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Association between serum triglyceride level and severity of acute biliary pancreatitis

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ABSTRACT

Background: Acute biliary pancreatitis (ABP) is the most common type of acute pancreatitis. However, the effect of serum triglyceride (TG) levels on the severity of ABP remains unclear. The aim of this study was to assess the correlation between serum TG levels and the severity of ABP.

Methods: Data from 526 ABP patients was analyzed in this study. The patients were divided into normal and elevated groups according to the TG level measured within 24 h after admission, and the elevated group was further divided into mild, moderate, and severe elevated groups. The demographic data and clinical outcomes of each group were compared.

Results: Of the 526 ABP patients, 394 were in the normal TG group and 132 were in the elevated TG group (36 mild, 57 moderate, and 39 severe). The elevated group was younger (51.5 ± 12.9 vs. 58.9 ± 13.9), predominantly male (66.7% vs. 45.2%), had more history of diabetes (22.7% vs. 12.4%) and hyperlipidemia (19.7% vs. 0.8%), and developed systemic inflammatory response syndrome (SIRS) (25.8% vs. 15.5%), persistent organ failure (POF) (11.4% vs. 2.8%), and local complications (62.9% vs. 42.1%) more frequently compared to the normal group ($P < 0.05$). The incidence of SIRS, POF, acute peripancreatic fluid collection (APFC), and acute necrotic collection (ANC) increased with increasing TG levels ($P_{trend} < 0.05$). In multivariate analysis, TG was independently associated with POF, APFC, and ANC in increments of 100 mg/dl ($P < 0.05$), and there was a linear relationship between TG levels and POF, APFC, and ANC (non-linear $P > 0.05$, P overall <0.05). In addition, nonalcoholic fatty liver disease is not a risk factor for POF, ANC, and APFC in ABP patients.

Conclusions: Elevated serum TG levels were independently associated with more severe ABP. The incidence of POF, APFC, and ANC in ABP patients increased with the increase of TG levels, with a linear relationship.

1. Introduction

Acute pancreatitis (AP) is a critical clinical disease that commonly affects the pancreas, peripancreatic tissues, and distant organs. Its global incidence rate ranges from 4.9 to 80 cases per 100,000, and hospitalization rates are steadily increasing [1]. AP can be triggered by several factors, including biliary tract diseases, alcoholism, and lipid metabolism disorders, however, acute biliary pancreatitis (ABP) is the most prevalent cause, accounting for 46.3% of cases worldwide [2]. While mild AP typically resolves on its own and has a positive prognosis, severe cases have high mortality rates of 20–40% [3,4]. As such, early identification of high-risk patients is crucial to reducing morbidity and mortality rates and improving patient outcomes.

Hypertriglyceridemia (HTG) is a common lipid metabolism disease that is divided into primary and secondary. Primary HTG is a genetic disorder characterized by severe chylomicronemia and recurrent pancreatitis [5], whereas secondary HTG is triggered by various environmental factors. Alcohol can stimulate the liver to secrete very low-density lipoprotein and decrease lipoprotein lipase

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activity, which is considered one of the common risk factors for secondary HTG [6,7]. Recent research suggests that serum triglyceride (TG) levels play a significant role in the occurrence and progression of AP. Elevation of serum TG levels to a certain threshold can directly induce acute hypertriglyceridemic pancreatitis (HTG-AP), and the incidence of AP increases with increasing TG levels [8–10]. Besides, serum TG levels can also impact the severity and prognosis of HTG-AP, with elevated levels increasing the incidence of persistent organ failure (POF), local complications, and mortality [11,12]. Notably, TG is not inherently toxic, and studies have shown that unsaturated long-chain nonesterified fatty acids (NEFA) hydrolyzed from unsaturated fatty acids (UFA) in TG can lead to harmful signal propagation, lipotoxic inflammation, and organ failure (OF), which is the main factor in aggravating AP [13,14].

However, elevated serum TG levels are also common in patients with AP caused by other factors [15]. Some ABP patients have HTG before the onset of the disease, and there is an increase in TG levels in the early stage of ABP [16,17]. Despite this, few studies have examined the role of serum TG levels in the clinical outcome of ABP. Thus, this study aims to investigate the association between serum TG levels and the severity of ABP.

