RESEARCH

The role of comorbid hypertriglyceridemia and abdominal obesity in the severity of acute pancreatitis: a retrospective study

Xiaoxi Yang[1,2†], Jiajun He[1†], Shuli Ma[1,2,3†], Tingting Wang[1], Quping Zhu[1], Fei Cao[1], Yuanhao Li[1], Chuting Yang[1], Chaowu Chen[1], Guotao Lu[4], Lianghao Hu[5], Jun Liu[1] and Weiwei Chen[1*]

Abstract

Background: The effect of comorbid hypertriglyceridemia (HTG) and abdominal obesity (AO) on acute pancreatitis (AP) remains unclear. The aim of this study was to explore the effect of comorbid HTG and AO and discuss which is the dominant disorder.

Methods: In this study, 1219 AP patients who presented with HTG or AO were stratified into four groups: non-HTG + non-AO, HTG + non-AO, non-HTG + AO, and HTG + AO.

Results: The 328 patients with comorbid HTG + AO were much younger (42.29 ± 11.77), mainly male (79.57%), and had higher TG levels, larger waist circumferences, and more past medical histories than the patients in the other three non-comorbid groups ($P < 0.001$). The comorbidity group developed more incidences of persistent organ failure and local complications ($P < 0.05$). Multivariate logistic regression analysis showed that AO (OR = 3.205, 95% CI = 1.570–6.544), mild HTG (OR = 2.746, 95% CI = 1.125–6.701), and moderate to very severe HTG (OR = 3.649, 95% CI = 1.403–9.493) were independent risk factors for persistent respiratory failure ($P < 0.05$). Age > 60 years (OR = 1.326, 95% CI = 1.047–1.679), AO (OR = 1.701, 95% CI = 1.308–2.212), diabetes mellitus (OR = 1.551, 95% CI = 1.063–2.261), mild HTG (OR = 1.549, 95% CI = 1.137–2.112), and moderate to very severe HTG (OR = 2.810, 95% CI = 1.926–4.100) were independent risk factors associated with local complications ($P < 0.05$). Moreover, HTG seemed to be more dangerous than AO. The higher the serum TG level was, the greater the likelihood of persistent respiratory failure and local complications.

Conclusions: Comorbid HTG and AO will aggravate the severity and increase the incidence of local complications of AP. HTG may play a dominant role of risk in the condition of comorbidity.

Chinese clinical trial registry: ChiCTR2100049566. Registered on 3rd August, 2021. Retrospectively registered, https://www.chictr.org.cn/edit.aspx?pid=127374&htm=4.

Keywords: Hypertriglyceridemia, Abdominal obesity, Acute pancreatitis

* Correspondence: cww1984@126.com
†Xiaoxi Yang, Jiajun He and Shuli Ma contributed equally to this work.
[1]Department of Gastroenterology, Clinical Medical College, Yangzhou University, No 98, Nantong West Rd, Yangzhou, Jiangsu Province 225000, China
Full list of author information is available at the end of the article

Introduction

Acute pancreatitis is a common inflammatory disease in the digestive system [1]. The global incidence of AP is approximately 4.9–80/100,000, and it has been increasing worldwide [2]. Generally, mild acute pancreatitis (MAP) is characterized by a short duration and good prognosis. However, once severe acute pancreatitis (SAP) develops, the mortality rate is as high as 30–50% [3, 4]. Therefore, early and accurate identification of high-risk AP patients is of great significance to reduce mortality and improve prognosis.
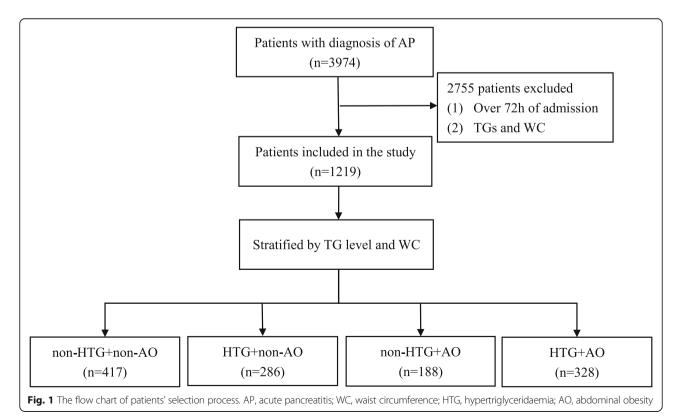
Recently, studies have indicated that abnormal lipid metabolism is closely associated with AP [5, 6]. As a key lipometabolic disorder, hypertriglyceridemia (HTG) has been recognized to be a cause of AP and an aggravating factor in AP progression [7]. Clinical studies have shown that the level of serum triglycerides (TGs) is an independently risk factors for persistent organ failure (POF) in AP patients [1]. In addition, obesity has been proven to be an independent risk factor for AP [8, 9], which aggravates the severity, prolongs hospital stay, and increases mortality [10, 11], especially for patients with abdominal obesity (AO) caused by excessive visceral fat [12]. However, few studies have researched the effect of comorbid HTG and AO on the severity and local complications of AP. Therefore, the objective of this study is to explore the influence of these comorbidities and discuss which is the dominant disorder.

