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A retrospective study for prediction severity of hypertriglyceridemia-associated acute pancreatitis patients and association with in-hospital mortality

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Abstract

Background: Hypertriglyceridemia-associated acute pancreatitis (HTG-AP) is the second leading cause of acute pancreatitis (AP) in China. This study aimed to identify HTG-AP severity and clarify the association between the triglyceride-glucose (TyG) index and in-hospital mortality in severe acute pancreatitis (SAP) patients.

Method: A total of 289 HTG-AP patients were separated into SAP (n=104) and non-SAP (n=185) groups in Xuanwu Hospital from 2014 to 2023. Multivariable logistic regression analyses were used to developed a formula based on laboratory tests and clinical assessments for predicting the severity of AP. Restricted cubic spline (RCS) was used to elucidate the link between the TyG index and in-hospital mortality.

Results: Both SAP and non-SAP patients had a median onset age of 39 years (68.2% male). SAP patients presented higher serum levels of D-Dimer, triglycerides, glucose, blood urea nitrogen, creatinine, procalcitonin, C-reactive protein, and interleukin-6, along with lower levels of calcium and ALB, accompanied by significant values of the TyG index and scores of the acute physiology and chronic health evaluation (APACHE-II) and modified computed tomography severity index ($p<0.05$). The multivariable logistic regression demonstrated superior predictive performance, with an AUC of

0.940, a specificity of 0.784, and a sensitivity of 0.990. A non-linear relationship was observed between the TyG index within 24 hours of admission and in-hospital mortality across Days 7, 30, and 120.

Conclusion: This study developed a multivariable logistic regression model incorporating the TyG index, APACHE II score, and serum creatinine to predict SAP and highlight the prognostic value of the TyG index in HTG-AP.

Keywords: hypertriglyceridemia-associated acute pancreatitis; triglyceride-glucose index; prediction; clinical outcome

1. Introduction

Acute pancreatitis (AP) is a common gastrointestinal disease caused by damage to the acinar cells and activation of digestive enzymes resulting in autodigestion of pancreatic parenchyma and systemic inflammation, which can lead to hospital admission, mortality, and socioeconomic issues [1,2]. The global incidence of AP in previous reviews has been reported 23-49 cases per 100,000 general population per year throughout the world and varying greatly in different regions [3,4].

AP patients suffer from acute epigastric pain in the upper abdomen radiating to the back, accompanied by elevated serum lipase and/or amylase, or typical imaging findings [5,6]. According to the revised Atlanta classification, AP severity is divided into mild, moderately severe, and severe. Severe acute pancreatitis (SAP) is defined as persistent organ failure over 48 hours [7]. Approximately 15% of patients with AP develop to SAP, which has a higher mortality rate of 2-9%. Gallstones, alcohol abuse, and hypertriglyceridemia (HTG) are the main causes of AP. In recent years, the increasing prevalence of HTG has become the second etiology of AP in China[8]. Patients with hypertriglyceridemia-associated acute pancreatitis (HTG-AP) are more likely to experience severe disease progression and persistent organ failure[9]. The prompt recognition of SAP induced by HTG is essential in initial treatment and management.

The triglyceride and glucose (TyG) index is a marker of insulin resistance and related metabolic abnormalities, which is reported as an independent prognostic factor

in AP patients and could be used as a reliable biomarker for SAP[10]. Triglyceride glucose-body mass index (TyG-BMI) has also been proposed as an effective predictor of in-hospital and intensive care unit (ICU) mortality in patients with severe AP [11].

However, the relationship between the TyG index and in-hospital mortality in severe HTG-AP patients has not been reported before. This study aimed to compare baseline data of AP and SAP patients with HTG, explore predictive indicators for HTG-SAP patients by multiple logistic regression, and investigate the relationship between mortality rate and TyG index in SAP patients during short-term and long-term follow-up.

2. Methods

2.1 Study Design

Patients with first diagnosis of HTG-AP were consecutively enrolled in the Department of General Surgery at the Xuanwu Hospital from January 2014 to December 2023.The cohort included detailed clinical records of 104 SAP patients and 185 non-SAP patients. Exclusion criteria include patients under 18 years of age, incomplete clinical records, acute or chronic pancreatitis due to other causes (e.g., gallstones, alcoholic pancreatitis, autoimmune pancreatitis); severe comorbidities, such as advanced malignancy, end-stage hepatic or renal failure, or acute myocardial infarction; pregnancy or lactation.

