Assessment of Computed Tomography-Defined Muscle and Adipose Tissue Features in Relation to Length of Hospital Stay and Recurrence of Hypertriglyceridemic Pancreatitis

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Research Article

Keywords: Hypertriglyceridemic pancreatitis, Recurrent pancreatitis, Length of hospital stay, Body composition, Subcutaneous fat area

DOI: https://doi.org/10.21203/rs.3.rs-132306/v1

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Abstract

**Background:** Analytic morphometric assessment has recently been proposed to be applied to the study of acute pancreatitis (AP). However, the relationship between body composition and the outcomes of hypertriglyceridemic pancreatitis (HTGP) is still unclear. The aim of this study was to evaluate body composition in relation to the length of hospital stay (LOS) and recurrence of HTGP.

**Methods:** Patient characteristics, admission examination data, body composition parameters, LOS, and recurrence within 1 year were collected from the institutional pancreatitis database and follow-up records. Logistic regression analysis was used to identify risk factors for LOS and recurrence of HTGP.

**Results:** Of the 196 included patients, 158 (80.6%) were men and 53 (27.0%) were sarcopenic. The average LOS was 15.83±10.02 days. The recurrence rate of HTGP was 36.7%. Multivariate analysis with multiple linear regression suggested that subcutaneous fat area (SFA) (p=0.019) and high-density lipoprotein-cholesterol (HDL-C) (p=0.001) were independently associated with the LOS for HTGP after adjusting for age and sex. The multivariate adjusted hazard ratios for SFA and HDL-C, with respect to the relationship between body parameters and LOS, were 1.008 (95% confidence interval [CI], 1.001–1.015) and 0.090 (95% CI, 0.022–0.361), respectively. No significant differences were observed between the AP and recurrent AP (RAP) groups in terms of characteristics, admission examination data, and body composition parameters.

**Conclusion:** SFA and HDL-C are associated with LOS in patients with HTGP. The body composition of patients at the first symptom onset of HTGP cannot predict recurrence.

Background

Acute pancreatitis (AP), a common inflammatory disease, progresses to organ dysfunction in 10–20% of patients, with increasing incidence and a high mortality rate [1–4]. The most common etiologies of AP are gallstones and alcoholism [2]. Hypertriglyceridemic pancreatitis (HTGP), which accounts for up to 10% of AP cases, occurs in the presence of hypertriglyceridemia with no signs of other causes [5]. Recent reports have indicated that the incidence of HTGP in Asia is increasing [3, 6], and is higher than that reported in Western countries [7].

Clinical and experimental data have shown that obesity is a risk factor for AP [4, 8–13]. However, most studies did not distinguish between visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). The study of fat distribution is crucial to understanding the metabolic implications of excess adiposity [14–17]. Computed tomography (CT) is a reliable method for the analysis of fat distribution and the measurement of adipose tissues [18].

In addition, most studies did not classify the etiological patterns of AP. Previous studies have shown that the prognosis and severity of AP seem to vary depending on etiology, and different etiologies have different pathophysiological mechanisms [19]. HTGP is associated with more complications, a longer
and more severe disease, and a higher recurrence rate [7, 20, 21]. Therefore, it is important to distinguish the etiology of AP. The aim of the present study was to assess the impact of body composition on the length of hospital stay (LOS) and risk of recurrence of HTGP.

**Methods**

**Study population**

We retrospectively evaluated consecutive patients with HTGP who were admitted to our pancreatitis center between September 2016 and August 2019. The diagnosis of AP was made if at least two of the following three features were present: (1) acute abdominal pain, (2) serum amylase and/or lipase levels three or more times the upper limit of normal, and (3) evidence of pancreatitis on abdominal imaging [22]. The diagnosis of HTGP was confirmed if patients had AP with serum total triglyceride (TG) >11.3 mmol/L (1000 mg/dL), or a serum TG level of 5.65–11.3 mmol/L accompanied by chylous serum and the absence of other risk factors for AP [5]. This study was performed with approval from the ethics committee of the First Affiliated Hospital of Wenzhou Medical University.

**Clinical data**

Clinical data such as age, sex, body mass index (BMI), umbilical waist circumference (WC), pre-existing comorbidity (including hypertension, diabetes mellitus, and alcoholism), and admission laboratory test data (including TG, total cholesterol, high-density lipoprotein-cholesterol [HDL-C], and low-density lipoprotein-cholesterol [LDL-C]) were retrospectively collected. The outcomes were LOS and recurrence (defined as hospital admission within 1 year after discharge).