Materials and methods

Study population

This retrospective observational study was carried out in the Department of Gastroenterology and was approved by the ethics committee of the hospital on August 4th, 2020 (No. 2020ky-047). Written informed consent was obtained from each patient. The research protocol was complied with the ethical guidelines of the 1975 Declaration of Helsinki. It was registered in the Chinese Clinical Trial Registry (Registration number: ChiCTR2100049566). The data were obtained from hospital information system (HIS) between January 1st, 2016, and December 31st, 2020. Patients with AP aged 18 to 80 years old were included in this study. They were hospitalized within 7 days of onset, with TG levels and waist circumference (WC) available in the first 3 days. The diagnosis and classification of AP was made according to the revision of the Atlanta classification [4]. Exclusion criteria were a. serious comorbidities at admission, such as chronic renal failure, b. any history of cancer, c. participation in other clinical trials that might interfere with this study, or d. pregnancy or parturient women. The screening process for patients is shown in Fig. 1.

Definition and classification of HTG and AO

According to the Endocrine Society Clinical Practice Guidelines [13], HTG level was determined above 1.7 mmol/L [13–16]. In this study, HTG was divided into two groups according to TG levels: mild (1.7 mmol/L ≤

Fig. 1 The flow chart of patients' selection process. AP, acute pancreatitis; WC, waist circumference; HTG, hypertriglyceridaemia; AO, abdominal obesity

TG < 5.65 mmol/L) and moderate to severe (TG ≥ 5.65 mmol/L).

AO was defined by WC, which was estimated by abdominal CT imaging. The horizontal and vertical axes of the navel on abdominal CT were measured. Then, the WC was calculated using the standard ellipse formula (WC = the elliptical coefficient × (short axis + long axis) ÷2)) [17]. Based on the Chinese criteria of AO for adults, men with WC ≥ 90 cm or women with WC ≥ 85 cm are considered to have AO.

In this study, four groups were established based on the above criteria: Group 1 (non-HTG + non-AO): TG < 1.7 mmol/L, WC < 90 cm (for men) or WC < 85 cm (for women), Group 2 (HTG + non-AO): TG ≥ 1.7 mmol/L, WC < 90 cm (for men) or WC < 85 cm (for women), Group 3 (non-HTG + AO): TG < 1.7 mmol/L, WC ≥ 90 cm (for men) or WC ≥ 85 cm (for women), and Group 4 (HTG + AO): TG ≥ 1.7 mmol/L, WC ≥ 90 cm (for men) or WC ≥ 85 cm (for women).

Data collection
Data analysed in this study included demographic data such as sex, age, WC, aetiology, episodes of AP, past medical history, clinical features and vital signs, laboratory indices, and image data. All data were obtained from the HIS and recorded in the unified case report form. Quality control was carried out in data collection to ensure accuracy.

Statistical analysis
Statistical analysis was performed with IBM Statistical Packages for the Social Sciences (SPSS®) 26.0. Normally distributed data are expressed as the mean ± standard deviation, and nonnormally distributed data are expressed as the median and extreme ranges. Categorical data were analysed by χ^2 test or 2-tailed Fisher's exact test. One-way ANOVA was applied between the four groups. Mann–Whitney U tests were used for pairwise comparisons among the groups. Multivariate binary logistic regressions (Wald's test) were performed to evaluate the risk factors for persistent respiratory failure and local complications. Statistical significance was determined with P value of < 0.05.

Results
Patients' demographics and clinical characteristics
There were 1219 AP patients included in this study. The 328 patients with comorbid HTG and AO were much younger (42.29 ± 11.77) and mainly male (79.57%) compared to patients in the other three groups. The TG levels in the two HTG groups were much higher than those in the two non-HTG groups, whereas the WC was

Table 1 Patients' demographics and clinical characteristics in the four groups of AP

