although strong associations between AIP and clinical outcomes were established, the underlying mechanistic pathways remain to be completely elucidated.

Conclusions

To summarize, AIP is consistently and strongly related to the higher incidence of AKI and severity of AP among the Chinese population. These findings suggest that the routine monitoring of AIP could be a valuable clinical tool to identify high-risk patients for AKI and severe AP early. The clinical implications of the association between AIP, AKI, and severe AP highlight the importance of routine AIP monitoring in clinical practice. By recognizing individuals at high risk, healthcare providers can implement early interventions and personalized care strategies, ultimately improving patient outcomes and contributing to the growing body of research surrounding AIP.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02520-x.

Supplementary Material 1

Acknowledgements

We extend our gratitude to Dr. Liu Jie (People's Liberation Army of China General Hospital, Beijing, China), for his insightful review and comments on the manuscript.

Author contributions

Wen Wu and Yiming Li conceived, designed the study, Yupei Zhang, Chunzhen Zhang, Xing Chen, Xingguang Qu, and Zhaohui Zhang obtained the data, which was analyzed by Wen Wu. Yiming Li and Wen Wu interpreted the data and results and drafted the manuscript. Zhiyong Peng and Rong Zhang critically revised the manuscript for intellectual content. All authors contributed to revising the article and approved the final version.

Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial, or not-for profit sector.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The present retrospective study was approved by the Ethics Committee of Yichang Central People's Hospital, the First College of Clinical Medical Science of China Three Gorges University (ethical approval number: 2023-130-01), and performed following Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Critical Care Medicine, Zhongnan Hospital of Wuhan University, Wuhan430071, Hubei, China
[2]Clinical Research Center of Hubei Critical Care Medicine, Wuhan 430071, Hubei, China
[3]Department of Emergency and Critical Care Medicine, Yichang Central People's Hospital, The First College of Clinical Medical Science of China Three Gorges University, Yichang 443003, Hubei, China
[4]The First College of Clinical Medical Science, China Three Gorges University, Yichang 443003, Hubei, China

Received: 7 January 2025 / Accepted: 10 March 2025
Published online: 25 March 2025

References

1. Oiva J, et al. Acute pancreatitis with organ dysfunction associates with abnormal blood lymphocyte signaling: controlled laboratory study. Crit Care. 2010;14:R207.
2. Forsmark CE. Acute pancreatitis. N Engl J Med (2016).
3. Nassar TI, Qunibi WY. AKI associated with acute pancreatitis. CJASN. 2019;14:1106–15.

