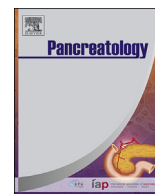




Contents lists available at ScienceDirect

## Pancreatology

journal homepage: [www.elsevier.com/locate/pan](http://www.elsevier.com/locate/pan)

## Impact of body fat and muscle distribution on severity of acute pancreatitis

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## ARTICLE INFO

## Article history:

Received 12 October 2016

Received in revised form

20 January 2017

Accepted 4 February 2017

Available online xxx

## Keywords:

Pancreas

Inflammation

Prognosis

Sarcopenia

## ABSTRACT

**Background/Objectives:** Obesity is a well-established risk factor for severe acute pancreatitis (AP); however, the impact of visceral obesity or sarcopenic obesity on severity of AP has not been well studied. We compared the relationship between severity of AP and various body parameters including body weight, body mass index (BMI), subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and visceral fat-to-muscle ratio (VMR).

**Methods:** We analyzed the data of patients who were diagnosed with AP from 2009 to 2015. Image analysis software program (Aquarius Workstation software) was used to calculate individual VAT, SAT, and skeletal muscle areas from abdominal computed tomography scans at L3 vertebral levels. Revised Atlanta Classification was adopted to define severity of AP. Receiver operating characteristics (ROC) curves were constructed to determine the optimal threshold for predicting the severity.

**Results:** Among 203 patients, 13 (6.4%) patients had severe AP and 62 (30.5%) patients had moderately severe cases. VMR demonstrated the highest area under the ROC curve [0.757, (95% confidence interval: 0.689–0.825)] in predicting moderately severe or severe AP. The optimal threshold of VMR for predicting severity was 1. The prevalence of various local complications and persistent organ failure were higher in patients with VMR over 1.

**Conclusions:** High visceral fat with low skeletal muscle volume was strongly correlated with AP severity. VMR had a stronger correlation with AP severity than body weight or BMI. This simple grading system would be useful if incorporated into future predictive scoring models.

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### 1. Introduction

Acute pancreatitis (AP) is a common inflammatory disease that involves the pancreas. Its incidence is increasing, ranging from 13 to 45 per 100,000 [1]. AP is usually a mild disease, but about one fifth of patients may develop severe courses with a mortality rate of 10–20% [2–4]. It is important to identify severe cases early because

they may require more aggressive intensive care and early nutritional support. Several scoring systems have been developed for predicting adverse outcomes in AP, such as the Acute Physiology and Chronic Health Evaluation II (APACHE-II) [5] or the Ranson score [6]. However, each score has certain shortcomings. The APACHE-II score is complex and the Ranson score is finally measured at 48 h after admission.

Obesity is a well-known risk factor for AP and is also related to a more severe course. Two meta-analyses showed that obesity is related to a high incidence of local complication, organ failure, and mortality [7,8]. Another previous study showed that the power of APACHE-II for predicting AP severity was improved by adding a score for obesity [9]. In most reports that investigated the relationship between obesity and AP severity, obesity was surrogated by high body mass index (BMI) [9–12]. Some recent reports showed that visceral fat volume is more strongly correlated with

**Abbreviations:** AP, acute pancreatitis; APACHE-II, Acute Physiology and Chronic Health Evaluation II; AUC, area under the curve; BMI, body mass index; CT, computed tomography; ROC, receiver operating characteristics; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; VMR, visceral fat-to-muscle ratio.

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<http://dx.doi.org/10.1016/j.pan.2017.02.002>

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severe AP than obesity defined as a high BMI [13,14]. However, these studies only measured subcutaneous and visceral fat, and skeletal muscle area was not assessed. In addition, they did not propose an optimal threshold in predicting severe AP. Therefore, their clinical usefulness is rather limited.

The Acute Pancreatitis Classification Working Group modified the Atlanta classification system to improve clinical assessment and treatment of AP in 2012 [15]. Because the revised Atlanta classification mainly focuses on morphologic manifestations of AP, radiologic imaging has become increasingly important in evaluating and following-up patients with AP [16]. Contrast-enhanced computed tomography (CT) is the primary tool for assessing and monitoring AP. CT scan also is the most widely used method in body composition evaluation. It can delineate various parameters associated with sarcopenic obesity, such as areas of subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), skeletal muscle, and visceral fat to muscle ratio (VMR). We assumed that these parameters related to body fat and muscle distribution might be more precise than BMI for predicting AP severity. We aimed to investigate the relationship between various parameters of body composition and AP severity and to determine the single best predictor among them.