Variables	non-HTG + non-AO (n = 417)	HTG + non-AO (n = 286)	non-HTG + AO (n = 188)	HTG + AO (n = 328)	P
Sex (n, %)					< 0.001
Male	220 (52.76)	182 (63.64) [a]	80 (42.55) [b]	261 (79.57) [a b c]	
Female	197 (47.24)	104 (36.36) [a]	108 (57.45) [a b]	67 (20.43) [a b c]	
Age (Years) (mean ± SD)	60.26 ± 16.08	48.65 ± 12.06 [a]	60.00 ± 16.67 [b]	42.29 ± 11.77 [a b c]	< 0.001
TG (mmol/L) [median (range)]	0.82 (0.15–1.69)	4.69 (1.71–116.38) [a]	1.06 (0.28–1.68) [a b]	7.31 (1.72–85.60) [a c]	< 0.001
WC (cm) (mean ± SD)	78.86 ± 6.29	81.83 ± 6.31 [a]	93.14 ± 5.98 [a b]	96.59 ± 6.70 [a b c]	< 0.001
Aetiologies (n, %)					< 0.001*
Biliary	274 (65.71)	54 (18.88) [a]	127 (67.55) [b]	59 (17.99) [a c]	
Hypertriglyceridemia	0 (0.00)	156 (54.55) [a]	0 (0.00) [b]	196 (59.76) [a c]	
Alcoholic	12 (2.88)	17 (5.94)	5 (2.66)	15 (4.57)	
ERCP	2 (0.48)	0 (0.00)	0 (0.00)	1 (0.30)	
Idiopathic	99 (23.74)	49 (17.13)	48 (25.53)	46 (14.02) [a c]	
Mixedness	1 (0.24)	4 (1.40)	1 (0.53)	6 (1.83)	
Others	29 (6.95)	6 (2.10) [a]	7 (3.72)	5 (1.52) [a]	
Recurrence≥2 (Times) (n, %)	35 (8.39)	33 (11.54)	10 (5.32)	54 (16.46) [a c]	< 0.001
Diabetes mellitus (n, %)	44 (10.55)	68 (23.78) [a]	26 (13.83) [b]	84 (25.61) [a c]	< 0.001
Alcoholism (n, %)	54 (12.95)	67 (23.43) [a]	21 (11.17) [b]	92 (28.05) [a c]	< 0.001
Smoker (n, %)	51 (12.23)	54 (18.88)	16 (8.51) [b]	91 (27.74) [a c]	< 0.001
Hospital stay (Day) (mean ± SD)	9.41 ± 4.61	9.21 ± 4.81	9.61 ± 4.76	9.66 ± 5.46	0.690

TG: serum triglyceride; WC: waist circumference; ERCP: endoscopic retrograde cholangiopancreatography; [a] $P < 0.05$, compared with the non-HTG + non-AO group; [b] $P < 0.05$, compared with the HTG + non-AO group; [c] $P < 0.05$, compared with the non-HTG + AO group; * Fisher's exact test

significantly higher in the obesity groups than in the non-AO groups. In terms of aetiology, biliary was the main cause in the non-HTG + non-AO and non-HTG + AO group (65.71 and 67.55%, respectively), whereas HTG was the major cause in the HTG + non-AO and HTG + AO groups (54.55 and 59.76%, respectively). In past medical history, recurrence ≥2 times and proportions of diabetes mellitus, alcoholism, and smokers were much higher in the comorbid group than in the other three groups, followed by the HTG + non-AO group. However, there were no significant differences between the non-HTG + non-AO group and the non-HTG + AO group. No significant difference was found in hospital stay (P = 0.690). The patients' demographics were shown in Table 1.

Clinical outcomes

The 1219 AP patients included 831 (68.17%) patients with moderately severe acute pancreatitis (MSAP), 54 (4.43%) patients with SAP with POF, 33 (2.71%) patients with transient organ failure (TOF), and 205 (16.82%) patients with systemic inflammatory response syndrome (SIRS). A significant difference was found in the severity of AP among the four groups (P < 0.001). There was 75.30% MSAP and 7.32% SAP in the HTG + AO comorbidity group, followed by the HTG + non-AO group with 75.52% MSAP and 2.45% SAP, the non-HTG + AO group with 65.96% MSAP and 4.79% SAP, and the non-HTG + non-AO group with 58.51% MSAP and 3.36% SAP. There was no significant difference in TOP. However, a significant difference was found in POF. The incidence of persistent respiratory failure was significantly higher in the comorbid group than in the other three

groups (P = 0.002). Similarly, the incidence of SIRS (25.91%) was the highest and significantly different in the comorbid group (P < 0.001) (Table 2).

Additionally, 885 (72.60%) patients developed local complications, and 842 (69.07%) had acute peripancreatic fluid collection (APFC), 55 (4.51%) suffered from acute necrotic collection (ANC), 31 (2.54%) developed pancreatic pseudocysts (PPCs), 4 (0.33%) had walled-off necrosis (WON), and 1 (0.08%) endured infectious pancreatic necrosis (IPN). Significant differences were found among the four groups for local complications (P < 0.001). In particular, the incidences of APFC and ANC were higher in the comorbid group than in the other three groups (P < 0.05). It was high up to 79.88% of APFC and 8.23% of ANC in the HTG + AO comorbidity group, followed by the HTG + non-AO group with 73.78% of APFC and 3.85% of ANC, the non-HTG + AO group with 69.68% of APFC and 3.72% of ANC, and the non-HTG + non-AO group with 57.07% of APFC and 2.40% of ANC. No significant differences were identified in PPC, WON, or IPN among the four groups. The MCTSI score was significantly different among the four groups (P < 0.001). However, there was no difference between the comorbid group and the HTG + non-AO group (Table 3).

