

The Association of Body Composition Parameters and Laboratory Markers With The Severity of Hypertriglyceridemia-Induced Pancreatitis

Lifang Chen

The First Affiliated Hospital of Wenzhou Medical University

Yingbao Huang

The First Affiliated Hospital of Wenzhou Medical University

Huajun Yu

The First Affiliated Hospital of Wenzhou Medical University

Kehua Pan

The First Affiliated Hospital of Wenzhou Medical University

Zhao Zhang

The First Affiliated Hospital of Wenzhou Medical University

Yi Man

The First Affiliated Hospital of Wenzhou Medical University

Dingyuan Hu (✉ dingyuan.hu@wzhealth.com)

The Second Affiliated Hospital of Wenzhou Medical University

Research

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Abstract

Background: Hypertriglyceridemia has arisen as the third leading cause of acute pancreatitis. This study aimed at exploring the association between the severity of hypertriglyceridemia-induced pancreatitis (HTGP) and computed tomography (CT)-based body composition parameters and laboratory markers.

Methods: Clinical parameters were collected from 242 patients with HTGP between 2017 and 2020. Severity of HTGP was evaluated by original or modified CT severity index. Body composition parameters such as area and radiodensity of muscle, subcutaneous adipose tissue and visceral adipose tissue were calculated by CT at the third lumbar vertebra level. Parameters between mild and moderately severe to severe HTGP were compared. Uni-variate and multi-variate Logistic regression analyses were employed to assess the risk factors of the severity of HTGP.

Results: Seventy patients with HTGP (28.9%) were mild. Body mass index, waist circumference and all CT-based body composition parameters differed between male and female patients. None was associated with the severity of HTGP, neither in the male nor in the female. Uni-variate and multi-variate Logistic regression analysis showed that low serum albumin (<35g/L) and high C-reactive protein (>90 mg/L) were risk factors of moderately severe to severe HTGP ($P<0.001$, OR=4.846, 95%CI=2.122-11.068; $P<0.001$, OR=4.230, 95%CI=2.050-8.727, respectively). Low serum albumin was also associated with pancreatic necrosis, longer hospital stay and higher scores of APACHE II, Ranson and Marshall in HTGP patients (all $P<0.05$).

Conclusions: Low serum albumin and high C-reactive protein upon admission are associated with the severity of HTGP. However, none of the body composition parameters is associated with the severity of HTGP.

Background

Acute pancreatitis (AP) is the inflammation of the pancreas with unpredictable clinical outcome. Although most of acute pancreatitis is mild and can be cured successfully, some can lead to local complications, systematic inflammatory response syndrome and organ failure, which are associated with higher mortality. Gallstones and alcohol abuse are currently the most frequent causes of AP. Notably, the proportion of hypertriglyceridemia (HTG)-induced pancreatitis (HTGP) in AP is increasing during the decades [1], which now ranks as the third leading causes for AP [2, 3]. HTGP accounts for approximately 9% of all cases and as much as 56% of AP cases during pregnancy [4]. It possesses similar clinical course with other forms of AP with the only distinguishing clinical presentation observed initially being HTG [5]. Although debates exist, HTGP tends to be more severe than AP caused by other etiology [4]. It has been postulated that HTGP may specifically benefit from the plasmapheresis treatment [4].

The precise pathophysiology underlying HTGP remain unclear. However, it is generally believed that the deposition of free fatty acids hydrolyzed by pancreatic lipase from triglyceride (TG) drives the occurrence of the disease [6]. The fatty acids can be bound to the albumin in the serum whereas the exceeded free

fatty acids exert a detergent-like role and attacks platelets, vascular endothelium, and acinar cells. Although some studies have recognized the effect of albumin on the severity and the organ failure in AP, it has not been included as a risk factor of AP in most studies and clinical practice. Furthermore, there are few studies investigating the association of serum albumin with HTGP, despite that serum albumin might be more closely linked to the deposition of free fatty acids and the severity of HTGP.