## 2. Materials and methods

### 2.1. Subjects and study design

Patients diagnosed with AP between July 2009 and June 2015 at Seoul St. Mary's Hospital, Seoul, Korea were retrospectively analyzed. Diagnosis criteria for AP were the presence of at least 2 of the 3 following factors: (1) abdominal pain characteristic of AP, (2) serum amylase and/or lipase levels  $\geq 3$  times the upper limit of normal, and (3) characteristic findings of AP on a CT scan [3]. For patients who were admitted to the hospital for AP more than once during the study period, only the first visit was included. Exclusion criteria for the study were AP after endoscopic retrograde cholangiopancreatography, patients with definite chronic pancreatitis, AP caused by periampullary tumor, cases without CT scan, referred cases from other hospitals without an early CT study, and missing BMI data. The Institutional Review Board approved this study (KC15RSSI0927).

### 2.2. Severity assessment of acute pancreatitis

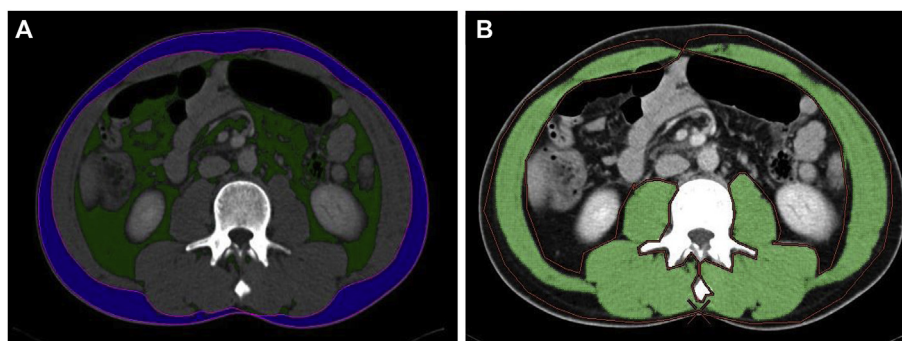
Based on the revised Atlanta Classification, AP severity was stratified into three groups: mild, moderately severe, and severe [15]. Mild AP was identified as the absence of organ failure and the

absence of local or systemic complications. Moderately severe AP was characterized by the presence of transient organ failure resolving within 48 h and/or local or systemic complications without persistent organ failure. Severe AP was defined as persistent organ failure lasting more than 48 h or death. Local complications included acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection, and walled off necrosis. Diagnosis of local complication was re-assessed by a radiologist specializing in abdominal imaging (MH. C.) who had 7 years of experience. All abdominal imaging studies performed during or after hospitalization were reviewed. Systemic complications included worsening of pre-existing co-morbidities related to AP. The length of hospital stay was also assessed as an outcome parameter of AP.

### 2.3. CT technique and image analysis

In our institution, initial CT scan is routinely performed in all AP patients on the day of admission for the purpose of diagnosing AP. CT examinations were performed from the domes of the diaphragm to the iliac crest using 64-detector computed tomography (Somatom Sensation 64/Definition AS+, Siemens Healthcare, Erlangen, Germany, or Discovery CT750HD, GE Healthcare, Milwaukee, Wisconsin, USA). The CT images were obtained with 100 kV tube voltage with 170 mAs reference tube current. Tube voltage was not changed according to the patients' BMI. Instead, automatic tube current modulation was used to optimize image quality according to patients' body habitus. CT examinations were routinely enhanced after injection of 110 mL iomeprol (Iomeron 350; Bracco, Milan, Italy) by the antecubital vein at a speed of 3–4 ml/s. Contrast media could not be used in 7 (3.4%) patients because of renal dysfunction or allergy. Thickness of reconstructed axial image was 5 mm.

Initial CT images were retrospectively retrieved from a picture archiving and communication and these images were reviewed by a radiologist (MH.C.) blinded to clinical and demographic data. Two consecutive axial CT slices at the level of the L3 vertebra body were used to measure fat and muscle cross-sectional areas. The results from the two images were averaged. SAT and VAT areas were automatically measured using Aquarius Workstation software (TeraRecon Inc., San Mateo, CA, USA). Skeletal muscle area was measured, including psoas, paraspinal, and abdominal wall muscles and excluding intra-abdominal visceral muscles (Fig. 1). The windows for adipose tissue and skeletal muscle were  $-190$  to  $-30$  and  $-29$  to  $+150$  Hounsfield units, respectively, in keeping with previously published articles [17,18]. VMR was calculated by dividing VAT by skeletal muscle area.



**Fig. 1.** (A) Subcutaneous visceral tissue (blue) and visceral adipose tissue (green) areas automatically measured in axial CT image at level of L3 vertebral body. (B) Axial CT at same level depicting skeletal muscle area (yellow green) excluding intra-abdominal visceral fat.

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