Early fluid therapy was used to treat AP patients with Lactated Ringer's solution until the resuscitation goals were reached, with urinary output over 0.5ml/kg/hour. Once SAP was suspected, the patient was transferred to the ICU team for further management [5,12]. This research was approved by the Ethics Committee of Beijing Xuanwu Hospital. Informed consent was obtained from all patients. Patients were followed until death or 120 days after first admission. All mortality outcomes were assessed during hospitalization. Once patients with suspected or confirmed SAP were continuously managed in the ICU and no deaths occurred after discharge, the 7-day, 30-day, and 120-day mortality endpoints represented time-specific in-hospital mortality.

2.2 HTG-AP and SAP Definitions

HTG-AP was diagnosed based on the following criteria:(1) Conforming to the

2012 revised Atlanta definitions of AP which require at least two of the following three features: acute onset of persistent abdominal pain radiating to the back; serum lipase at least three times higher than the upper limit of normal; characteristic imaging findings of AP on contrast-enhanced computed tomography and magnetic resonance imaging or transabdominal ultrasonography. (2) First serum triglyceride (TG) level is over 1000mg/dL, or over 500mg/dL accompanied with chylous blood. According to the Atlanta classification, all HTG-AP patients were divided into SAP and non-SAP groups, in which SAP was defined as persistent organ failure (one or more organs) over 48 hours [7].

Secondary outcomes were assessed during the 120-day follow-up period. Recurrent acute pancreatitis (RAP) was identified with the definition that a syndrome of multiple distinct acute inflammatory responses originating within the pancreas experienced 2 or more episodes of documented AP, separated by at least 3 months [13]. New onset diabetes mellitus secondary to AP was diagnosed according to the American Diabetes Association criteria: glycated hemoglobin ≥ 6.5% or two-hour plasma glucose ≥ 11.1 mmol/L during oral glucose tolerance test in patients without a history of diabetes [14]. Pancreatic exocrine insufficiency was diagnosed based on values of FE-1 expressed in stools (Levels < 200 μg/g). No delay is recommended in confirming the diagnosis of PEI after recovery from AP [15,16].

2.3 Participant Baseline

We collected the epidemiological characteristics of the patients, including age, sex, and body mass index (BMI). Medical history was recorded as circulatory disease, pulmonary disease, renal disease, diabetes mellitus, hyperlipidemia, and tobacco or alcohol abuse. Laboratory parameters were tested at first admission and before initiation of treatment: white blood count, hematocrit, neutrophil count, lymphocyte count, platelet count, TG, blood urea nitrogen (BUN), albumin (ALB), procalcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6), serum total cholesterol. To ensure the independence of observations, only data from the initial hospitalization were included in the analysis. 39 patients who experienced recurrent AP and retreated, data from subsequent admissions were excluded. Missing values were 0 for all variables

include in the analyses.

2.4 Assessment of AP

The formula for calculating the TyG index was Ln[TG(mg/dL) × plasma glucose(mg(dL)/2] [17]. The TyG-BMI index was Ln [1/2 plasma glucose (mg/dL) × triglycerides (mg/dL)] × BMI [18]. The acute physiology and chronic health evaluation (APACHE-II) score was utilized to assess and monitor AP based on 12 physiologic measurements, age, and previous health status, ranging from 0 to 71, with higher scores indicating more severe complications. The APACHE II score was calculated based on clinical and laboratory data recorded during the first admission [19,20]. The modified computed tomography severity index (mCTSI) was used to grade severity of pancreatitis by categorizing the as mild (0-2 points), moderate (4-6 points), or severe (8-10 points) [21].

2.5 Statistical Analysis

The SPSS version 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) was applied for statistical analyses. Shapiro-Wilk test was used to evaluate data normality. The Mann-Whitney U-test was used for comparisons between the SAP group and non-SAP group with non-normal distribution, while Student's t-test was used for normal distributions. Fisher's exact test was used for qualitative data analysis. For non-normally distributed data, Spearman's analysis was used for correlation analysis. For non-linear correlation analysis, the associations between the TyG index and mortality risk among patients with SAP were assessed by restricted cubic spline (RCS) with 4 knots. R package plotRCS and ggplot2. (version 4.4.1) To further characterize the nonlinear association between TyG and mortality, the first derivative of the RCS curve was calculated. Apparent inflection regions were identified according to changes in the slope of the fitted curve, and the corresponding TyG values were used to define the range over which mortality risk increased more rapidly. Potential inflection points were determined as the values of TyG corresponding to a first derivative equal to zero. The interval bounded by these inflection points was defined as the range over which TyG exhibited a positive association with mortality risk. Power analysis was performed using G*Power 3.1.9.7.