2. Materials and methods

2.1. Study population

Consecutive cases of ABP patients admitted to Northern Jiangsu People's Hospital from January 2016 to December 2020, with data obtained from the hospital information system (HIS), were analyzed in this retrospective study.

The inclusion criteria for this study were: (1) 18 years ≤ age ≤80 years; (2) admission within 3 days after the onset of disease; and (3) lipid levels measured within 24 h after admission. Exclusion criteria were (1) history of any malignancy; (2) history of pancreatic trauma and biliopancreatic surgery; (3) long-term use of hormones and immunosuppressants; (4) being in the advanced or terminal stage of any disease; (5) pregnant or lactating women; and (6) incomplete information. The screening process for patients is shown in Fig. 1.

Written informed consent was obtained from each patient and approved by the Institutional Ethics Committee for this study (2023KY-039). The study protocol was conducted according to the 1975 Declaration of Helsinki guidelines and registered with the Chinese Clinical Trials Registry (registration number: ChiCTR2300070394).

2.2. Definition of AP and ABP

The diagnosis and classification of AP were performed according to the 2012 revised Atlanta criteria [18].

The diagnosis of ABP was based on the criteria proposed in the literature [19]: (1) meeting the diagnostic criteria of AP; (2) abdominal ultrasound, computed tomography, magnetic resonance cholangiopancreatography, or endoscopic ultrasonography suggested cholelithiasis or cholestasis, or alanine aminotransferase (ALT) more than twice the upper limit of normal, or imaging suggested dilatation of the common bile duct (age ≤75 years, diameter >8 mm; age >75 years, diameter >10 mm).

2.3. Definition of nonalcoholic fatty liver disease (NAFLD)

The diagnosis of fatty liver was made by computed tomography (CT) findings with a liver/spleen CT ratio <1 [20,21], and NAFLD was defined as fatty liver without alcohol and other definite liver damage factors.

2.4. Grouping based on TG level

All patients were divided into a normal group (<150 mg/dl) and an elevated group (≥150 mg/dl) according to the highest TG level within 24 h after onset. The elevated group was further divided into three groups depending on the National Cholesterol Education

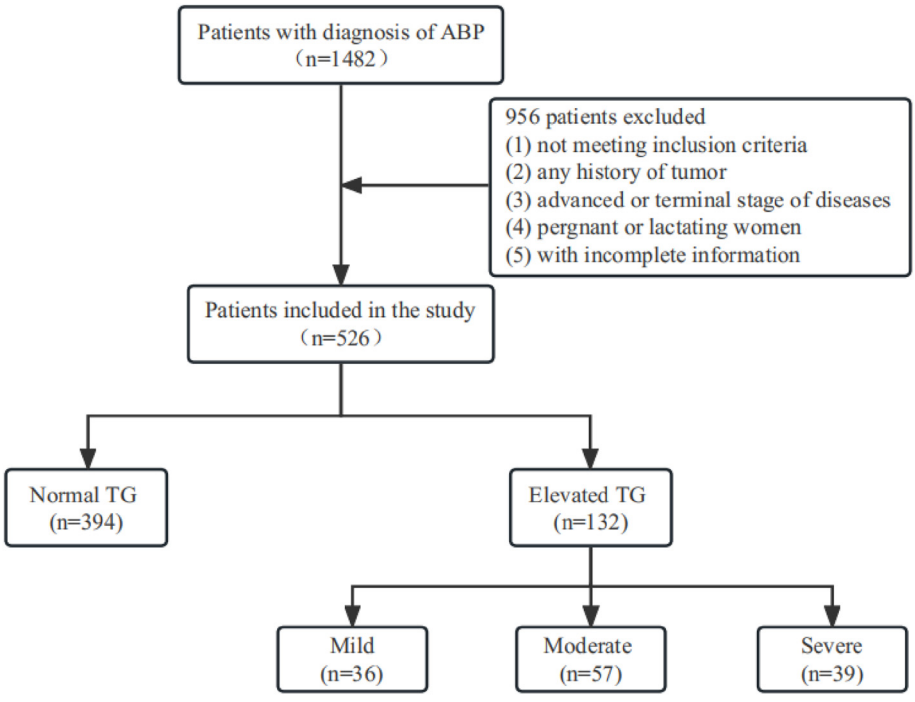

Fig. 1. The flow chart of patients' selection process. ABP: acute biliary pancreatitis; TG: serum triglyceride.