Since the prognosis and clinical intervention of AP differs largely in mild AP and severe AP, the early prediction of the severity in AP has been a great concern and research focus for clinicians. A host of predictors, including clinical, laboratory and radiological markers and various scoring systems, have been proposed. Current guidelines recommend the persistent systemic inflammatory response syndrome or organ failure for at least 48 hours to predict the severity of AP [7]. Other recognized risk factors for development of severe AP include elevated hematocrit, blood urea nitrogen and creatinine and body mass index [8, 9]. Several scoring systems, such as Acute Physiology and Chronic Health Evaluation II (APACHE II), the Bedside Index for Severity in Acute Pancreatitis (BISAP), and Ranson's Criteria have proven their correlation with the severity of AP, but their clinical utilities are still limited due to the low predictive values [10, 11]. Computed tomography (CT) on admission has the similar predictive accuracy for the severity of AP as clinical scoring systems [12]. Although not recommended by the guidelines [7], abdominal CT upon admission is often conducted in AP in real-world practice, especially in emergent situation. Contrast-enhanced CT is advantageous to delineate pancreatic or peripancreatic fluid collections and necrosis. It is the most applied method in clinic to re-evaluate the severity of cases in which deteriorated manifestation and laboratory findings are indicated.

Recent studies have suggested that the severity of AP is also linked to some radiological parameters for the body composition [13]. Yoko Yashima and colleagues found that larger peripancreatic volume of visceral adipose tissue (VAT) is associated with severe AP [14]. Another study from Korean reported that high visceral fat with low skeletal muscle volume was strongly correlated with AP severity [15]. A most recent systematic review, which included 11 studies, concluded that VAT is an important prognostic indicator of the severity of AP and may be incorporated into the prognostic scoring systems of AP [16]. Nevertheless, Hanna Sternby and colleagues found that muscle radiodensity, rather than VAT and subcutaneous adipose tissue (SAT), correlates with severe acute pancreatitis [17]. Notably, by stratifying AP into HTGP and non-HTGP, Ting Ji and colleagues revealed that VAT and VAT/SAT were valuable factors for predicting the severity in HTGP but not non-HTGP [18].

With a focus on HTGP, a subgroup of AP with rising incidence, this study aimed at exploring body composition parameters and clinical risk factors for the severity of HTGP, which may help predict the prognosis of HTGP.

Methods

Patients

A total of 242 hospitalized patients with HTGP were retrospectively studied from the First Affiliated Hospital of Wenzhou Medical University between July 2017 and August 2020. The diagnosis of AP was established according to the Revised Atlanta Definitions of AP [19], when 2 of the following 3 characteristics were met: (1) the symptoms of abdominal pain are consistent with AP, (2) the levels of amylase and/or lipase are at least 3 times above the upper limit of normal, and (3) abdominal imaging is consistent with changes in AP. HTGP is considered in AP patients when the level of serum TG is (1) over 11.3 mmol/L; (2) between 5.65 mmol/L and 11.3 mmol/L, milky serum, with no other etiology of AP; (3) not tested, but the patient, without any known etiology, has previously been diagnosed as HTGP. The inclusion criteria of patients in this study were (1) the diagnosis of HTGP was established; (2) abdominal CT scanning 72 h before the occurrence of symptom; exclusion criteria were (1) poor CT imaging of the abdomen; (2) indication of biliary, alcoholic, autoimmune, drug-induced or pancreatic tumor-related etiology of AP; (3) pregnancy.

Contrast-enhanced CT scanings of abdomen were performed in 177 (73.1%) of the studied patients when deterioration of the disease was indicated during the course. The severity of HTGP was evaluated by modified CT severity index (MCTSI) if contrast-enhanced CT scanning has been conducted, otherwise by the CT severity index based on unenhanced CT scanning.

Clinical parameters of each patient were retrieved from the Electronic Health Record System, including sex, gender, body mass index, length of hospital stay, and C-reactive protein level, serum albumin, TG concentration upon the admission. The levels of CRP, albumin and TG were categorized as high and low with the cutoff of 90 mg/L, 35 g/L and 22.4 mmol/L [20], respectively. APACHE II, BISAP, Ranson and Marshall scorings of the patients were calculated when possible.

Ct Scanning And Body Composition Parameters

CT scanning was performed by 64-slice spiral CT scanner (Lightspeed VCT, GE healthcare, USA) or Aquilion ONE 320 Slice CT scanner (Toshiba, Japan). The scanning covered the whole abdomen region. The slice thickness was 0.625 mm for 64-slice spiral CT scanner (pitch 0.984, single-turn spiral time 0.5 s, 100 kV, 500 mA) and 0.5 mm for the 320 Slice CT scanner (single-turn spiral time 0.5 s, 100 kV, 300 mA). For contrast-enhanced CT, an auto-injector was used to inject 60 mL of non-ionic contrast agent (iopromide 300mgI/mL) and 30 mL of saline at a speed of 4.0 mL/s, and the scanning was triggered intelligently by monitoring of the abdominal aorta, the arterial phase was delayed for 30–35 s, and the portal phase was delayed for 60–70 s. The imaging data was transferred to the post-processing workstation (Version 4.5, GE healthcare).