The odds ratios (ORs) and confidence intervals (CIs) for developing SAP were estimated using multivariable logistic regression, adjusting for confounding variables. The Hosmer-Lemeshow goodness-of-fit test and Akaike's Information Criterion (AIC) were applied to evaluate the performance in predicting SAP. Receiver operating characteristic (ROC) curves were used to assess the index's ability to predict SAP. The comparison of the area under the curve (AUC) between different indicators was established using the Delong test. A p-value of less than 0.05 was considered statistically significant. Continuous Net Reclassification Improvement (NRI) without arbitrary cutoff values was calculated to quantify incremental predictive performance. Internal validation and calibration performance were performed using bootstrap resampling (1,000 repetitions).

TABLE 1. Demographic Characteristics of the HTG-AP Patients

Variables	Non-SAP (n=185)	SAP (n=104)	*F/Z/χ2/t*	*P**
Total no. n (%)	185 (64.0%)	104 (36.0%)		
Epidemiology				
Age, median (IQR), y	39 (32, 46)	39 (33, 46)	-0.026	0.979[1]
Sex, male, n (%)	129 (69.7%)	68 (65.4%)	0.579	0.447[2]
BMI, mean ± SD, kg/m^2	25.78±4.58	25.79±4.66	0.009	0.981[3]
Medical history, n (%)				
Circulatory disease	60 (32.4%)	30 (28.8%)	0.399	0.527[2]
Pulmonary disease	0 (0.0%)	2 (1.9%)	3.582	0.058[2]
Renal disease	0 (0.0%)	1 (1.0%)	1.785	0.182[2]
Diabetes mellitus	58 (31.4%)	32 (30.8%)	0.011	0.918[2]
Hyperlipidemia	65 (35.1%)	36 (34.6%)	0.008	0.929[2]
Substance abuse, n (%)				
Tobacco	61 (33.0%)	31 (29.8%)	0.307	0.579[2]
Alcohol	64 (34.6%)	31 (29.8%)	0.691	0.406[2]
Laboratory				
WBC (10^9/L)	10.01 (6.42, 13.81)	10.95 (7.78, 13.84)	-1.480	0.139[1]
HCT (%)	41 (28, 47)	35 (29, 41)	0.824	0.411[1]
Neut (10^9/L)	8.17 (4.78, 11.66)	8.75 (5.98, 12.09)	-1.585	0.113[1]
Lymph (10^9/L)	1.86±0.58	1.18±0.05	1.253	0.384[3]
PLT (10^9/L)	254 (183, 322)	249 (167, 353)	-0.685	0.493[1]
D-Dimer (ug/ml)	3.80 (1.23, 4.46)	4.46 (2.41, 7.84)	-3.340	0.001*[1]
Ca^{2+} (mmol/L)	2.12 (1.99, 2.23)	2.01 (1.83, 2.22)	-3.214	0.001*[1]

Variables	Non-SAP (n=185)	SAP (n=104)	*F/Z/χ2/t*	*P**
HTG (mmol/L)	14.0 (8.0, 22.1)	16.4 (12.9, 23.0)	-3.987	0.000*[1]
Glucose (mmol/L)	10.3 (7.4, 13.6)	14.4 (12.0, 18.2)	-6.804	0.000*[1]
BUN (mmol/L)	4.22 (2.91, 5.57)	6.53 (3.90, 13.35)	-5.637	0.000*[1]
Creatinine (umol/L)	55 (46.0, 71.0)	69.5 (44.0,138.0)	-2.864	0.004*[1]
TCL(mmol/L)	4.60 (3.08,7.00)	3.99 (3.14,5.46)	-1.375	0.169[1]
ALB (g/L)	34.63±6.01	31.52±6.55	-4.083	0.000*[3]
PCT (ng/ml)	0.40 (0.20, 0.44)	0.65 (0.30, 3.61)	-4.819	0.000*[1]
CRP (mg/L)	75 (9, 163)	129 (79, 201)	-3.706	0.000*[1]
IL-6 (pg/ml)	65.2 (29.0,99.0)	126.7 (51.4,197.3)	-4.527	0.000*[1]
Assessment				
TyG	11.61(11.11,12.28)	12.41(11.87,12.53)	-6.516	0.000*[1]
TyG-BMI	295.21(260.64,337.13)	305.61(273.08,349.08)	-1.820	0.069[1]
APACHEII	6 (4, 9)	15.5(14, 18.5)	-11.186	0.000*[1]
mCTSI	6 (2, 8)	8 (6, 10)	-5.995	0.000*[1]

**P* value obtained with univariate regression analysis. Data are presented as the number of patients (%), average ±standard deviation or median (interquartile range). WBC, white blood count; HCT, hematocrit; Neut, neutrophil count; Lymph, lymphocyte count; PLT, platelet count; HTG, hypertriglyceridemia; BUN, blood urea nitrogen; ALB, albumin; PCT, procalcitonin; CRP, C-reactive protein; IL-6, interleukin-6; TCL,Serum total cholesterol; 1Mann-Whitney U test;2Fisher's exact test;3Student's t-test