Program-Adult Treatment Panel III (NCEPATP III) [22]: a mildly elevated group (150 mg/dl ≤ TG < 200 mg/dl), a moderately elevated group (200 mg/dl ≤ TG < 500 mg/dl), and a severely elevated group (TG ≥ 500 mg/dl).

2.5. Data collection

Demographic data, laboratory indicators, imaging data, and clinical findings were recorded for each patient in this study. All data were obtained from HIS and recorded on uniform case report forms. Quality control was performed during the data collection process to ensure the accuracy of the data. Among these, persistent organ failure was the outcome indicator we focused on, as assessed by the revised Atlanta Classification Criteria [18].

2.6. Statistical analysis

Continuous variables were described using mean ± standard deviation, compared between groups using the student's t-test, and trend changes were assessed using the Cuzick test. Categorical data were expressed as percentages, compared between groups using the chi-square test or Fisher exact test, and trend changes were assessed using the proportional trend test. A logistic regression model was used to evaluate the correlation of TG levels with POF, and local complications, with TG as a quantitative variable, assessed in increments of 100 mg/dl. Before building the multivariate model, we calculated generalized variance inflation factors (GVIF) to examine collinearity, and covariates were selected according to the following principles: (1) matched odds ratio changes more than 10% if variables were introduced into the base model or removed from the full model; (2) variables with p-values <0.2 in the univariate model; and (3) the clinical significance of the variables and the number of outcome events in the study population. Restricted cubic splines (RCS) were used to assess potential non-linear associations between TG levels, and POF and local complications.

All analyses were performed using R statistical software (http://www.r-project.org, the R Foundation) and IBM SPSS Statistics 25 statistical software, and a two-sided P value < 0.05 was considered statistically significant.

3. Results

3.1. Patients' demographics and clinical characteristics

There were 526 ABP patients included in this study: 394 in the normal group and 132 in the elevated group. Patients in the elevated group were younger (51.5 ± 12.9 vs. 58.9 ± 13.9), more often male (66.7% vs. 45.2%), and had a higher BMI (25.6 ± 3.3 vs. 24.3 ± 3.5) and WC (88.7 ± 9.6 vs. 83.7 ± 8.7) ($P < 0.05$) compared to the normal group. In addition, in terms of past medical history, the elevated group had significantly higher rates of combined diabetes mellitus (22.7% vs. 12.4%), alcoholism (22.7% vs. 10.2%), smoking (21.2% vs. 9.6%), recurrence ≥2 times of AP (31.8% vs. 15.0%), and HTG (19.7% vs. 0.8%) than the normal group ($P < 0.05$). There was no significant difference in hypertension (38.6% vs. 30.7%) or NAFLD (24.2% vs. 18.0%) ($P > 0.05$), as shown in Table 1.

3.2. Clinical outcomes

Overall, mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP) occurred in 271 (51.5%), 229 (43.5%), and 26 (4.9%) patients, respectively. Among them, the incidence of SAP in the elevated TG group (11.4% vs. 2.8%) was significantly higher than in the normal group ($P < 0.05$). With respect to OF, the overall incidence of POF and transient OF (TOF) in ABP patients was 4.9% and 4.0%, respectively. Comparison between groups revealed that the elevated group was more likely to have POF (11.4% vs. 2.8%), especially the incidence of persistent respiratory failure (9.1% vs. 2.3%) and persistent renal failure (5.3% vs. 1.3%), which was significantly higher than the normal group ($P < 0.05$), while the incidence of TOF was not statistically different between the two groups ($P > 0.05$). Regarding local complications, the global incidence was 47.3%. Comparison between the two groups showed a higher incidence of overall local complications in the elevated group (62.9% vs. 42.1%), with a significantly higher incidence of acute peripancreatic fluid collection (APFC) (50.0% vs. 36.3%) and acute necrotic collection (ANC) (8.3% vs. 3.6%) in particular than in the normal group ($P < 0.05$). No significant differences were identified in pancreatic pseudocyst, walled-off necrosis, or infectious pancreatic necrosis ($P > 0.05$). In addition, the incidence of systemic inflammatory response syndrome (SIRS) in the elevated and normal groups was 25.8% and 15.5%, respectively, with statistically significant differences ($P < 0.05$). There was no significant difference in the ICU admission rate between the two groups ($P > 0.05$), as shown in Table 2.