**Anthropometric measurements by CT image analysis**

All patients in this study underwent abdominal CT within 1 week of symptom onset for the quantitative assessment of body composition. Two experienced radiologists (with 5 years of imaging experience), who were blinded to the patients’ clinical data, analyzed the CT images using a postprocessing station (GE Healthcare Advantage Workstation, version 4.6) with the axial image at the level of the L3 vertebra. The predetermined Hounsfield unit (HU) thresholds were -29 to -150 HU for total abdominal muscle area (TAMA), -30 to -190 HU for subcutaneous fat area (SFA), and -50 to -150 HU for visceral fat area (VFA) (Fig.1).

**Statistical analyses**

Statistical analyses were performed using SPSS (version 26.0; IBM Corp., Armonk, NY, USA). We used the Kolmogorov-Smirnov test to assess whether the variables were normally distributed. Student’s t-test and the nonparametric Mann-Whitney U-test were used for comparisons of continuous variables. Categorical variables were analyzed using Pearson's chi-square and Fisher's exact tests. Continuous variables are expressed as mean±standard deviation, and categorical variables are presented as percentages. Logistic regression analysis was used to identify the risk factors.
Results

Characteristics of subjects

A total of 196 patients were considered eligible for the study (158 men and 38 women; mean age, 40.52 ± 9.72 years). Men accounted for 80.6% of all patients. The average LOS was 15.83 ± 10.02 days. The recurrence rate of HTGP was 36.7%. According to predefined sex-specific cutoff values [23], 53 patients (27%) were sarcopenic. The baseline demographic characteristics, clinical characteristics, and body composition of patients with HTGP are summarized in Table 1.
### Table 1
Baseline Demographic and Characteristics of 196 Patients Who Underwent CT for HTGP

| Parameter                        | Datum          |
|----------------------------------|----------------|
| Age (y)                          | 40.52 ± 9.72   |
| Sex                              |                |
| Women                            | 38 (19.4%)     |
| Men                              | 158 (80.6%)    |
| Body mass index (kg/m\(^2\))     | 25.83 ± 3.31   |
| < 18.5                           | 1 (0.5%)       |
| 18.5–24.9                        | 79 (39.9%)     |
| 25.0–29.9                        | 96 (48.5%)     |
| ≥ 30.0                           | 20 (10.1%)     |
| Pre-existing comorbidity         |                |
| Hypertension                     | 63 (32.1%)     |
| Diabetes                         | 123 (62.1%)    |
| Alcoholism                       | 89 (45.4%)     |
| Laboratory test at diagnosis     |                |
| Triglycerides (mmol/L)           | 21.46 ± 25.04  |
| Total cholesterol (mmol/L)       | 10.29 ± 6.44   |
| HDL-C (mmol/L)                   | 0.64 ± 0.25    |
| LDL-C (mmol/L)                   | 2.32 ± 1.17    |
| Body composition at diagnosis    |                |
| Total abdominal muscle area (TAMA), cm\(^2\) | 155.58 ± 33.46 |
| Subcutaneous fat area (SFA), cm\(^2\) | 132.64 ± 51.11 |
| Visceral fat area (VFA), cm\(^2\) | 174.00 ± 107.83 |
| Total abdominal fat area (TAFA), cm\(^2\) | 307.65 ± 124.18 |
| Umbilical waist circumference (WC), cm | 88.20 ± 9.09   |

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LOS, length of hospital stay.
### Comparisons Of Characteristics According To Los

The LOS was dichotomized at 14 days, based on the median LOS of the entire population. Patients in the short LOS group (≤ 14 days) and those in the long LOS group (> 14 days) were compared to evaluate the association between LOS and demographic characteristics, clinical characteristics, and body composition (Table 2). The short and long LOS groups comprised 94 and 102 patients, respectively. No statistical difference was observed with respect to age, sex, BMI, and pre-existing comorbidity (hypertension, diabetes mellitus, or alcoholism) between the two groups (all p > 0.05). Patients in the long LOS group presented higher total cholesterol (11.15 ± 7.00 vs. 9.36 ± 5.66 mmol/L, p = 0.043) and triglycerides (24.76 ± 27.20 vs. 17.87 ± 22.5 mmol/L, p = 0.021). The mean HDL-C level of patients with long LOS was lower than that of patients with short LOS (0.57 ± 0.24 vs. 0.72 ± 0.24 mmol/L, p < 0.001) (Fig. 2B). A significant association between LOS and individual SFA was observed. SAT was significantly higher in the long LOS group than in the short LOS group (142.77 ± 50.57 vs. 121.64 ± 49.65 p = 0.001) (Fig. 2A). Other body composition parameters, including TAMA, VFA, TAFA, WC, and sarcopenia, were also similar between the two groups (all p > 0.05). Multivariate analysis with multiple linear regression suggested that SAT (p = 0.019) and HDL-C (p = 0.001) were independently associated with the LOS for HTGP after adjusting for age and sex (Table 3). The multivariate adjusted hazard ratios for SAT and HDL-C, with respect to the relationship between body parameters and LOS, were 1.008 (95% confidence interval [CI], 1.001–1.015) and 0.090 (95% CI, 0.022–0.361), respectively.
Table 2
Comparison of baseline characteristics between Short LOS (≤ 14 days) and Long LOS (>14 days) groups.