3. Results

3.1 Demographic characteristics of the study

The demographic characteristics encompassed 289 HTG-AP patients, comprising 185 non-SAP and 104 SAP patients, as presented in Table 1. α=0.05, target power=0.95, sample sizes of 185 and 104 for the two groups, the minimal detectable effect size was calculated as 0.4537 (approximating medium effect size as 0.5).The median age of onset for HTG-AP was 39 years in both SAP and non-SAP patients. The data indicated a predominance of male patients among all HTG-AP patients (68.2%). Approximately 34.9% of HTG-AP patients had a history of hyperlipidemia. Compared to the non-SAP group, patients in the SAP group were more likely to have higher serum levels of D-Dimer, TG, Glucose, BUN, Creatinine, ALB, PCT, CRP, and IL-6, along with lower levels of calcium. Furthermore, the SAP group exhibited significant values of the TyG index within 24 h upon admission and scores of APACHE-II and mCTSI ($p<0.05$).

3.2 Multivariable logistic regression analysis for predicting severe acute pancreatitis

All indicators with statistical differences were included in multivariable analysis, resulting in only 3 variables remaining: TyG, Creatinine, and APACHE-II (as shown in Table 2). The formula for predicting SAP in HTG-AP patients is: *Y=1.349*TyG+0.013*Creatinine+0.382*APACHEII-22.255*.The optimal cutoff value of 0.199 (specificity=0.784, sensitivity=0.990, as shown in Figure 1). The value closer to 1 demonstrated a higher probability of SAP occurrence.

We compared the predictive performance between significant variables and the multivariable model and confirmed that the multivariable model showed superior predictive accuracy for SAP among all HTG-AP patients, with an AUC of 0.940 (as shown in Figure 1, DeLong test between multivariable regression model and APACHE-II: $Z = -4.1503$, $p = 3.32 \times 10^{-5} < 0.05$). In addition, the APACHE-II and TyG index also demonstrated good performance in prediction, with AUC values of 0.893 and 0.731. Compared with the APACHE-II, the multivariable model significantly improved patient risk classification, as reflected by a continuous NRI of 0.713, indicating that approximately 71.3% of patients were more appropriately reclassified,as shown in Supplementary Table 1.

The model demonstrated excellent stability with minimal optimism (optimism-corrected Dxy = 0.8667; optimism = 0.0045). The bootstrap-corrected C-statistic was 0.9334, indicating outstanding discriminative performance. Calibration suggested minimal overfitting with a calibration slope of 0.972 and an intercept of 0.006.

The bias-corrected calibration curve demonstrated good agreement between predicted and observed probabilities across the range of predicted risks, supporting acceptable calibration and prediction accuracy of the model. (mean absolute error = 0.053, mean squared error = 0.00415, and 90% of prediction errors were below 0.11; calibration plot was shown in supplementary Figure1). Hosmer–Lemeshow test indicated acceptable model calibration of observed risks ($\chi^2 = 15.16$, df = 8, $p = 0.056$).

TABLE 2. Multivariable logistic regression analysis for SAP

Characteristic	B	OR[1]	95% CI[1]	p-value
TyG	1.349	3.853	2.134, 6.956	0.000*
Creatinine	0.013	1.013	1.003, 1.022	0.010*

Characteristic	B	OR[1]	95% CI[1]	p-value
APACHEII	0.382	1.465	1.331, 1.612	0.000*

3.3 Clinical characteristics and outcomes of the HTG-AP patients

The SAP group revealed a higher risk of ICU admission, prolonged ICU duration, extended in-hospital duration, and increased in-hospital mortality (17.3%), compared to the non-SAP group (as shown in Table 3). Despite intensive care treatment, SAP patients suffered from persistent single-organ insufficiency and mutiple-organ failure syndrome, especially persistent pulmonary failure was diagnosed in 65.4% of SAP patients. 66.3% of SAP patients(69/104) were diagnosed with infected necrotizing pancreatitis(INP) based on contrast-enhanced computed tomography(CT) presenting gas configurations within pancreatic and peripancreatic necrosis in first 14 days[22], while only 26.5% non-SAP patients(49/185) were diagnosed with INP. Due to the standard treatment for INP being a surgical step-up approach[23], 47 patients with SAP (45.2%) and 27 patients with non-SAP (14.6%) underwent surgery and were diagnosed with INP. Among the SAP patients, 30 patients experienced postoperative hemorrhage, 21 patients suffered pancreatic fistula, and 12 patients required intervention for bleeding. Among the non-SAP patients, only 1 patient experienced postoperative hemorrhage, 7 patients suffered pancreatic fistula, and no patient required intervention for bleeding. Variables with statistically significant differences are shown in Table 3 ($p < 0.005$). The clinical outcomes, including new-onset diabetes, recurrence, and exocrine insufficiency, did not differ between the SAP and non-SAP group.