Logistic regression analysis

Logistic regression analysis was applied to explore the risk factors for persistent respiratory failure and local complications. The univariate analysis indicated that AO, diabetes mellitus, and HTG were risk factors for persistent respiratory failure (P < 0.05, Table 4). Furthermore, sex (male), age (> 60 years), AO, diabetes mellitus,

Table 2 Comparison of the severity in the four group in patients with AP

Variables	non-HTG + non-AO (*n* = 417)	HTG + non-AO (*n* = 286)	non-HTG + AO (*n* = 188)	HTG + AO (*n* = 328)	*P*
Atlanta classification (n, %)					< 0.001
MAP	159 (38.13)	63 (22.03) [a]	55 (29.25)	57 (17.38) [a c]	
MSAP	244 (58.51)	216 (75.52) [a]	124 (65.96)	247 (75.30) [a c]	
SAP	14 (3.36)	7 (2.45)	9 (4.79)	24 (7.32) [a b]	
OF (n, %)	24 (5.76)	15 (5.24)	14 (7.45)	32 (9.76)	0.100
POF (n, %)	14 (3.36)	7 (2.45)	9 (4.79)	24 (7.32) [a b]	0.016
Persistent respiratory failure	8 (1.92)	6 (2.10)	7 (3.72)	22 (6.71) [a b]	0.002
Persistent heart failure	2 (0.48)	0 (0.00)	1 (0.53)	1 (0.30)	0.277[*]
Persistent renal failure	5 (1.20)	2 (0.70)	4 (2.13)	3 (0.91)	0.564[*]
TOF (n, %)	12 (2.88)	8 (2.80)	5 (2.66)	8 (2.44)	0.986
SIRS (n, %)	49 (11.75)	48 (16.78)	23 (12.23)	85 (25.91) [a b c]	< 0.001

OF: organ failure; POF: persistence organ failure; TOF: transient organ failure; SIRS: systemic inflammatory response syndrome; [a] P < 0.05, compared with the non-HTG + non-AO group; [b] P < 0.05, compared with the HTG + non-AO group; [c] P < 0.05, compared with the non-HTG + AO group; * Fisher's exact test

Table 3 Comparison of local complications in the four groups in patients with AP

Variables	non-HTG + non-AO (n = 417)	HTG + non-AO (n = 286)	non-HTG + AO (n = 188)	HTG + AO (n = 328)	P
Local Complications (n, %)	259 (62.11)	218 (76.22) [a]	139 (73.94)	269 (90.24) [a] [c]	< 0.001
APFC (n, %)	238 (57.07)	211 (73.78) [a]	131 (69.68)	262 (79.88) [a] [c]	< 0.001
ANC (n, %)	10 (2.40)	11 (3.85)	7 (3.72)	27 (8.23) [a]	0.001
PPC (n, %)	7 (1.68)	6 (2.10)	4 (2.13)	14 (4.27)	0.135
WON (n, %)	0 (0.00)	1 (0.35)	0 (0.00)	3 (0.91)	0.098[*]
IPN (n, %)	0 (0.00)	1 (0.35)	0 (0.00)	0 (0.00)	0.407[*]
MCTSI (mean ± SD)	4.09 ± 2.25	4.94 ± 1.75 [a]	4.29 ± 2.07 [b]	4.74 ± 1.86 [a] [c]	< 0.001

APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection; PPC: pancreatic pseudocyst; WON: walled-off necrosis; IPN: infectious pancreatic necrosis; OF: organ failure; POF: persistent organ failure; TOF: transient organ failure; SIRS: systemic inflammatory response syndrome; MCTSI: modification of CT severity index; [a] $P < 0.05$, compared with the non-HTG + non-AO group; [b] $P < 0.05$, compared with the HTG + non-AO group; [c] $P < 0.05$, compared with the non-HTG + AO group; * Fisher's exact test

alcoholism, smoking, and HTG were also risk factors for local complications, with significant differences ($P < 0.05$, Table 5).

To avoid confounding factors, stepwise multivariate logistic regression analyses of risk factors for persistent respiratory failure and local complications were performed. The results are summarized in Table 6 and Table 7. AO (OR = 3.205, 95% CI = 1.570–6.544), mild HTG (OR = 2.746, 95% CI = 1.125–6.701), and moderate to very severe HTG (OR = 3.649, 95% CI = 1.403–9.493) were indicated as independent risk factors for persistent respiratory failure ($P < 0.05$) (Table 6). Age > 60 years (OR = 1.326, 95% CI = 1.047–1.679), AO (OR = 1.701, 95% CI = 1.308–2.212), diabetes mellitus (OR = 1.551, 95% CI = 1.063–2.261), mild HTG (OR = 1.549, 95% CI = 1.137–2.112), and moderate to very severe HTG (OR = 2.810, 95% CI = 1.926–4.100) were independent risk factors associated with local complications ($P < 0.05$) (Table 7). Moreover, HTG seemed to be more dangerous than AO ($P < 0.05$). The higher the serum TG level was, the greater the likelihood of persistent respiratory failure and local complications.