| Parameter                  | Short LOS (≤ 14 days) (n = 94) | Long LOS (>14 days) (n = 102) | P value |
|----------------------------|---------------------------------|--------------------------------|---------|
| Age (y)                    | 41.45 ± 8.8                     | 39.67 ± 10.4                   | 0.201   |
| Sex                        |                                 |                                | 0.244   |
| Women                      | 15(16.0%)                       | 23(22.5%)                      |         |
| Men                        | 79(84.0%)                       | 79(77.5%)                      |         |
| Body mass index (kg/m²)    | 25.73 ± 3.00                    | 25.92 ± 3.58                   | 0.685   |
| < 18.5                     | 0(0.0%)                         | 1(1.0%)                        |         |
| 18.5–24.9                  | 36(38.3%)                       | 43(42.2%)                      |         |
| 25.0–29.9                  | 50(53.2%)                       | 46(45.1%)                      |         |
| ≥ 30.0                     | 8(8.5%)                         | 12(11.8%)                      |         |
| Pre-existing comorbidity   |                                 |                                |         |
| Hypertension               | 26(27.7%)                       | 37(36.3%)                      | 0.197   |
| Diabetes                   | 25(26.6%)                       | 29(28.4%)                      | 0.774   |
| Alcoholism                 | 41(43.6%)                       | 48(47.1%)                      | 0.629   |
| Laboratory test at diagnosis|                               |                                |         |
| Triglycerides (mmol/L)     | 17.87 ± 22.5                    | 24.76 ± 27.20                  | 0.021   |
| Total cholesterol(mmol/L)  | 9.36 ± 5.66                     | 11.15 ± 7.00                   | 0.043   |
| HDL-C (mmol/L)             | 0.72 ± 0.24                     | 0.57 ± 0.24                    | < 0.001 |
| LDL-C (mmol/L)             | 2.43 ± 1.26                     | 2.23 ± 1.08                    | 0.243   |
| Body composition at diagnosis|                               |                                |         |
| Total abdominal muscle area (TAMA), cm² | 158.25 ± 32.48 | 153.12 ± 34.31 | 0.285 |
| Subcutaneous fat area (SFA), cm² | 121.64 ± 49.65 | 142.77 ± 50.57 | 0.001 |
| Visceral fat area (VFA), cm²  | 171.77 ± 67.47 | 178.00 ± 134.20 | 0.579 |
| Total abdominal fat area (TAFA), cm² | 293.42 ± 94.94 | 320.78 ± 145.30 | 0.200 |

LOS, length of hospital stay.
Parameter | Short LOS (≤ 14 days) (n = 94) | Long LOS (>14 days) (n = 102) | P value  
--- | --- | --- | ---  
Umbilical waist circumference (WC), cm | 89.26 ± 9.03 | 87.24 ± 9.08 | 0.120  
Sarcopenia | 24(25.5%) | 29(28.4%) | 0.648  

LOS, length of hospital stay.

Table 3  
Multivariate analyses of risk factors for LOS of HTGP.

| Parameter | OR | P value  
--- | --- | ---  
Age (y) | 0.999(0.967–1.031) | 0.937  
Sex | 0.793(0.355–1.773) | 0.572  
Triglycerides (mmol/L) | 0.996(0.973–1.020) | 0.767  
Total cholesterol (mmol/L) | 1.041(0.953–1.137) | 0.375  
HDL-C (mmol/L) | 0.090(0.022–0.361) | 0.001  
Subcutaneous fat area (SFA), cm² | 1.008(1.001–1.015) | 0.019  

Comparisons Of Characteristics According To Ap Recurrence

No significant differences were observed between the AP and RAP groups in age, sex, BMI, and pre-existing comorbidity (hypertension, diabetes mellitus, or alcoholism). The laboratory test values for TG, total cholesterol, HDL-C, and LDL-C were not significantly different between the two groups. The body composition parameters TAMA, SFA, VFA, and total abdominal fat area (TAF A), as well as WC and sarcopenia, were not significantly different between the two groups (all p > 0.05) (Table 4).
Table 4
Comparison of baseline characteristics between AP and RAP groups.