TABLE 3. Clinical characteristics and outcomes of the Present Cohort

Variables	Non-SAP (n=185)	SAP (n=104)	*Z/χ2*	*P**
Total no. n (%)	185 (64.0%)	104 (36.0%)		
Hospitalization course				
ICU admission, n (%)	80 (43.2%)	88 (84.6%)	46.819	0.000*[2]
ICU duration (days)	0 (0, 6)	9 (2, 20)	-7.788	0.000*[1]
In-hospital duration (days)	11 (7,15)	19 (9,33)	-4.384	0.000*[1]
In-hospital mortality (%)	0 (0.0%)	18 (17.3%)	34.146	0.000*
Complication on admission, n (%)				
Persistent circulatory failure	0 (0.0%)	53 (51.0%)	115.452	0.000*[2]

Variables	Non-SAP (n=185)	SAP (n=104)	*Z/χ2*	*P**
Persistent pulmonary failure	0 (0.0%)	68 (65.4%)	158.180	0.000*[2]
Persistent renal failure	0 (0.0%)	37 (35.6%)	75.481	0.000*[2]
Multiple organ failure	0 (0.0%)	45 (43.3%)	94.811	0.000*[2]
INP	49 (26.5%)	69 (66.3%)	43.782	0.000*[2]
Intervention				
Surgery	27(14.6%)	47(45.2%)	32.720	0.000*[2]
Postoperative hemorrhage	1(0.5%)	30 (28.8%)	55.701	0.000*[2]
Colon involvement	1(0.5%)	4 (3.8%)	2.555	0.110[2]
Colon fistula	1 (0.5%)	4 (3.8%)	2.555	0.110[2]
Biliary stricture	3 (1.6%)	4 (3.8%)	0.612	0.434[2]
Splanchnic vein thrombosis	18 (9.7%)	12 (11.5%)	0.234	0.628[2]
Pancreatic fistula	7(3.8%)	21(20.2%)	20.485	0.000*[2]
Pancreatic portal hypertension	8(4.3%)	9(8.7%)	2.254	0.133[2]
Bleeding requiring intervention	0 (0.0%)	12 (11.5%)	22.271	0.000*[2]
Clinical outcomes, n (%)				
New-onset diabetes	24 (13.0%)	22 (21.2%)	3.329	0.068[2]
Recurrence	28 (15.1%)	11 (10.6%)	1.185	0.276[2]
Exocrine insufficiency	8 (4.3%)	3 (2.9%)	0.086	0.769[2]

**P* value obtained with univariate regression analysis. Data are presented as the number of patients (%), or median (interquartile range). SAP, severe acute pancreatitis; INP, infected necrotizing pancreatitis; 1Mann-Whitney U test;2Fisher's exact test

3.4 The relationship between TyG, creatinine, and APACHE-II with in-hospital mortality in SAP patients at different time points

For the in-hospital mortality of SAP patients, RCS analyses using four knots demonstrated a non-linear relationship between TyG and in-hospital mortality, with time points at 7 days, 30 days, and 120 days. TyG, which ranged from 11.87 to 12.22, tended to increase the possibility of in-hospital mortality over the 120-day follow-up. This range was different from the short-term results (as shown in Figure 2). Mortality risk tended to increase progressively at higher TyG levels, with an apparent inflection region around TyG values of approximately 11.78–12.29 during the 7-day follow-up and 11.87- 12.28 during the 30-day follow-up. Creatinine and the APACHE II score showed a weak positive link with in-hospital mortality in SAP (Creatinine: Spearman=0.173, p=0.050; APACHE II: Spearman=0.176, p=0.003).

4. Discussion

Our study retrospectively analyzed the baseline data between non-SAP and SAP patients from 289 HTG-AP patients in Xuanwu Hospital over 9 years and constructed a multivariable logistic regression model, including the TyG index, APACHE II, and creatinine for predicting SAP among HTG-AP patients. Furthermore, we investigated the relationship between the TyG index and in-hospital mortality rate in SAP patients during 7-day, 30-day, and 120-day follow-up. This study proposed a non-linear correlation between the TyG index and in-hospital mortality risk during initial admission.