The elevated group was further divided into mildly elevated (n = 36), moderately elevated (n = 57), and severely elevated (n = 39) groups. A comparison of the severity of different TG levels in ABP patients is shown in Table 3. The incidence of SAP increased with increasing TG levels ($P_{trend}<0.05$). The incidence of POF was 2.8%, 5.6%, 8.8%, and 20.5% in the four groups, respectively ($P_{trend} < 0.001$). Concerning local complications, the overall incidence in the four groups was 42.1%, 52.8%, 57.9%, and 79.5%, respectively ($P_{trend} < 0.05$), with the incidence of APFC and ANC increasing with higher TG levels ($P_{trend} < 0.05$). Moreover, the incidence of SIRS and ICU transfer rates were higher in patients with severely elevated levels of ABP, accounting for 48.7% and 5.1%, respectively ($P_{trend} < 0.05$).

Table 1
Population baseline characteristics of ABP patients in the normal versus elevated TG groups.

Variables	Normal TG (N = 394)	Elevated TG (N = 132)	*P*
Age(Years) (mean ± SD)	58.9 ± 13.9	51.5 ± 12.9	<0.001
Sex (Man) (n, %)	178 (45.2)	88 (66.7)	<0.001
BMI (kg/m2) (mean ± SD)	24.3 ± 3.5	25.6 ± 3.3	<0.001
WC (cm) (mean ± SD)	83.7 ± 8.7	88.7 ± 9.6	<0.001
Medical history (n, %)			
Recurrence≥2 (Times)	59 (15.0)	42 (31.8)	<0.001
Alcoholism	40 (10.2)	30 (22.7)	<0.001
Smoker	38 (9.6)	28 (21.2)	<0.001
Diabetes mellitus	49 (12.4)	30 (22.7)	0.004
Hypertension	121 (30.7)	51 (38.6)	0.093
Hyperlipidemia	3 (0.8)	26 (19.7)	<0.001
NAFLD	71 (18.0)	32 (24.2)	0.119

ABP: acute biliary pancreatitis; TG: serum triglyceride; BMI, body mass index; WC: waist circumference; NAFLD: nonalcoholic fatty liver disease.

Table 2
Comparison of severity between the normal and elevated TG groups of ABP patients.

Variables	Normal TG (N = 394)	Elevated TG (N = 132)	*P*
Atlanta classification (n, %)			<0.001
MAP	223 (56.6)	48 (36.4)	<0.001
MSAP	160 (40.6)	69 (52.3)	0.019
SAP	11 (2.8)	15 (11.4)	<0.001
POF (n, %)	11 (2.8)	15 (11.4)	<0.001
Persistent heart failure	2 (0.5)	3 (2.3)	0.197
Persistent respiratory failure	9 (2.3)	12 (9.1)	0.001
Persistent renal failure	5 (1.3)	7 (5.3)	0.019
TOF (n, %)	16 (4.1)	5 (3.8)	0.890
Local Complications (n, %)	166 (42.1)	83 (62.9)	<0.001
APFC	143 (36.3)	66 (50.0)	0.005
ANC	14 (3.6)	11 (8.3)	0.025
PPC	8 (2.0)	4 (3.0)	0.507
WON	1 (0.3)	2 (1.5)	0.157
IPN (n, %)	0 (0.0)	0 (0.0)	1.000
SIRS (n, %)	61 (15.5)	34 (25.8)	0.008
Admission to ICU (n, %)	2 (0.5)	3 (2.3)	0.104

ABP: acute biliary pancreatitis; TG: serum triglyceride; MAP: mild acute pancreatitis; MSAP: moderately severe acute pancreatitis; SAP: severe acute pancreatitis; POF: persistence organ failure; TOF: transient organ failure; APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection; PPC: pancreatic pseudocyst; WON: walled-off necrosis; IPN: infectious pancreatic necrosis; SIRS: systemic inflammatory response syndrome; ICU: intensive care unit.

Table 3
Comparison of severity of different TG levels in ABP patients.