| Parameter                        | AP (n = 124)       | RAP (n = 72)     | P value |
|----------------------------------|--------------------|-----------------|---------|
| Age (y)                          | 41.39 ± 9.92       | 39.03 ± 9.25    | 0.891   |
| Sex                              |                    |                 | 0.719   |
| Women                            | 25(20.2%)          | 13(18.1%)       |         |
| Men                              | 99(79.8%)          | 59(81.9%)       |         |
| Body mass index (kg/m$^2$)       | 26.14 ± 3.45       | 25.28 ± 3.00    | 0.079   |
| < 18.5                           | 0(0.0%)            | 1(1.4%)         |         |
| 18.5–24.9                        | 47(37.9%)          | 32(44.4%)       |         |
| 25.0–29.9                        | 60(48.4%)          | 36(50.0%)       |         |
| ≥ 30.0                           | 17(13.7%)          | 3(4.2%)         |         |
| Pre-existing co-morbidity        |                    |                 |         |
| Hypertension                     | 40(32.3%)          | 23(31.9%)       | 0.964   |
| Diabetes                         | 34(27.4%)          | 21(29.2%)       | 0.793   |
| Alcoholism                       | 60(48.4%)          | 29(40.3%)       | 0.272   |
| Laboratory test at diagnosis     |                    |                 |         |
| Triglycerides (mmol/L)           | 18.21 ± 18.82      | 27.04 ± 32.52   | 0.143   |
| Total cholesterol (mmol/L)       | 9.86 ± 5.10        | 11.03 ± 8.25    | 0.894   |
| HDL-C (mmol/L)                   | 0.64 ± 0.24        | 0.65 ± 0.28     | 0.978   |
| LDL-C (mmol/L)                   | 2.37 ± 1.04        | 2.25 ± 1.38     | 0.147   |
| Body composition at diagnosis    |                    |                 |         |
| Total abdominal muscle area (TAMA), cm$^2$ | 155.36 ± 33.81     | 155.97 ± 33.07 | 0.903   |
| Subcutaneous fat area (SFA), cm$^2$ | 137.98 ± 52.82    | 123.44 ± 46.98 | 0.054   |
| Visceral fat area (VFA), cm$^2$  | 180.41 ± 126.55    | 162.95 ± 63.21 | 0.359   |
| Total abdominal fat area (TAFA), cm$^2$ | 320.00 ± 140.33   | 286.40 ± 86.68 | 0.097   |
| Umbilical waist circumference (WC), cm | 87.95 ± 9.25     | 88.63 ± 8.86   | 0.615   |
| Sarcopenia                       | 34(27.4%)          | 19(26.4%)       | 0.876   |

AP, acute pancreatitis; RAP, recurrent acute pancreatitis.
Discussion

AP is a common disease of the abdomen necessitating emergency department visits [3, 24, 25]. Biliary tract stones and alcoholism are the most common etiologies of AP [2]. Recent reports have indicated an increasing prevalence of HTGP in Asia [3, 6]. Jin et al. showed that from 2001 to 2016, the prevalence of HTGP increased from 14.0–34.0% [3]. These changes may be related to caloric intake and an increasing incidence of diabetes [26].

A plethora of clinical and experimental data have identified obesity as a risk factor for AP [4, 8–13]. Hansen et al. studied 118,000 patients with AP and confirmed that BMI is an independent factor of AP [9]. Blaszczak et al. reported that class III obesity seems to have an adverse mortality effect in patients with AP [11]. A recent study by Thavamani et al. suggested that morbid obesity is an independent risk factor for clinical outcomes in pediatric AP [12]. The mechanism by which obesity aggravates pancreatitis has been investigated. Pérez et al. revealed that obesity may result in reduced pancreatic peroxisome proliferator-activated receptor-γ coactivator 1α (PGC-1α) levels by decreasing the binding of PGC-1α to the p65 subunit of nuclear factor-κB, and potentiating oxidative and interleukin-6-mediated inflammatory damage during AP attacks [13]. Ye et al. demonstrated that obesity may aggravate AP through damaging the intestinal mucosal barrier by decreasing the binding of intestinal leptin and its receptor (ObR-b), increasing intestinal inflammatory injury, and resulting in insufficient intestinal epithelial cell proliferation in rats [27]. However, most studies did not distinguish between VAT and SAT depots. The study of fat distribution is crucial to understanding the metabolic implications of excess adiposity. More and more researchers have realized that the study of fat distribution is important in obesity research [14–17]. CT imaging is a reliable method for the analysis of fat distribution and the measurement of adipose tissues [18]. The axial CT image at L3 is known to represent muscle tissues and fat distribution [18, 28]. Blaszczak et al. conducted a study in 68,158 individuals, among whom 424 developed AP, and demonstrated that greater abdominal adiposity is associated with a higher severity of AP [29]. O’Leary et al. showed a similar finding in 214 patients with AP [30]. However, many studies have suggested that VAT is not significantly associated with AP [31–33]. Duarte-Rojo et al. have shown that both SAT and VAT independently predict a severe outcome of AP [34]. The differences in results across different studies may be explained by several factors. First, the studies involved a heterogeneous population of patients, including those from Southeast Asia, Europe, and North America. Second, different software programs were used to analyze body composition, which may be an additional confounding factor. Third, most studies did not classify the etiological patterns of AP, which may be mainly because of the different proportions of the etiological patterns in previous studies. Therefore, studies on the etiologies of AP are needed. To our knowledge, this is the first study on the impact of body composition on the outcomes of HTGP.