Body composition parameters were measured based on the non-enhanced CT scanning. Muscle and adipose tissue at the third lumbar vertebra level (L3) with supine position were analyzed by Image J software [21]. A range of -29 to 150 Hounsfield units (HU) was set to highlight muscle, a range of -190 to -30 HU was set to highlight SAT, and -150 to 50 HU for VAT. The area and density of the region of interest (ROI) were calculated automatically. Waist circumference was measured at the navel plane. CT

measurements were performed by 2 experienced radiologists blinded to the clinical information. Re-measurement took place when disagreement of the measurements occurred.

Statistical analysis

Parameters between mild and moderately severe to severe HTGP were compared. Comparisons of categorical data were performed using Chi-square test or Fisher's exact test. Continuous data were expressed as mean \pm standard deviation and compared by the student's t test when normal distribution was justified, otherwise expressed as median (interquartile range) and compared by Mann Whitney U test. Uni-variate and multi-variate Logistic regression analyses were employed to assess the risk factors for the severity of HTGP. To test the predictive capacity of the measured parameters, receiver operating characteristic (ROC) curves with corresponding areas under the curves (AUC) were calculated. P-value of < 0.05 was considered statistically significant. All the statistics were performed using SPSS 18.0 (IBM. SPSS Statistics for Windows, USA).

Results

Body Composition Parameters were divergent between male and female patients with pancreatitis

Notably, differences existed apparently between the male and female patients regarding all the body composition parameters studied in our study, including BMI, muscle area, muscle radiodensity, SAT area, SAT radiodensity, VAT area, VAT area/total adipose tissue area and waist circumference (all $P < 0.05$). The mean values of each parameter in male and female patients with HTGP were shown in Table 1. For the subsequent analyses, all body composition parameters were categorized as high and low subgroups using corresponding median value in the male or the female as the cutoff. There were no differences of age, CRP value, albumin concentration and TG concentration between the male and female patients (all $P > 0.05$).

Table 1

Comparisons of body composition parameters and clinical data in patients with mild and moderately severe to severe hypertriglyceridemia-induced pancreatitis.

Variables	HTGP	Mild HTGP	Moderately severe to Severe HTGP	<i>P</i> values
Sex				0.141
Male	193	60 (85.7)	133 (77.3)	
Female	49	10 (14.3)	39 (22.7)	
Age (years)	40 (34–47)	42 (35–49)	39 (33–46)	0.101
Body mass index				
Male	26.3 ± 3.3	26.3 ± 2.8	26.3 ± 3.5	0.885
female	24.5 ± 3.8	24.4 ± 5.8	24.5 ± 3.2	0.912
muscle area (mm ²)				
Male	166.3 ± 27.5	165.4 ± 27.6	166.7 ± 27.5	0.763
female	110.1 ± 16.6	107.7 ± 13.0	110.7 ± 17.5	0.612
muscle radiodensity (HU)				
Male	43.5 ± 6.0	44.8 ± 4.8	42.9 ± 6.4	0.020
female	39.6 ± 5.8	42.0 ± 4.6	39.0 ± 6.0	0.158
SAT area (mm ²)				
Male	123.5 ± 45.0	1213 ± 45.3	124.5 ± 49.3	0.664
female	167.5 ± 64.5	157.6 ± 80.0	170.0 ± 61.0	0.592
SAT radiodensity (HU)				
Male	-95.8 ± 7.7	-97.7 ± 5.7	-95.0 ± 8.4	0.009
female	-99.8 ± 5.4	-101.2 ± 3.9	-99.5 ± 5.7	0.368
VAT area (mm ²)				
Male	181.9 ± 66.9	187.9 ± 63.7	179.2 ± 68.4	0.405
female	122.8 ± 52.6	105.5 ± 41.8	127.2 ± 54.6	0.248
VAT area /TAT area				

HTGP: hypertriglyceridemia-induced pancreatitis. SAT: subcutaneous adipose tissue. TAT: total adipose tissue. VAT: visceral adipose tissue. ^a There were 21 missing values. ^b There were 12 missing values.