Discussion

With the improvement in living standards and the adjustment of dietary structure, the incidence of hypertriglyceridemic AP (HTG-AP) has increased significantly, and HTG has become the second major cause of AP in China [18]. Abdominal adiposity has an adverse impact on AP [19] and shows an obvious trend of increasing severity. Although HTG and AO have been associated with the severity of AP in previous studies, few studies have examined the effect of comorbid HTG and AO on AP. This study first proposed an association between comorbid HTG and AO and the severity of AP. The study demonstrated that HTG and AO were independent risk factors associated with persistent respiratory failure and local complications in AP patients. Moreover, the risk of HTG was higher than that of AO. The higher the serum TG level was, the greater the likelihood of persistent respiratory failure and local complications, which suggested that HTG may play a dominant role in AP risk.

This study found that 42.17% of patients exhibited biliary AP, followed by 28.88% with HTG-AP, indicating that HTG is the second major cause of AP in the centre.

Table 4 Univariate Logistic regression analysis of persistent respiratory failure in AP patients

Variable	B (S.E)	Adjusted OR	95% CI	P
Male	0.363	1.437	0.776–2.663	0.249
Age > 60 years	0.254	1.290	0.666–2.498	0.451
AO	1.272	3.567	1.808–7.037	< 0.001
Diabetes mellitus	0.731	2.076	1.061–4.062	0.033
Recurrence ≥2 times	0.148	0.863	0.303–2.457	0.782
Alcoholism	0.366	0.694	0.289–1.666	0.413
Smoking	0.411	1.508	0.730–3.118	0.267
HTG	0.420	1.522	1.062–2.181	0.022
Mild	0.546	1.726	0.788–3.779	0.172
Moderate to severe	0.844	2.325	1.119–4.829	0.024

Table 5 Univariate Logistic regression analysis of local complications in AP patients

Variable	B (S.E)	Unadjusted OR	95% CI	P
Male	1.075	2.931	2.485–3.457	< 0.001
Age > 60 years	0.818	2.266	1.834–2.799	< 0.001
AO	1.338	3.813	3.082–4.718	< 0.001
Diabetes mellitus	1.455	4.286	3.063–5.996	< 0.001
Recurrence ≥2 times	0.094	1.099	0.728–1.659	0.654
Alcoholism	0.556	1.744	1.225–2.482	0.002
Smoking	0.682	1.978	1.354–2.892	< 0.001
HTG	0.573	1.774	1.649–1.908	< 0.001
Mild	1.039	2.835	2.189–3.645	< 0.001
Moderate to severe	1.736	5.674	4.147–7.762	< 0.001

Table 6 Multiple Logistic regression analysis of persistent respiratory failure in AP patients

Variable	B (S.E)	Unadjusted OR	95% CI	P
AO	1.165	3.205	1.570–6.544	0.001
Diabetes mellitus	0.462	1.587	0.779–3.233	0.203
HTG				
Mild	1.010	2.746	1.125–6.701	0.026
Moderate to severe	1.295	3.649	1.403–9.493	0.008

Patients with comorbid HTG and AO were significantly younger and were mainly male, which was consistent with a previous study [20]. This study also showed that recurrence, metabolic comorbidity of diabetes, and a life-style of drinking and smoking were much higher in the comorbid group. This pattern may be related to long-term drinking, a high-fat diet, a lack of exercise and other poor living habits among young men [21], thus leading to abnormal fat metabolism and other phenomena.

Additionally, the results showed that patients with co-morbid HTG and AO had higher incidences of SAP, persistent organ failure, SIRS, and local complications, especially APFC and ANC. Study demonstrated that elevated TG may lead to respiratory insufficiency by affecting pulmonary gas exchange [22]. The results of the study were consistent with those of Chen et al. [23], who pointed out that HTG and obesity are definitely risk factors for the local complications of AP. Patel et al. also showed that mild AP develops into SAP in obese mice with increased MOF [24]. In addition, this study also found that HTG was a more dangerous pathogenic factor than AO. The higher the serum TG level was, the greater the likelihood of persistent respiratory failure and local complications, which suggested that HTG may play a dominant role of risk in the condition of comorbidity. This finding has never been reported before.

Table 7 Multiple Logistic regression analysis of local complications in AP patients

Variable	B (S.E)	Unadjusted OR	95% CI	P
Male	0.166	1.180	0.925–1.507	0.183
Age > 60 years	0.282	1.326	1.047–1.679	0.019
AO	0.531	1.701	1.308–2.212	< 0.001
Diabetes mellitus	0.439	1.551	1.063–2.261	0.023
Alcoholism	0.216	1.241	0.805–1.915	0.329
Smoking	0.444	1.559	0.984–2.469	0.059
HTG				
Mild	0.438	1.549	1.137–2.112	0.006
Moderate to severe	1.033	2.810	1.926–4.100	< 0.001