In this study, we investigated the impact of body composition on LOS and recurrence in patients with HTGP. Our results revealed that SAT and HDL-C were independent predictors of LOS, and there was no significant association between body composition and the recurrence of HTGP. Patients in the long LOS group (> 14 days), based on the median LOS of the entire sample, had higher SAT than patients in the
short LOS group (≤ 14 days). Previous studies have also determined that patients with LOS > 14 days have more severe pancreatitis [29]. Szentesi et al. studied 1,257 individuals with AP, and reported that obese patients had longer LOS than non-obese patients [35]. Murata et al. showed a similar finding in pediatric AP [36]. However, they did not conduct further analysis on fat distribution and etiological classification. Fujisawa et al. suggested that SAT may be an especially important factor related to the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis; however, they did not investigate its relationship with LOS [37]. Few studies have been conducted on the correlation between obesity and the recurrence of pancreatitis. Shimonov et al. found that higher amounts of VAT and TAMA were significantly associated with a lower recurrence rate of AP in 158 patients; however, no significance was identified in our study [38]. HTGP may be different from other etiologies of pancreatitis in terms of the effect of body composition. The doctor's medical advice for TG control after discharge may be another reason because the body composition of the patients after 1 year may be different from that at the first hospitalization. Dynamic changes in body composition may be the direction of future research. In addition, many studies have shown that alcoholism, cigarette smoking, hypertriglyceridemia, and local complications are risk factors for recurrent pancreatitis [39, 40]. Our study showed no significant association between hypertriglyceridemia and recurrence of HTGP.

This study had some limitations. First, the number of patients with HTGP within categories by pancreatitis type was small; thus, studies with larger sample sizes are required. Second, as our study results were derived from a retrospective single-center analysis, further prospective and multicenter studies should be conducted in the future. Finally, the outcome of recurrence was assessed within 1 year after discharge, which may not reflect the long-term outcome of patients.

**Conclusion**

In the present study, we found that SFA and HDL-C are associated with LOS in patients with HTGP. The CT-defined body composition may help identify patients at a high risk of long-term hospitalization and assist in treatment decision making. In addition, we found that the body composition of patients at the first symptom onset of HTGP cannot predict the recurrence of the disease. Future studies should investigate strategies focusing on dynamic changes in body composition.

**Abbreviations**

AP
Acute pancreatitis (AP); HTGP: Hypertriglyceridemic pancreatitis; LOS: Length of hospital stay; VAT: Visceral adipose tissue; SAT: Subcutaneous adipose tissue; TAMA: Total abdominal muscle area; VFA: Visceral fat area; SFA: Subcutaneous fat area; TASA: Total abdominal fat area; CT: Computed tomography; BMI: Body mass index; WC: Waist circumference; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein-cholesterol; PGC-1α: Proliferator-activated receptor-γ coactivator 1α

**Declarations**
Declaration of Conflicting Interest

No conflicts of interest exist.

Acknowledgements

The authors are grateful to Zhefeng Leng for help in imaging. We would like to thank Editage (www.editage.cn) for English language editing.

Author Contributions

Weizhi Xia, Huajun Yu and Yunjun Yang: concept and design. Yingbao Huang and Yunjun Yang: analysis and interpretation of the data. Weizhi Xia and Huajun Yu: drafting of the article. Yingbao Huang, Lifang Chen and LiuZhi Shi: collection and assembly of data. All authors: critical revision of the article for important intellectual content. All authors: final approval of the article.

Funding

This study was carried out with the support of Wenzhou Science and Technology Project (2019Y0062).

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by The First Affiliated Hospital of Wenzhou Medical University Biomedical Research Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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