Variables	HTGP	Mild HTGP	Moderately severe to Severe HTGP	<i>P</i> values
Male	0.589 ± 0.110	0.604 ± 0.088	0.581 ± 0.118	0.187
female	0.418 ± 0.091	0.409 ± 0.091	0.421 ± 0.092	0.725
waist circumference (cm)				
Male	90.1 ± 8.6	89.8 ± 8.4	90.2 ± 8.77	0.766
female	83.9 ± 10.4	82.4 ± 7.7	84.3 ± 11.1	0.613
C-reactive protein ^a				< 0.001
< 90	91	43 (69.4)	48 (30.2)	
≥ 90	130	19 (30.6)	111 (69.8)	
Albumin	36.54 ± 6.56	40.38 ± 4.89	34.98 ± 6.52	< 0.001
< 35	103	11 (15.7)	92 (53.5)	< 0.001
≥ 35	139	59 (84.3)	80 (46.5)	
Triglyceride (mmol/L) ^b	12.74 (8.18–25.12)	10.64 (6.69–21.50)	13.34 (9.45–26.10)	0.008
High (< 22.4 mmol/L)	163	50 (76.9)	113 (68.5)	0.205
Very high (≥ 22.4 mmol/L)	67	15 (23.1)	52 (31.5)	
Length of hospital stay (days)	13 (9–20)	9 (7–11.5)	17 (11–21)	< 0.001
< 14	131	61 (88.4)	70 (40.7)	< 0.001
≥ 14	110	8 (11.6)	102 (59.3)	
HTGP: hypertriglyceridemia-induced pancreatitis. SAT: subcutaneous adipose tissue. TAT: total adipose tissue. VAT: visceral adipose tissue. ^a There were 21 missing values. ^b There were 12 missing values.				

Parameters Associated With The Severity Of Htgp

To investigate the association of the severity of HTGP with the body composition parameters, laboratory parameters and clinical data, comparisons were made between patients with mild HTGP and those with moderately severe to severe HTGP. Age and gender distribution showed no difference between the two

groups (all $P > 0.05$). However, the serum CRP and TG level were significantly higher in patients with moderately severe to severe HTGP than those with mild HTGP (all $P < 0.05$). Besides, serum albumin concentration was significantly lower in the severe group (mean 34.98 vs. 40.38 g/L, $P < 0.001$). Since body composition parameters were significantly gender dependent, stratified comparisons in either male or female patients were performed. Consequently, the muscle radiodensity (mean 42.9 vs. 44.8 HU, $P = 0.020$) was lower while SAT radiodensity (mean -95.0 vs. -97.7 HU, $P = 0.009$) was higher in male patients with moderately severe or severe HTGP than those with mild HTGP.

ROC analysis showed the AUC of muscle radiodensity ($P = 0.004$, AUC = 0.625), SAT radiodensity ($P = 0.066$, AUC = 0.580), CRP ($P < 0.001$, AUC = 0.743), serum albumin ($P < 0.001$, AUC = 0.759) and TG ($P = 0.027$, AUC = 0.596) for the prediction of HTGP severity (Fig. 1). Among these parameters, albumin had the largest AUC for the prediction of HTGP severity. A cutoff of 36.65 g/L for albumin concentration achieved the sensitivity of 0.786 and specificity of 0.651. With the cutoff of 35.0 g/L, the sensitivity and specificity were of 0.843 and 0.535, respectively.

Logistic regression analyses of risk factors of the severity of HTGP

Uni-variate Logistic regression analysis was applied to explore parameters associated with the severity of HTGP in either male or female subgroups of patients. In male patients with HTGP, age, CRP and albumin were associated with the CT-based severity of the disease (all $P < 0.05$, Table 2). In female patients, high CRP and TG level, but none of the body composition parameters, were associated with the severity of HTGP (Table 2).

Table 2

Uni-variate Logistic analysis of risk factors associated with the severity of hypertriglyceridemia-induced pancreatitis in male and female patients.