Variables	Serum TG Level (mg/dL) within 24 h of hospital admission				P_{trend}
	Normal (n = 394)	Mild (n = 36)	Moderate (n = 57)	severe (n = 39)	
Atlanta classification (n, %)					<0.001
MAP	223 (56.6)	17 (47.2)	23 (40.4)	8 (20.5)	<0.001
MSAP	160 (40.6)	17 (47.2)	29 (50.9)	23 (59.0)	0.011
SAP	11 (2.8)	2 (5.6)	5 (8.8)	8 (20.5)	<0.001
POF (n, %)	11 (2.8)	2 (5.6)	5(8.8)	8 (20.5)	<0.001
Persistent heart failure	2 (0.5)	0 (0.0)	1 (1.8)	2 (5.1)	0.010
Persistent respiratory failure	9 (2.3)	1 (2.8)	3 (5.3)	8 (20.5)	<0.001
Persistent renal failure	5 (1.3)	2 (5.6)	2 (3.5)	3 (7.7)	0.006
TOF (n, %)	16 (4.1)	1 (2.8)	2 (3.5)	2 (5.1)	0.937
Local Complications (n, %)	166 (42.1)	19 (52.8)	33 (57.9)	31(79.5)	<0.001
APFC	143 (36.3)	17 (47.2)	25 (43.9)	24 (61.5)	0.002
ANC	14 (3.6)	1 (2.8)	3 (5.3)	7 (17.9)	0.001
PPC	8 (2.0)	0 (0.0)	4 (7.0)	0 (0.0)	0.560
WON	1 (0.3)	1 (2.8)	1 (1.8)	0 (0.0)	0.371
IPN (n, %)	0 (0.0)	0 (0.0)	0(0.0)	0 (0.0)	1.000
SIRS (n, %)	61 (15.5)	4 (11.1)	11 (19.3)	19 (48.7)	<0.001
Admission to ICU (n, %)	2 (0.5)	1 (2.8)	0 (0.0)	2 (5.1)	0.036

ABP: acute biliary pancreatitis; TG: serum triglyceride; MAP: mild acute pancreatitis; MSAP: moderately severe acute pancreatitis; SAP: severe acute pancreatitis; POF: persistence organ failure; TOF: transient organ failure; APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection; PPC: pancreatic pseudocyst; WON: walled-off necrosis; IPN: infectious pancreatic necrosis; SIRS: systemic inflammatory response syndrome; ICU: intensive care unit.

3.3. Correlation analysis of serum TG level with POF, APFC and ANC

Univariate and multivariate logistic regression analyses were performed to determine the association of serum TG levels with POF, APFC, and ANC, and the rules for covariate screening are described in detail in the methods section. We found that TG, assessed in 100 mg/dl increments, was associated with the development of POF (OR = 1.05, 95% CI 1.02–1.08, $P = 0.001$), APFC (OR = 1.04, 95% CI 1.01–1.08, $P = 0.008$), and ANC (OR = 1.04, 95% CI 1.01–1.07, $P = 0.008$), and was independently associated with the development of POF (OR = 1.06, 95% CI 1.02–1.09, $P = 0.001$), APFC (OR = 1.04, 95% CI 1.01–1.07, $P = 0.019$), and ANC (OR = 1.03, 95% CI 1.00–1.07, $P = 0.039$) after controlling for potential confounding variables, as shown in Table 4. A RCS model was developed to describe the nonlinear relationship between serum TG levels and POF, APFC, and ANC. The model showed a linear relationship (P for non-linearity >0.05), as shown in Fig. 2 A-C.

4. Discussion

ABP is the most common type of AP, with an abrupt onset, rapid progression, and a tendency to develop SIRS and multiple organ dysfunction syndrome (MODS) [23]. Recent studies have shown that HTG is closely associated with the development and progression of HTG-AP [24,25]. However, fewer studies have focused on the effect of serum TG levels on the severity of ABP. Therefore, our objective was to investigate the correlation between different serum TG levels and the severity of ABP. In our study, we found that elevated serum TG levels aggravated the severity of ABP patients, and the higher the serum TG levels, the greater the risk of SIRS, POF, and local complications in ABP patients. Moreover, the elevated serum TG level was independently associated with the occurrence of POF, APFC, and ANC in ABP patients, with a linear relationship.