4. Sims EK, Carr ALJ, Oram RA, DiMeglio LA. Evans-Molina, C. 100 years of insulin: celebrating the past, present and future of diabetes therapy. Nat Med. 2021;27:1154–64.
5. Dobiášová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate inapob-lipoprotein-depleted plasma (FERHDL). Clin Biochem. 2001;34:583–8.
6. Krishna SG, et al. Morbid obesity is associated with adverse clinical outcomes in acute pancreatitis: A Propensity-Matched study. Am J Gastroenterol. 2015;110:1608–19.
7. Mazidi M, Katsiki N, Mikhailidis DP, Banach M. Association of ideal cardiovascular health metrics with serum uric acid, inflammation and atherogenic index of plasma: A population-based survey. Atherosclerosis. 2019;284:44–9.
8. Zheng X, Zhang X, Han Y, Hu H, Cao C. Nonlinear relationship between atherogenic index of plasma and the risk of prediabetes: a retrospective study based on Chinese adults. Cardiovasc Diabetol. 2023;22:205.
9. Banks PA, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–11.
10. Khwaja AKDIGO. Clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120:c179–84.
11. Annane D, et al. Hydrocortisone plus fludrocortisone for adults with septic shock. N Engl J Med. 2018;378:809–18.
12. Ferreira FL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001;286:1754.
13. von Elm E, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370:1453–7.
14. Zhang Z. Multiple imputation with multivariate imputation by chained equation (MICE) package. Annals Translational Med 4, (2016).
15. Wu W et al. Predictive value of C-Reactive protein/albumin ratio for acute kidney injury in patients with acute pancreatitis. J Inflamm Res.
16. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiology-Endocrinology Metabolism. 1979;237:E214.
17. Qin Z. The atherogenic index of plasma plays an important role in predicting the prognosis of type 2 diabetic subjects undergoing percutaneous coronary intervention: results from an observational cohort study in China. (2020).
18. Tan MH, Johns D, Glazer NB. Pioglitazone Reduces Atherogenic Index of Plasma in Patients with Type 2 Diabetes. *Clinical Chemistry* (2004).
19. Hirschler V, Maccallini G, Sanchez M, Gonzalez C, Molinari C. Association between triglyceride to HDL-C ratio and insulin resistance in Indigenous Argentinean children: TG/HDL-C and insulin resistance in Indigenous children. Pediatr Diabetes. 2015;16:606–12.
20. Bello-Chavolla OY, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur J Endocrinol. 2018;178:533–44.
21. Xu S, et al. The association between the AIP and undiagnosed diabetes in ACS patients with different body mass indexes and LDL-C levels: findings from the CCC-ACS project. Cardiovasc Diabetol. 2024;23:77.
22. Qin M, Chen B. Association of atherogenic index of plasma with cardiovascular disease mortality and all- cause mortality in the general US adult population: results from NHANES 2005–2018. (2024).
23. Yin B et al. Non-linear association of atherogenic index of plasma with insulin resistance and type 2 diabetes: a cross-sectional study. (2023).
24. Qu L, et al. Association between atherogenic index of plasma and new-onset stroke in individuals with different glucose metabolism status: insights from CHARLS. Cardiovasc Diabetol. 2024;23:215.
25. Liu Y, et al. The relation between atherogenic index of plasma and cardiovascular outcomes in prediabetic individuals with unstable angina pectoris. BMC Endocr Disord. 2023;23:187.
26. Feng X, et al. The combined predictive power of the atherogenic index of plasma and serum glycated albumin for cardiovascular events in postmenopausal patients with acute coronary syndrome after percutaneous coronary intervention. Lipids Health Dis. 2024;23:352.
27. Xue Y, Xu J, Li M, Gao Y. Potential screening indicators for early diagnosis of NAFLD/MAFLD and liver fibrosis: triglyceride glucose index–related parameters. Front Endocrinol. 2022;13:951689.
28. Váncsa S, et al. Metabolic-associated fatty liver disease is associated with acute pancreatitis with more severe course: post hoc analysis of a prospectively collected international registry. UEG J. 2023;11:371–82.
29. Hosaka M, Kubo T, Matsuoka T, Hasegawa T. Severe acute pancreatitis rapidly developed into pulmonary edema and diffuse alveolar hemorrhage leading to respiratory failure: an autopsy case. Cureus. 2023. https://doi.org/10.7759/cureus.46560.
30. Cho SK, Kim JW, Huh JH, Lee KJ. Atherogenic Index of Plasma Is a Potential Biomarker for Severe Acute Pancreatitis: A Prospective Observational Study. (2020).
31. Sivgin H, Çetin S. Effect of empagliflozin use on monocyte high-density lipoprotein ratio and plasma atherogenic index in obese and non-obese type 2 diabetic patients.
32. Chen JW, et al. The role of monocyte to High-Density lipoprotein cholesterol ratio in prediction of carotid Intima-Media thickness in patients with type 2 diabetes. Front Endocrinol. 2019;10:191.
33. Cho SK, Huh JH, Yoo JS, Kim JW, Lee K. J. HOMA-estimated insulin resistance as an independent prognostic factor in patients with acute pancreatitis. Sci Rep. 2019;9:14894.
34. Lee Y-H, Pratley RE. The evolving role of inflammation in obesity and the metabolic syndrome. Curr Diab Rep. 2005;5:70–5.
35. Pirro M, et al. Lipoprotein(a) and inflammation: A dangerous duet leading to endothelial loss of integrity. Pharmacol Res. 2017;119:178–87.
36. Chan Y-H, Ramji DP. Probing inflammasome activation in atherosclerosis. In: Ramji D vol, editor. Atherosclerosis. Volume 2419. New York, NY: Springer US; 2022. pp. 313–31.
37. Gasiorowska A, et al. Subclinical inflammation and endothelial dysfunction in patients with chronic pancreatitis and newly diagnosed pancreatic cancer. Dig Dis Sci. 2016;61:1121–9.
38. Dumnicka P et al. The Interplay between Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. *IJMS* 18, 354 (2017).

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.