Variables	Male		Female	
	<i>P</i> values	HR (95%CI)	<i>P</i> values	HR (95%CI)
Age(>40 years)	0.020	0.476 (0.254–0.890)	0.727	0.778 (0.018–3.196)
BMI (>26)	0.618	1.168 (0.634–2.154)	0.602	1.571 (0.287–8.595)
muscle area (> median)	0.327	1.358 (0.736–2.504)	0.438	1.750 (0.426–7.190)
muscle radiodensity (> median)	0.070	0.565 (0.304–1.049)	0.438	0.571 (0.139–2.348)
SAT area (> median)	0.327	1.358 (0.736–2.504)	0.147	3.020 (0.678–13.442)
SAT radiodensity (> median)	0.110	1.652 (0.892–3.060)	0.623	1.425 (0.347–5.851)
VAT area (> median)	0.377	0.759 (0.412–1.399)	0.147	3.020 (0.678–13.442)
VAT area/TAT area (> median)	0.377	0.759 (0.412–1.399)	0.438	1.750 (0.426–7.190)
waist circumference (> median)	0.327	1.358 (0.736–2.504)	0.942	1.053 (0.262–4.224)
CRP (> 90 mg/L)	< 0.001	5.244 (2.618–10.506)	0.027	11.733 (1.326–103.795)
Albumin (< 35 g/L)	< 0.001	6.894 (3.140–15.140)	0.118	3.800 (0.714–20.224)
Triglyceride (\geq 22.4 mmol/L)	0.687	1.156 (0.572–2.333)	0.025	1.565 (1.224–2.001)
HTGP: hypertriglyceridemia-induced pancreatitis. SAT: subcutaneous adipose tissue. TAT: total adipose tissue. VAT: visceral adipose tissue.				

Multi-variate Logistic analysis confirmed that CRP and albumin remained to be associated with the severity of HTGP in male patients, while CRP was found to be the only parameter associated with the severity of HTGP in female patients (all $P < 0.01$, Table 3). By enrolling parameters of gender, age, muscle radiodensity, CRP, albumin and TG, the multi-variate Logistic analyses on patients of both genders showed that high CRP [$P < 0.001$, odds ratio (OR) = 4.230, 95% confidence interval (CI) = 2.050–8.727] and low albumin ($P < 0.001$, OR = 4.846, 95%CI = 2.122–11.068) were associated the severity of HTGP (Table 3).

Table 3
Multi-variate Logistic analysis of parameters associated with the severity of hypertriglyceridemia-induced pancreatitis.

Variables	P values	HR (95%CI)
Male ^a		
CRP (> 90)	0.002	3.380 (1.587–7.199)
Albumin (< 35 g/L)	< 0.001	5.443 (2.195–13.498)
Female ^b		
CRP (> 90)	0.006	25.600 (2.544-257.566)
Combined ^c		
Gender	0.087	0.454 (0.184–1.120)
CRP (> 90)	< 0.001	4.230 (2.050–8.727)
Albumin (< 35 g/L)	< 0.001	4.846 (2.122–11.068)
Triglyceride	0.035	2.277 (1.057–4.902)
^a Variables included age, muscle radiodensity, CRP and albumin.		
^b Variables included CRP and triglyceride.		
^c Variables included gender, age, muscle radiodensity, CRP, albumin and triglyceride.		

Analyses Of Risk Factors For Occurrence Of Pancreatic Necrosis

A total of 178 patients, comprising 37 female and 141 male patients, underwent enhanced CT scanning. Of them, 37 presented with necrosis in pancreas, including 6 female and 31 male patients. In the female, higher TG was the only parameter associated with the risk of pancreatic necrosis [83.3% (5/6) vs 24.1% (7/29), $P = 0.019$, OR = 15.714, 95%CI = 1.561-158.211] by uni-variate Logistic regression analysis. In the male, the risk of pancreatic necrosis was associated with SAT radiodensity ($P < 0.001$, OR = 4.312, 95%CI = 1.770-10.505), CRP ($P = 0.005$, OR = 4.539, 95%CI = 1.472–13.991), low serum albumin concentration ($P < 0.001$, OR = 5.770, 95%CI = 2.285–14.572) and TG concentration ($P = 0.038$, OR = 0.262, 95%CI = 0.074–0.929) by uni-variate Logistic analyses, while SAT radiodensity ($P = 0.004$, OR = 4.268, 95%CI = 1.572–11.589), serum albumin concentration ($P = 0.006$, OR = 4.062, 95%CI = 1.483–11.128) and TG concentration ($P = 0.018$, OR = 0.194, 95%CI = 0.050–0.757) remained to be significant risk factors of necrosis by multi-variate Logistic analyses. In all population, SAT radiodensity ($P < 0.001$, OR = 3.864, 95%CI = 1.737–8.593), low serum albumin ($P < 0.001$, OR = 4.350, 95%CI = 1.952–9.691) and CRP ($P =$

0.014, OR = 3.069, 95%CI = 1.254–7.513) correlated with the risk of pancreatic necrosis by uni-variate Logistic analyses, whereas the former two variates remained statistically correlated with the risk of necrosis in pancreas (for SAT radiodensity: $P = 0.004$, OR = 3.349, 95%CI = 1.456–7.703; for low serum albumin: $P = 0.002$, OR = 3.745, 95%CI = 1.633–8.589).