The present study has revealed that ABP patients with elevated serum TG levels were typically younger, predominantly male, and

Table 4
Univariate and multivariate analyses to evaluate the association between TG levels (assessed in increments of 100 mg/dl) and POF, APFC and ANC.

	Univariate analysis		Multivariate analysis	
	OR(95%CI)	*P*	OR(95%CI)	*P*
POF				
Female	0.53 (0.23–1.20)	0.127	0.50 (0.21–1.21)	0.124
Age≥60 years	1.79 (0.80–4.02)	0.159	3.64 (1.35–9.78)	0.011
BMI	1.13 (1.03–1.24)	0.007	1.13 (1.03–1.25)	0.011
Recurrence ≥2 times	1.95 (0.82–4.61)	0.131	2.47 (0.99–6.18)	0.053
Hypertension	1.82 (0.82–4.03)	0.139	1.14 (0.48–2.72)	0.768
NAFLD	1.55 (0.63–3.79)	0.337	1.63 (0.61–4.30)	0.328
TG(per 100 mg/dl)	1.05(1.02–1.08)	0.001	1.06 (1.02–1.09)	0.001
APFC				
Female	0.74 (0.52–1.06)	0.097	0.86 (0.59–1.27)	0.461
Age≥60 years	0.80(0.56–1.13)	0.204	0.85 (0.59–1.24)	0.403
BMI	1.03 (0.98–1.08)	0.246	1.02 (0.96–1.07)	0.537
Alcoholism	1.52 (0.91–2.51)	0.106	1.08 (0.58–2.00)	0.810
Smoking	1.61 (0.96–2.71)	0.070	1.33 (0.72–2.49)	0.363
NAFLD	0.82 (0.52–1.28)	0.378	0.76 (0.47–1.22)	0.257
TG(per 100 mg/dl)	1.04 (1.01–1.08)	0.008	1.04 (1.01–1.07)	0.019
ANC				
Female	1.32 (0.59–2.96)	0.502	2.21 (0.85–5.75)	0.104
Age≥60 years	0.50 (0.21–1.17)	0.109	0.51 (0.20–1.28)	0.151
BMI	1.05 (0.95–1.16)	0.359	1.01 (0.89–1.13)	0.924
Alcoholism	1.68 (0.61–4.62)	0.318	2.98 (0.87–10.22)	0.082
Hypertension	1.97 (0.88–4.41)	0.100	2.41 (1.02–5.69)	0.045
NAFLD	2.01 (0.84–4.80)	0.115	2.15 (0.81–5.66)	0.123
TG(per 100 mg/dl)	1.04 (1.01–1.07)	0.008	1.03 (1.00–1.07)	0.039

TG: serum triglyceride; POF: persistence organ failure; APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection; BMI, body mass index; NAFLD: nonalcoholic fatty liver disease.

had a higher incidence of comorbid diabetes mellitus. Many previous studies have analyzed the clinical data of HTG-AP and showed that HTG-AP was also the majority of a young male population, combined with more metabolic complications [9,26,27]. Thus, various types of AP patients with elevated TG levels may commonly have this population characteristic. This may be related to the unhealthy lifestyle habits and dietary structure of young men, such as chronic alcohol consumption, smoking, high-calorie diets, and insufficient physical activity, which can lead to abnormal lipid metabolism and decreased glucose tolerance [28]. We also found a greater history of HTG in the elevated TG group, which was consistent with the research findings of Sue et al. [10], who pointed out that AP patients with high TG levels on admission may have had elevated TG levels prior to admission.

SIRS is a syndrome that can effectively reflect the systemic inflammatory conditions of the body. Relevant evidences suggested that SIRS was closely related to the occurrence of one or multiple organ failures and deaths in AP patients [29,30]. Local complications are correlated with pancreatic cell and tissue damage and are important factors in assessing the severity of AP. Sternby et al. [31] showed that any local complication occurrence was independently associated with an increased risk of POF compared to no local complication. POF is the most significant determinant of disease severity, and its occurrence suggests a poor patient prognosis. This study revealed that the incidence of SIRS and local complications was higher in ABP patients with elevated TG levels. Furthermore, the incidence of POF, particularly persistent respiratory failure and persistent renal failure, was significantly higher in the elevated TG group than in the normal TG group. Multivariate analysis demonstrated that elevated TG levels were independently associated with the occurrence of APFC, ANC, and POF.