The mechanisms by which HTG and AO aggravate AP may include adipokines, cytokines, unsaturated fatty acid (UFA)-mediated lipotoxicity, and oxidative stress. Previous studies reported that the severity of AP is related to an increase in visceral fat [25, 26], which accounts for 1–10% of body weight [27]. TG oversteps more than 80% of adipocyte mass [28], which is hydrolysed into free fatty acid (FFA) and results in lipotoxicity of acinar cells. Insoluble TG may result in pancreatic microthrombi, ischaemia and infarction. Exocrine pancreatic acinar cells are rich in lipase, which is responsible for hydrolysing TG into UFAs [29]. UFAs may worsen inflammatory conditions and release intracellular calcium, thereby causing acinar necrosis by decreasing ATP levels [8]. It can also aggregate into micelles and cause pancreatic ischaemia [30], which activates lysosomal pepsine-B and trypsinogen, resulting in acidosis, pancreatic self-digestion, and injury [31]. Excessive UFAs induce apoptosis of alveolar epithelia and renal tubular injury [1, 32]. In addition, FFA directly influence on pancreatic acinus [33], stimulating the secretion of TNF-α, IL-1β, MCP-1, IL-18, and others [34]. In addition, high-fat diet-induced hyperlipidaemia is related to oxidative stress and ROS, which are considered key factors causing tissue damage and the inflammatory response in AP [35]. All the above results indicated that comorbid HTG and AO would aggravate the severity of AP. AO may act through HTG. Thus, HTG may play a primary role of risk in comorbidities.

Comparisons with other studies and what the current work adds to existing knowledge

Ding et al. [36] pointed out that the waist phenotype of HTG was related to the severity of AP. Kiss et al. showed in a meta-analysis that the presence of HTG (even at mild levels) exacerbates the condition of AP [37]. Compared with previous studies, this study proved the influence of comorbid HTG and AO on the progression of AP. The complications of HTG and AO further aggravated the severity and increased the incidence of local complications of AP, especially persistent respiratory failure, APFC and ANC. Interestingly, there is a preliminary indication that HTG is more dangerous than AO in the course of AP.

Strengths and limitations

As described above, this study explored the influence of comorbid HTG and AO on the severity of AP and found that HTG was more dangerous than AO. However, there were also several limitations in the study. First, as TG levels decreased rapidly with fasting, the TG levels within the first three days after admission were underestimated. Therefore, unintended bias may have occurred. Second, abdominal CT was not the most appropriate

Yang *et al. Lipids in Health and Disease*   (2021) 20:171

Page 7 of 8

way to measure WC, but all subjects included adopted the same measurement method, which may avoid bias to some extent.

Conclusions

In conclusion, comorbid HTG and AO will aggravate the severity and increase the incidence of local complications of AP, especially persistent respiratory failure, APFC and ANC. HTG may play a dominant role of risk in comorbidities. More attention should be given to AP patients with comorbid HTG and AO in the future. In the early stage of AP, medical staff should pay close attention to such patients and give effective treatment in time to prevent complications. Additionally, in the recovery period, health education, such as diet management and AO slimming, should be carried out, and TG levels should be monitored regularly to reduce the recurrence of AP.

Abbreviations
AP: Acute pancreatitis; APFC: Acute peripancreatic fluid collection; ANC: Acute necrotic collection; CRF: Case report form; ERCP: Endoscopic retrograde cholangiopancreatography; FFA: Free fatty acid; HTG: Hypertriglyceridemia; HTG-AP: Hypertriglyceridemic acute pancreatitis; IPN: Infectious pancreatic necrosis; MAP: Mild acute pancreatitis; MCTSI: Modification of CT severity index; OR: Odds ratio; OF: Organ failure; POF: Persistence organ failure; PPCs: Pancreatic pseudocysts; SAP: Severe acute pancreatitis; SIRS: Systemic inflammatory response syndrome; TG: Serum triglyceride; TOF: Transient organ failure; UFAs: Unsaturated fatty acids; WC: Waist circumference; WON: Walled-off necrosis

Authors' contributions
XXY, JJH and SLM collected the data, performed statistical analysis, drafted the manuscript, and contributed equally to this work. TTW, QPZ, FC, YHL, and CTY participated in the data collection. CWC, GTL, LHH and JL checked the data and edited the manuscript. WWC conceived the study, checked the data and revised the manuscript. All authors have read and approved the final manuscript.

Availability of data and materials
All data are contained in the article. The raw data will be shared upon request: Contact corresponding author.

Declarations

Ethics approval and consent to participate
The study was approved by the ethics committee of Clinical Medical College of Yangzhou University on 4th August, 2020 (No. 2020ky-047).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no conflicts of interest.

Author details
[1]Department of Gastroenterology, Clinical Medical College, Yangzhou University, No 98, Nantong West Rd, Yangzhou, Jiangsu Province 225000, China. [2]School of Nursing, Yangzhou University, Yangzhou, China. [3]Department of Gastroenterology, Affiliated Hospital of Nantong University, Nantong, China. [4]Department of Gastroenterology, Affiliated Hospital of Yangzhou University, Yangzhou, China. [5]Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai, China.