Low serum albumin was associated with longer hospital stay and higher severity scorings of patients with HTGP

HTGP patients with low serum albumin had a significant longer hospital stay (median 18 days vs. 11 days, $P < 0.001$) and higher proportion of hospital stay over 2 weeks (67.0% vs. 29.7%, OR = 4.801, 95% CI = 2.771–8.318, $P < 0.001$) than those with high serum albumin (Table 4). After correction of other factors by multi-variate Logistic analysis, low albumin remained associated with longer hospital stay of HTGP (OR = 3.648, 95% CI = 1.904–6.988, $P < 0.001$). Besides, low serum albumin was also a risk factor of higher APACHE II, Ranson and Marshall scoring, both by uni-variate and multi-variate Logistic analyses (Table 4). In our study, there were 8 patients with BISAP scores ≥ 3 , who all presented with low serum albumin concentration.

Table 4

Uni- and multi-variate analyses of the association between albumin concentration and the length of hospital stay and clinical scoring parameters for patients with hypertriglyceridemia-induced pancreatitis.

Variables	Low albumin	High albumin	Uni-variate Logistic analyses		Multi-variate Logistic analyses		Missing value
			OR (95%CI)	P values	OR (95%CI)	P values	
Length of hospital stay							
< 2 weeks	34 (33.0)	97 (70.3)	4.801 (2.771– 8.318)	< 0.001	3.648 (1.904– 6.988)	< 0.001 a	1
≥ 2 weeks	69 (67.0)	41 (29.7)					
APACHE II							
< 8	61 (64.2)	94 (83.2)	2.758 (1.443– 5.268)	0.002	2.808 (1.254– 6.288)	0.012 b	34
≥ 8	34 (35.8)	19 (16.8)					
BISAP							
< 3	85 (91.4)	107 (100)	NA	0.002			42
≥ 3	8 (8.6)	0					
Ranson							
< 3	38 (40.9)	72 (67.3)	2.977 (1.670– 5.307)	< 0.001	2.601 (1.260– 5.369)	0.010 c	42
≥ 3	55 (59.1)	35 (32.7)					
Marshall							

^a Variables included age, CRP, albumin, TG and subcutaneous adipose tissue area.

^b Variables included gender, CRP, albumin, TG and muscle radiodensity.

^c Variables included CRP, albumin, TG and subcutaneous adipose tissue area.

^d Variables included albumin and muscle radiodensity.

Variables	Low albumin	High albumin	Uni-variate Logistic analyses	Multi-variate Logistic analyses	Missing value		
			OR (95%CI)	<i>P</i> values		OR (95%CI)	<i>P</i> values
< 2	74 (79.6)	104 (94.5)	4.450 (1.696– 11.682)	0.002	3.480 (1.279– 9.470)	0.015 ^d	39
≥ 2	19 (20.4)	6 (5.5)					
^a Variables included age, CRP, albumin, TG and subcutaneous adipose tissue area.							
^b Variables included gender, CRP, albumin, TG and muscle radiodensity.							
^c Variables included CRP, albumin, TG and subcutaneous adipose tissue area.							
^d Variables included albumin and muscle radiodensity.							

Discussion

This study showed that low albumin and high CRP levels upon admission of patients with HTGP were associated with the severity of the disease, while none of the CT-based body composition parameters was linked to the severity of HTGP. We further found that low albumin concentration was associated with pancreatic necrosis, longer hospital stay and higher APACHE II, Ranson and Marshall scorings of patients with HTGP. To our knowledge, this is the first study suggesting that low albumin may serve as a risk factor for moderately severe to severe HTGP. Our finding indicates that HTGP patients with low albumin should be kept under close surveillance of the disease progression, and may benefit from treatment aiming to normalize albumin concentration, such as albumin supplement.