The average age of presentation of HTG-AP patients was 39 years, with two-thirds comprised of males in our study. Similar results were reported in multinational research. A retrospective study established a cohort with 614 HTG-AP patients consisting mainly of males (72.1%), and the average age was mid-40s from China [24]. Multi-international centers combined 69 patients with HTG-AP and reported that 67% of patients were males and the median age was 40 years.[25]

HTG-induced AP has been widely recognized as a significant risk factor for severe pancreatitis, with previous studies estimating that patients with HTG have a 14% incidence of AP and an increased likelihood of developing severe forms of the disease [26,27]. A single-center study in China reported that HTG raised the incidence of AP by 33%, which became the second most common cause of AP [28]. Disease risk increase 4% incidence of AP for every 100mg/dL rise in serum TG levels beyond 1000mg/dL[9,29,30]. Zhang et al. demonstrated that severe HTG significantly increased the severity of AP and an association between TG grade and severity of AP[28]. Mild-to-moderate hypertriglyceridemia (≥177 mg/dL) has also been identified as a risk factor for AP [31]. Additionally, findings from univariable and multivariable Mendelian randomization articles have confirmed the association of an increased level of TG with the elevated risk of AP by the lipoprotein lipase pathway [32–35]. Reduced activity of lipoprotein lipase might lead to fewer TG removed from plasma, into higher levels of plasma TG, which was linked to a rising risk of AP. The pathophysiological

mechanisms underlying HTG-induced AP include hyperviscosity and chylomicronemia, which reduced capillary blood flow, leading to ischemia, acidification, and acute acid load. These conditions sensitize the pancreatic acinar cell to enhanced secretagogue-induced zymogen activation, ultimately increasing the risk and severity of AP [36,37]. Our study is consistent with the above concept that patients with SAP have higher levels of TG, reinforcing the role of HTG in disease development.

In addition, inflammatory bowel disease as well as higher TG were associated with increased risk of AP[34]. When the acinar cells were suffering cellular damage, apical secretion of digestive enzymes converted to basolateral exocytosis, meaning the disruption of the apical junctional barrier, thereby contributing to the increased levels of pancreatic enzymes and liberating free fatty acids in serum, which enhanced inflammation and was observed in the early course of AP [38]. Modrau et al. found that the CRP level after 48 h could be detected as severe AP[39]. PCT monitoring can reliably assess relevant INP and prognosis in AP[40]. In our study, we also indicated that the inflammatory markers (including PCT, IL-6, and CRP) in SAP patients were significantly higher compared to non-SAP patients.

TyG index could effectively diagnose AP and remained higher in the severe group[41–43]. SHapley additive explanations analysis of the XGBoost model illustrated impacts of CRP, TG, and TyG index at high levels in HTG, suggesting synergistic effects of inflammation and dyslipidemia[44]. However, Xu et al. established a Random Forest classification model in predicting SAP and highlighted the dominant contribution of inflammatory indicators(CRP and NLR) in predicting SAP compared to metabolic biomarkers (TyG) based on feature importance analysis[45]. This is inconsistent with our multivariable logistic analysis, possibly due to the AP patients in the study of Xu had mix etiologied, especially with gallstones being the most common cause(35%), while our study only enrolled AP patients caused by hypertriglyceridemia.

Our study aligned with the finding that the score of APACHE II could predict the severity of AP and aid in determining the need for tertiary care [30,46,47]. However, when assessing the severity of AP, APACHE II cannot distinguish between interstitial AP and necrotic AP, which is related to different prognoses.

The compartment model of SAP patients with multi-organ failure (MOF) had higher BUN and creatinine, but the ratio of BUN and creatinine distinguished from non-MOF, which verified the primary effect of MOF on the kidney was prerenal azotemia [48]. APACHE II and serum creatinine level within 24 h of admission could predict persistent organ failure in early AP[49]. During the first 48 hours of admission, serum creatinine concentration revealed low positive predictive values for separating necrotizing pancreatitis from the absence of pancreatic necrosis in AP patients[50]. These findings inferred that serum creatinine level might be a positive laboratory marker for predicting persistent organ failure in early AP, which was similar to our study.

Through restricted cubic splines, a threshold effect at a TyG-BMI value of 243 performed greater risks of in-hospital and ICU mortality in AP patients [51,52]. TyG index has shown an association with all-cause and cardiovascular mortality[53,54], stroke and its outcome[55–57], as well as acute kidney injury in AP[58]. Our study extends to explore the association between the TyG index within 24 h of admission and mortality in HTG-AP patients. However, no significant difference in the value of the TyG index was observed between the surgery and no-surgery group (p=0.115).