References
1. Nawaz H, Koutroumpakis E, Easler J, Slivka A, Whitcomb DC, Singh VP, et al. Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis. Am J Gastroenterol. 2015;110(10):1497–503. https://doi.org/10.1038/ajg.2015.261.
2. Garg SK, Sarvepalli S, Campbell JP, Obaitan I, Singh D, Bazerbachi F, et al. Incidence, admission rates, and predictors, and economic burden of adult emergency visits for acute pancreatitis: data from the national emergency department sample, 2006 to 2012. J Clin Gastroenterol. 2019;53(3):220–5. https://doi.org/10.1097/MCG.0000000000001030.
3. Forsmark CE, Vege SS, Wilcox CM. Acute pancreatitis. N Engl J Med. 2016; 375(20):1972–81. https://doi.org/10.1056/NEJMra1505202.
4. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102–11. https://doi.org/10.1136/gutjnl-2012-302779.
5. Li X, Guo X, Ji H, Niu J, Gao P. Relationships between metabolic comorbidities and occurrence, severity, and outcomes in patients with acute pancreatitis: a narrative review. Biomed Res Int. 2019;2019:2645926–8. https://doi.org/10.1155/2019/2645926.
6. Biczo G, Vegh ET, Shalbueva N, Mareninova OA, Elperin J, Lotshaw E, et al. Mitochondrial dysfunction, through impaired autophagy, leads to endoplasmic reticulum stress, deregulated lipid metabolism, and pancreatitis in animal models. Gastroenterology. 2018;154(3):689–703. https://doi.org/10.1053/j.gastro.2017.10.012.
7. Zhang R, Deng L, Jin T, Zhu P, Shi N, Jiang K, et al. Hypertriglyceridaemia-associated acute pancreatitis: diagnosis and impact on severity. HPB. (Oxford). 2019;21:1240–9.
8. Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. Sci Transl Med. 2011;3:107ra110.
9. Dobszai D, Mátrai P, Gyöngyi Z, Csupor D, Bajor J, Erőss B, et al. Body-mass index correlates with severity and mortality in acute pancreatitis: a meta-analysis. World J Gastroenterol. 2019;25(6):729–43. https://doi.org/10.3748/wjg.v25.i6.729.
10. Emerenziani S, Guarino MPL, Trillo Asensio LM, Altomare A, Ribolsi M, Balestrieri P, et al. Role of overweight and obesity in gastrointestinal disease. Nutrients. 2019;12(1). https://doi.org/10.3390/nu12010111.
11. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral adiposity index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care. 2010;33(4):920–2. https://doi.org/10.2337/dc09-1825.
12. Natu A, Stevens T, Kang L, Yasinow S, Mansoor E, Lopez R, et al. Visceral adiposity predicts severity of acute pancreatitis. Pancreas. 2017;46(6):776–81. https://doi.org/10.1097/MPA.0000000000000845.
13. Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH, et al. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(9):2969–89. https://doi.org/10.1210/jc.2011-3213.
14. de Pretis N, Amodio A, Frulloni L. Hypertriglyceridemic pancreatitis: epidemiology, pathophysiology and clinical management. United European Gastroenterol J. 2018;6(5):649–55. https://doi.org/10.1177/2050640618755002.
15. Scherer J, Singh VP, Pitchumoni CS, Yadav D. Issues in hypertriglyceridemic pancreatitis: an update. J Clin Gastroenterol. 2014;48(3):195–203. https://doi.org/10.1097/01.mcg.0000436438.60145.5a.
16. Yin G, Cang X, Yu G, Hu G, Ni J, Xiong J, et al. Different clinical presentations of hyperlipidemic acute pancreatitis: a retrospective study. Pancreas. 2015; 44(7):1105–10. https://doi.org/10.1097/MPA.0000000000000403.
17. Joo I, Kwak MS, Park DH, Yoon SH. Fully automated waist circumference measurement on abdominal CT: comparison with manual measurements and potential value for identifying overweight and obesity as an adjunct

output of CT scan. PLoS ONE. 2021;16(7):e0254704. https://doi.org/10.1371/journal.pone.0254704.

18. Zheng Y, Zhou Z, Li H, Li J, Li A, Ma B, et al. A multicenter study on etiology of acute pancreatitis in Beijing during 5 years. Pancreas. 2015;44(3):409–14. https://doi.org/10.1097/MPA.0000000000000273.

19. Krishna SG, Behzadi J, Hinton A, El-Dika S, Groce JR, Hussan H, et al. Effects of bariatric surgery on outcomes of patients with acute pancreatitis. Clin Gastroenterol Hepatol. 2016;14:1001–1010.e1005.

20. Li X, Ke L, Dong J, Ye B, Meng L, Mao W, et al. Significantly different clinical features between hypertriglyceridemia and biliary acute pancreatitis: a retrospective study of 730 patients from a tertiary center. BMC Gastroenterol. 2018;18(1):89. https://doi.org/10.1186/s12876-018-0821-z.