Two early studies, with small sample sizes, investigated the impact of TG levels on clinical outcomes in ABP patients. Zeng et al. [32] found that the incidence of respiratory failure significantly increased in patients with TG levels ≥200 mg/dl compared to those with normal TG levels, and TG levels ≥500 mg/dl increased the incidence of pancreatic pseudocysts and pancreatic necrosis. Cheng et al. [17] explored the clinical significance of elevated TG levels in ABP patients during early hospitalization and found that the risk of respiratory failure and pancreatic abscess was significantly higher in patients with elevated TG levels. However, in comparison to previous studies, our study showed that elevated TG levels also increased the incidence of SIRS and persistent renal failure. Furthermore, this study found a linear relationship between elevated TG levels and the occurrence of organ failure as well as local complications through trend analysis and a linearity test. In other words, the higher the TG level, the higher the risk of organ failure, APFC, and necrosis.

It is worth exploring the mechanism by which HTG aggravates ABP. Durgampudi et al. [33] used ABP mice as a model to observe the effects of acute lipolysis of fatty acids on local and systemic complications of ABP by injecting TG analogues and found that UFA aggravated pancreatic necrosis and systemic inflammation, leading to SAP. Therefore, excess fatty acids produced by elevated TG levels are the main cause of severe ABP.

The specific mechanism may be as follows: During ABP, pancreatic injury releases lipase into the systemic circulation and surrounding adipose tissue. Notably, pancreatic triglyceride lipase is considered to be the main lipase for the hydrolysis of visceral adipose tissue and serum triglycerides and mediates the production of lipotoxic NEFA [34,35]. Excess unsaturated NEFA monomers can cause tissue microcirculatory disturbance and MODS through

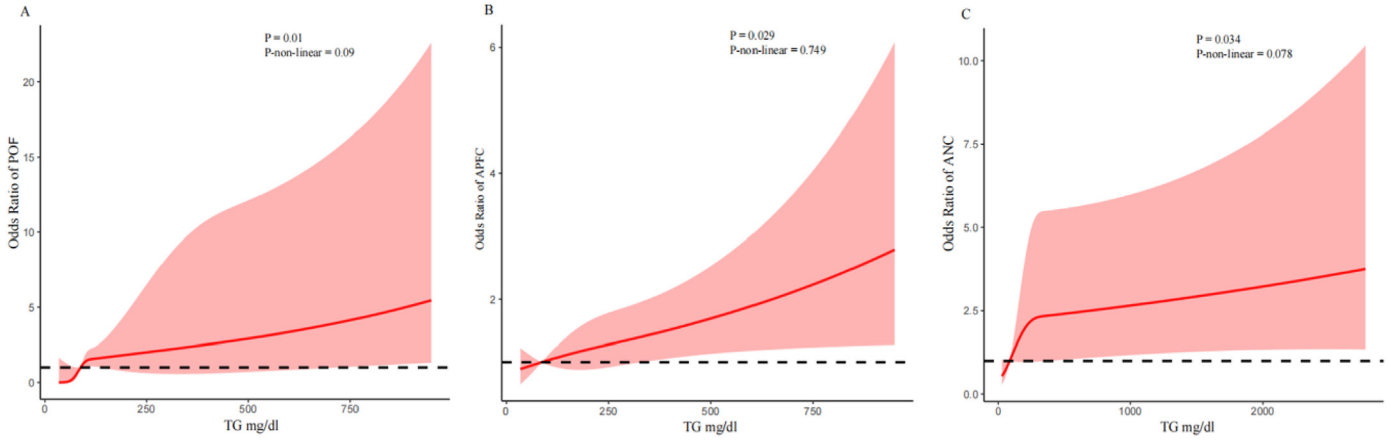

Fig. 2. Restricted cubic splines evaluate the non-linear relationship between TG and POF, APFC, and ANC. TG: serum triglyceride; POF: persistence organ failure; APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection.