Albumin has been suggested as a predictive factor for the severity of AP [22]. More recently, a study included 708 patients with AP and additional 477 patients from validation cohort, finding that albumin was an independent predictor for SAP and in-hospital mortality in AP patients [23]. Albumin has also been incorporated into some prediction panels which showed usefulness to predict the severity of AP [24, 25]. For example, serum albumin plus extrapancreatic fluid collections were suggested as the best indicator of severity of AP at the time of admission [26]. Another study suggested that combining blood urea nitrogen and albumin resulted in better prediction for SAP in pediatric patients [27]. Besides, low albumin is also helpful to predict organ failure of AP [28]. It has been shown that low serum albumin is independently associated with an increased risk of persistent organ failure and death in AP [29].

However, the association of albumin concentration with the severity of the subgroup of AP, HTGP, has not been investigated before. In HTGP, the deposition of free fatty acids hydrolyzed from TG plays a crucial role in the mechanism of pancreatitis. Theoretically, decrease of albumin, which can bind to the free fatty

acids in the serum, may result in accumulation of free fatty acid, thus contributing to the inflammatory progression. Decrease of albumin may also be a consequence of severe type of HTGP with larger amount of free fatty acid to be neutralized by albumin, and with higher vasopermeability which allows more albumin to permeate into tissue space [30]. Therefore, the albumin concentration may show a closer correlation with the severity of HTGP than AP caused by other etiology. In line with these assumptions, we found that HTGP patients with albumin lower than 35 g/L had four-times more possibility to be moderately severe or severe than those with albumin over 35 g/L. Notably, our stratification study in the female patients, the albumin showed no correlation with the severity of HTGP. This might be explained by the relative smaller number of female patients and underpower of the statistical analysis. Studies with larger sample size may be of value to ascertain the association between the albumin and the severity of HTGP.

CRP level upon admission was another laboratory parameter of predictive value for the severity of HTGP in our study. This finding was consistent with the study from Yu and colleagues, in which 159 HTGP Chinese patients were retrospectively enrolled and high CRP and BMI were postulated as risk factors for severe HTGP [31]. Indeed, CRP is one of the most widely utilized biomarkers in clinical practice for AP. CRP levels of > 150 mg/L 48 h after onset of symptoms have a high sensitivity for predicting severity of AP [32]. Stirling and colleagues reported that a rise of > 90 mg/dL from admission or an absolute value of > 190 mg/dL at 48 h predicted severe disease with the greatest accuracy [33]. However, it is generally thought that the initial CRP at time of admission is too early to be predictive for the severity of AP [34]. Our finding of the predictive role of CRP upon admission for the severity AP needs validation in more studies in the future.

The body composition parameters, especially VAT, have been reported to correlate with the severity of AP. Due to the involvement of lipoprotein metabolism in HTGP, we asked whether body composition parameters were associated with the severity of HTGP. Intriguingly, no association was found between the severity of HTGP and any of these body composition parameters, including CT-measured muscle area, muscle radiodensity, SAT area/radiodensity, VAT area, and body mass index and waist circumference. In comparison, another study from Ji et al. showed that VAT area was associated with the severity of HTGP. Several factors may contribute to the discrepancy. Firstly, our study noticed that gender has a significant impact on all these body composition parameters, which has been reported before [35]. Therefore, the cut-off of each body composition parameter and the subsequent statistical analysis were gender dependent in our study. Secondly, our study included HTGP with any severity, while Ji and colleagues' study included only moderately severe to severe patients from intensive care unit. Lastly, there is a difference of sample size between the two studies.

Pancreatic necrosis is a parameter for CT-based evaluation of the severity of AP, and is closely associated with the morbidity and mortality of AP [36]. The management of pancreatic necrosis has been highlighted due to its significance for the outcome of AP [37]. Grinsven et al. has investigated the association between body composition and mortality of AP with pancreatic necrosis, concluding that loss of skeletal muscle density within the first month after initial admission was significantly associated with increased

mortality [38]. It has been shown that patients with HTGP had higher incidence of pancreatic necrosis compared to AP with other etiology [39]. In HTGP, excess TG is hydrolyzed by lipase from pancreatic acinar cells to produce FFAs, which in turn cause acinar necrosis [3]. Our study suggested that high SAT radiodensity and low serum albumin were associated with pancreatic necrosis in patients with HTGP.