21. Sezgin O, Özdoğan O, Yaraş S, Üçbilek E, Altıntaş E. Evaluation of hypertriglyceridemia-induced acute pancreatitis: a single tertiary care unit experience from Turkey. Turk J Gastroenterol. 2019;30(3):271–7. https://doi.org/10.5152/tjg.2018.18292.

22. Kimura T, Toung JK, Margolis S, Permutt S, Cameron JL. Respiratory failure in acute pancreatitis: a possible role for triglycerides. Ann Surg. 1979;189(4):509–14.

23. Chen SM, Xiong GS, Wu SM. Is obesity an indicator of complications and mortality in acute pancreatitis? An updated meta-analysis. J Dig Dis. 2012;13(5):244–51. https://doi.org/10.1111/j.1751-2980.2012.00587.x.

24. Patel K, Trivedi RN, Durgampudi C, Noel P, Cline RA, DeLany JP, et al. Lipolysis of visceral adipocyte triglyceride by pancreatic lipases converts mild acute pancreatitis to severe pancreatitis independent of necrosis and inflammation. Am J Pathol. 2015;185(3):808–19. https://doi.org/10.1016/j.ajpath.2014.11.019.

25. Sadr-Azodi O, Orsini N, Andrén-Sandberg Å, Wolk A. Abdominal and total adiposity and the risk of acute pancreatitis: a population-based prospective cohort study. Am J Gastroenterol. 2013;108(1):133–9. https://doi.org/10.1038/ajg.2012.381.

26. Yashima Y, Isayama H, Tsujino T, Nagano R, Yamamoto K, Mizuno S, et al. A large volume of visceral adipose tissue leads to severe acute pancreatitis. J Gastroenterol. 2011;46(10):1213–8. https://doi.org/10.1007/s00535-011-0430-x.

27. Choh AC, Demerath EW, Lee M, Williams KD, Towne B, Siervogel RM, et al. Genetic analysis of self-reported physical activity and adiposity: the Southwest Ohio family study. Public Health Nutr. 2009;12(8):1052–60. https://doi.org/10.1017/S1368980008003583.

28. Garaulet M, Hernandez-Morante JJ, Lujan J, Tebar FJ, Zamora S. Relationship between fat cell size and number and fatty acid composition in adipose tissue from different fat depots in overweight/obese humans. Int J Obes. 2006;30(6):899–905. https://doi.org/10.1038/sj.ijo.0803219.

29. Zhang W, Zhao Y, Zeng Y, Yu X, Yao J, Zhao S, et al. Hyperlipidemic versus normal-lipid acute necrotic pancreatitis: proteomic analysis using an animal model. Pancreas. 2012;41(2):317–22. https://doi.org/10.1097/MPA.0b013e31822981fb.

30. Jeong YK, Kim H. A Mini-review on the effect of docosahexaenoic acid (DHA) on cerulein-induced and hypertriglyceridemic acute pancreatitis. Int J Mol Sci. 2017;18(11). https://doi.org/10.3390/ijms18112239.

31. Hahn SJ, Park JH, Lee JH, Lee JK, Kim KA. Severe hypertriglyceridemia in diabetic ketoacidosis accompanied by acute pancreatitis: case report. J Korean Med Sci. 2010;25(9):1375–8. https://doi.org/10.3346/jkms.2010.25.9.1375.

32. Noel P, Patel K, Durgampudi C, Trivedi RN, de Oliveira C, Crowell MD, et al. Peripancreatic fat necrosis worsens acute pancreatitis independent of pancreatic necrosis via unsaturated fatty acids increased in human pancreatic necrosis collections. Gut. 2016;65(1):100–11. https://doi.org/10.1136/gutjnl-2014-308043.

33. Guo YY, Li HX, Zhang Y, He WH. Hypertriglyceridemia-induced acute pancreatitis: progress on disease mechanisms and treatment modalities. Discov Med. 2019;27(147):101–9.

34. Garg PK, Singh VP. Organ failure due to systemic injury in acute pancreatitis. Gastroenterology. 2019;156(7):2008–23. https://doi.org/10.1053/j.gastro.2018.12.041.

35. Pereda J, Pérez S, Escobar J, Arduini A, Asensi M, Serviddio G, et al. Obese rats exhibit high levels of fat necrosis and isoprostanes in taurocholate-induced acute pancreatitis. PLoS ONE. 2012;7(9):e44383. https://doi.org/10.1371/journal.pone.0044383.

36. Ding Y, Zhang M, Wang L, Yin T, Wang N, Wu J, et al. Association of the hypertriglyceridemic waist phenotype and severity of acute pancreatitis. Lipids Health Dis. 2019;18(1):93. https://doi.org/10.1186/s12944-019-1019-2.

37. Kiss L, Fűr G, Mátrai P, et al. The effect of serum triglyceride concentration on the outcome of acute pancreatitis: systematic review and meta-analysis. Sci Rep. 2018;8(1):14096.

Publisher's Note