Nevertheless, our study still has some limitations. First, our research is a single-center retrospective study of the Asian population, which is susceptible to data bias. To enhance the generalizability of the findings, further inclusion of multicenter studies and independent external cohorts is required to validate. Second, we didn't measure serial changes in the TyG index and TyG-BMI following the progression of AP during the treatment. More observation parameters should be involved, including upper gastrointestinal bleeding and ventilator-assisted ventilation. Third, the APACHE II and mCTSI are inconvenient due to the completion upon admission of at least 24 hours for the final determination of AP severity, which may have an impact on the initial treatment for severe patients. Fourth, RCS analyses suggested potential nonlinear associations between TyG and in-hospital mortality in our study, which were associative and hypothesis-generating rather than ready for clinical implementation. The relatively small number of in-hospital mortality events (9, 13, and 18 deaths for the 7-day, 30-day, and 120-day endpoints, respectively) may limit the stability of the estimated curves and

the identification of potential inflection points. Larger prospective cohorts are required to confirm.

5. Conclusion

This study revealed the different laboratory indicators separating SAP from HTG-AP patients and established a multivariable logistic regression model including the TyG index, APACHE II, and serum creatinine for predicting SAP. The non-linear relationship between the TyG index upon admission within 24 h and in-hospital mortality emphasized that during Day 7, Day 30, and long-term follow-up (120 days). TyG index may be beneficial in early prediction of SAP and indicating the possibility of in-hospital mortality risk in SAP patients. External validation is required before clinical implement.

Declarations

Ethics approval and consent to participate

This research was approved by the Ethics Committee of Beijing Xuanwu Hospital. Informed consent was obtained from all patients in accordance with the declaration of Helsinki.

Availability of data and materials

The data analyzed during the current study are not available since we are still collecting more data for further study, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

Yuting Wang: Conceptualization, writing-original draft, Data visualization.

Ye Zhao: Investigation and methodology.

Wentong Mei: Data analysis and visualization.

Yuchen Jia: Polishing the draft and validation.

Zhi Zheng: Funding acquisition and supervision

Yixuan Ding: Experiment design, supervision, and data analysis.

All authors read and approved the final manuscript.

Yuting Wang and Ye Zhao contributed to the work equally and should be regarded as co-first authors.

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Not applicable.

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Use of AI and AI-assisted technologies statement

The authors declare that no artificial intelligence tools and and AI-assisted technologies were used in this research.

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Figure legends:

Figure 1. Receiver operating characteristic curve of different models for predicting SAP ROC curve value for different variables: TyG+Creatinine+APACHEII=0.940; TyG=0.731; TyG-BMI=0.565; APACHEII=0.893; mCTSI=0.705; HTG=0.641; Glucose=0.741; D-Dimer=0.618; Calcium=0.614; BUN=0.700; Creatinine=0.601; ALB=0.649; PCT=0.670; CRP=0.631; IL-6=0.66

Figure 2. The relationship between TyG and in-hospital mortality in SAP patients by RCS