Conclusions

We found that low serum albumin and high C-reactive protein upon admission were significantly associated with the severity of HTGP. Our study indicated that serum albumin may play a crucial role in the progression of HTGP, while supplement of albumin may be of therapeutic value. Besides, we noticed that gender has a significant impact on all body composition parameters, none of which was associated with the severity of acute HTGP. We also found that high SAT radiodensity and low serum albumin may act as an indicator for pancreatic necrosis in patients with HTGP. More studies are needed to confirm the predictive role of serum albumin and C-reactive protein in the severity of HTGP.

Abbreviations

AP: acute pancreatitis; APACHE: Acute Physiology and Chronic Health Evaluation; AUC: areas under the curves; BISAP: Bedside Index for Severity in Acute Pancreatitis; BMI: body mass index; CI: confidence interval; CRP: C-reactive protein; CT: Computed tomography; HTG: hypertriglyceridemia; HTGP: hypertriglyceridemia-induced pancreatitis; MCTSI: modified CT severity index; HU: Hounsfield units; OR: odds ratio; ROC: receiver operating characteristic; SAT: subcutaneous adipose tissue; TAT: total adipose tissue; TG: triglyceride; VAT: visceral adipose tissue.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of the First Affiliated Hospital of Wenzhou Medical University. Participant informed consent was waived given the retrospective study design.

Consent for publication

Not applicable.

Availability of data and material

All relevant data and materials are included in the manuscript. For the full detailed data, please contact the corresponding author.

Competing interests

The authors declare no conflicts of interest.

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Authors' contributions

Chen L performed the experiments, analyzed the data and wrote the initial draft of the manuscript; Huang YB analyzed the data and assisted in manuscript writing and study conception; Yu HJ collected the clinical data and follow-up of the patients; Pan KH, Zhang Z and Man Y critically revised the manuscript for important intellectual content; Hu DY conceived the study; all authors read and approved the final manuscript.

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Figures

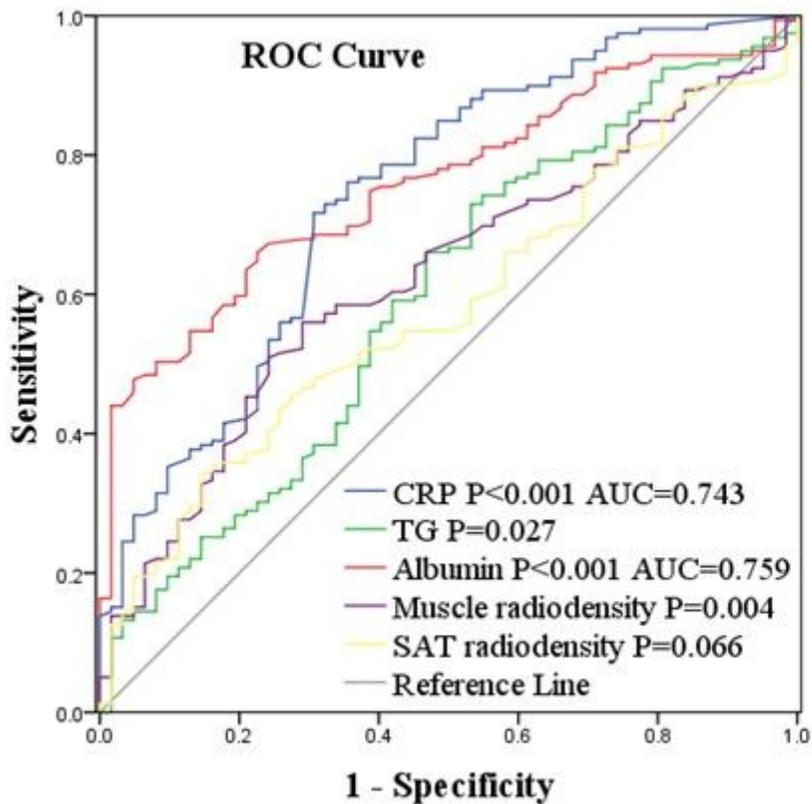


Figure 1

Receiver operating characteristic curves of parameters for the predictive capacity of the severity of HTGP. Albumin had the largest AUC (0.759) for the prediction of HTGP severity. AUC: areas under the curves; HTGP: hypertriglyceridemia-induced pancreatitis; SAT: subcutaneous adipose tissue; TG: Triglyceride.