sustained cytosolic Ca^{2+} elevation, inhibition of mitochondrial complexes I and V, and endoplasmic reticulum stress [36,37]. Excess UFA also exacerbates the inflammatory cascade mediated by chemokines and cytokines, thus aggravating the disease. The expression of neutrophil chemotactic factor mRNA was enhanced by excess UFA to promote neutrophil migration and aggregation, resulting in the activation of pancreatic trypsinogen and pro-inflammatory signaling [38–40]. In addition, the production of pro-inflammatory cytokines such as tumor necrosis factor-a (TNF-a) and interleukin-6 (IL-6) can also be upregulated by excess UFA [40]. TNF-a attacks acinar cells and other organ cells, causing ischemia, hemorrhage, necrosis, inflammation, and edema, mainly through direct cell-cell contact [41]. And IL-6 stimulates STAT3 activation in the pancreas via *trans*-signaling and induces acute-phase protein synthesis, worsening pancreatic injury and leading to systemic inflammation [42,43]. Moreover, recent studies have found that excess fatty acids can also affect macrophage-related functions, worsening the disease. Xia et al. [44] showed that pro-inflammatory polarization of macrophages can be induced by excess fatty acids, mediating pancreatic acinar cell inflammation and death. And Kostenko et al. [45] revealed that excess fatty acids can impair the phagocytic activity of macrophages through the uptake of membrane phospholipids, which impairs bacterial clearance and thus converts a sterile disease like pancreatitis to an infected one.

Clinicians do not routinely measure TG levels in AP patients during medical care, and several prospective, multicenter, large-sample cohort studies [2,8,15] have shown that up to 43.3%–50.1% of AP patients do not have TG values measured during hospitalization. It has become increasingly clear in recent years that HTG can induce AP and aggravate HTG-AP. As a result, physicians and scholars have begun paying attention to monitoring TG levels and administering lipid-lowering therapy to such patients. Unfortunately, the measurement of TG levels and the significance of elevated TG levels are often overlooked in patients diagnosed with ABP at an early stage. This study confirms that elevated serum TG levels are closely related to the progression and worsening of ABP disease. Therefore, early measurement and dynamic monitoring of TG levels in ABP patients should be emphasized in clinical practice. The higher the early TG levels, the greater the risk of SIRS, POF, and local complications, and relevant treatment should be given more actively.

Finally, we would like to clarify the diagnostic criteria for ABP in the study. At present, there is no clear international consensus on the specific diagnostic criteria for ABP, and the diagnostic criteria for ABP used in our study, as described in the methods, were based on a high-quality study published in the Lancet Journal in 2020 [19]. One of the criteria was ALT > 2-fold above the upper limit of normal on the basis of the occurrence of AP, and we took into account that ALT elevations could not be ruled out to be caused by NAFLD or other diseases, but according to our statistics, such patients accounted for only 3.9% of our study population, which may have little impact on the inclusion of ABP patients. Additionally, we compared the severity of the disease in patients with ALT > 2-fold the upper limit of normal only with those with imaging evidence, and there were no significant differences in the incidence of SAP, MSAP, overall local complications, or SIRS between the two types of patients (Supplementary File: Table S1). To further exclude the effect of NAFLD, we included NAFLD in the risk factor analysis and found that NAFLD was not a risk factor for POF, ANC, and APFC in ABP patients. Elevated TG levels remained independently associated with the development of POF, ANC, and APFC after controlling for the effect of NAFLD on outcome indicators.

There are some other limitations to this study. Firstly, we measured TG values within 24 h of patient admission, but the time between symptom onset and serum TG measurement was not the same in all patients, and although we selected patients with no more than 72 h from symptom onset to hospital admission, there was still some bias. Secondly, the study population was Chinese only, and race may have an effect on the variation of TG concentration. The applicability of the results to other races needs to be further confirmed. Thirdly, few patients had repeated measurements of serum TG levels during hospitalization, which limits our ability to evaluate the impact of changes in serum TG levels on the severity of ABP. Finally, this study was a single-center retrospective study, and the specific risk factors leading to elevated TG levels and the relevant results need to be further explored in a multicenter prospective study.

In conclusion, serum TG levels were found to be independently associated with more severe ABP in this study, and this association was linear. The higher the TG level, the higher the risk of POF, APFC, and ANC in ABP patients, and the more severe the disease. Therefore, for ABP patients with elevated serum TG levels, medical staff should pay close attention to these patients and provide timely and effective treatment to prevent complications.

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Declaration of competing interest

No conflict of interest was declared by the authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2024.02.001.

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