A.7-day follow-up B.30-day follow-up C.120-day follow-up in SAP patients

Figures

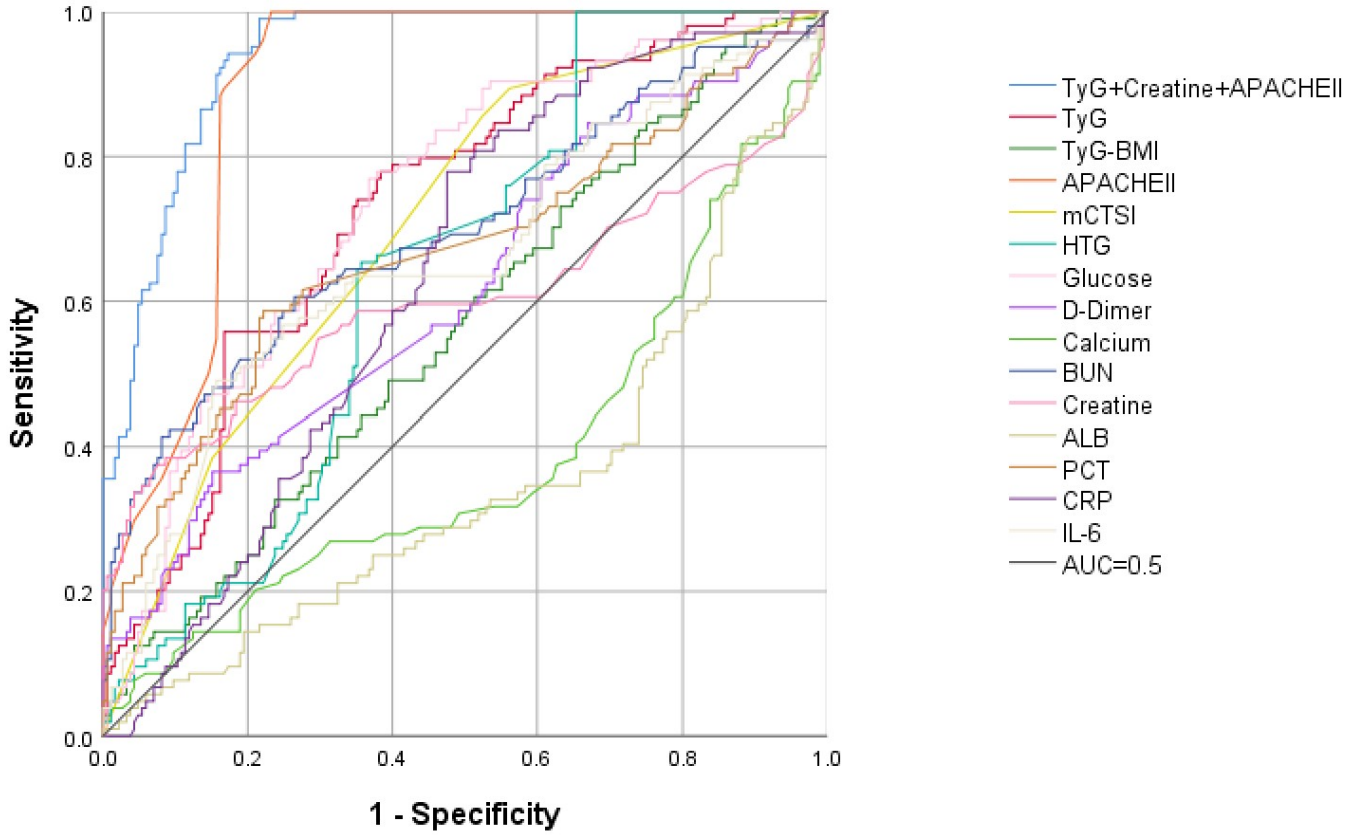


Figure 1

Receiver operating characteristic curve of different models for predicting SAP

ROC curve value for different variables: TyG+Creatinine+APACHEII=0.940; TyG=0.731; TyG-BMI=0.565; APACHEII=0.893; mCTSI=0.705; HTG=0.641; Glucose=0.741; D-Dimer=0.618; Calcium=0.614; BUN=0.700; Creatinine=0.601; ALB=0.649; PCT=0.670; CRP=0.631; IL-6=0.66

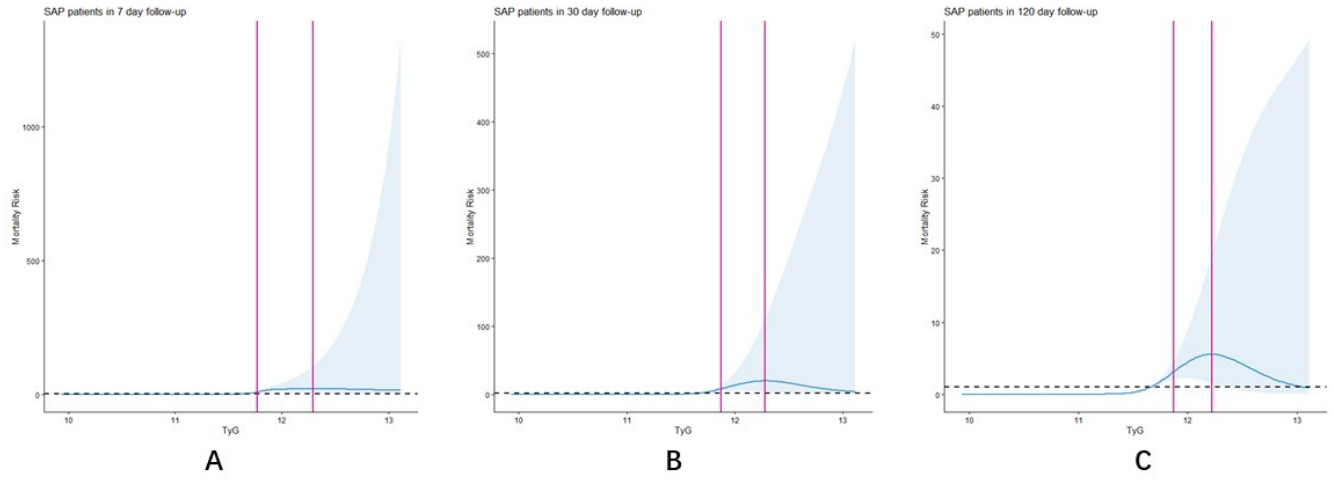


Figure 2

The relationship between TyG and in-hospital mortality in SAP patients by RCS

A.7-day follow-up B.30-day follow-up C.120-day follow-up in SAP patients

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