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# IMPACT OF BODY COMPOSITION, MEASURED BY COMPUTED TOMOGRAPHY SCAN, ON ACUTE PANCREATITIS COURSE

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*Severe acute pancreatitis occurs in 15–25% of all patients with acute pancreatitis (AP), and has a dismal prognosis. Recognition of severe AP risk factors could provide identification and resuscitation of patients with impending severe course of disease. Our study aim was to analyse body composition, measured by computed tomography (CT) scans, in acute pancreatitis patients and its impact on disease severity. The study was a prospective cohort study carried out in the period from January 2015 – April 2016. In total 100 patients underwent CT imaging. Body constitution was analysed by CT examinations using the ImageJ v1.49q standard software. The third lumbar vertebra was selected as the landmark measurement. Muscular, visceral, subcutaneous, and intramuscular adipose tissue area were measured. Values were normalised for stature to obtain lumbar skeletal muscle and adipose tissue indexes (cm$^2$/m$^2$). Acute pancreatitis severity was determined by Atlanta revised criteria (2012). Among the included patients, moderately severe AP occurred in 83% (83 patients) cases, and severe AP in 17% (17 patients). 38% of the patients had normal weight according to BMI, 33% were overweight 33%, and 28% were obese. Sarcopenia was detected in 51%. Sarcopenia was found in six patients (35%) with severe AP and in 45 patients (54%) with moderately severe AP. General linear model analysis showed that obesity (p value = 0.026) and increased intramuscular fat area (p value = 0.029) had effect on severe AP. In conclusion, body composition analysis showed that adiposity is a risk factor for severe AP, and higher intramuscular fat area seemed to be another risk factor for severe AP.*

**Key words:** *acute pancreatitis, nutritional status, sarcopenia, intramuscular adipose tissue, computed tomography.*

## INTRODUCTION

Severe acute pancreatitis occurs when local and/or systemic complications (organ failure) develop. It affects approximately 15–25% of all patients with acute pancreatitis (AP), and has a dismal prognosis with overall mortality rate about 2%, remaining much higher in subgroups of patients with severe disease (Fagenholz *et al*., 2007). Different scoring systems with many specific prognostic parameters and risk factors have been developed with the intention of ability to early predict severe acute pancreatitis. This could provide rapid identification and resuscitation of patients with impending severe course of disease.

Some studies can be found on body composition analysis of acute pancreatitis patients. Most of them, based on BMI and/or waist circumference measurements, concluded that adiposity is a risk factor of severe acute pancreatitis and mortality (De Waele *et al*., 2006; Martinez *et al*., 2006; Wang *et al*., 2011; O'Leary *et al*., 2012; Katuchova *et al*., 2014; Sawalhi *et al*., 2014). From another point of view obesity is a risk factor for acute pancreatitis (Blomgren *et al*., 2002).

Several studies have looked at the importance of adipose tissue distribution (Beasley *et al*., 2009; Duarte-Rojo *et al*., 2010) measured by computed tomography (CT) scans. Visceral adiposity has been identified as risk factor for more severe acute pancreatitis. Less data can be found about amount of intramuscular fat and its impact on acute pancreatitis. Adipose tissue depots in the abdominal cavity and in muscles have been associated with chronic inflammation, as well with impaired glucose tolerance, increased cholesterol level and decreased strength (Prior *et al*., 2007; Durheim *et al*., 2008; Koster *et al*., 2010; Addison *et al*., 2011; Dube *et al*., 2011; Tuttle *et al*., 2011; Tuttle *et al*., 2012).

Computed tomography is a promising reference method for the differentiation and quantification of various soft tissue depots (Pascot *et al*., 1999; Goodpaster *et al*., 2003; Goodpaster *et al*., 2005; Johnson *et al*., 2006) and have been used already in clinical studies on the impact of body composition alterations in many diseases and effect of aging on clinical outcomes. Visceral, subcutaneous, intramuscular adipose and muscular tissue areas can be measured per Hounsfield unit segmentation thresholds. Also, CT scan measurements can provide estimates of total fat mass, total lean body mass, fat and lean body mass indices (normalised for stature), subcutaneous fat-to-muscle ratio and visceral-to-subcutaneous adipose tissue ratio (Mitsiopoulos *et al*., 1998; Mourtzakis *et al*., 2008; Yip *et al*., 2015).

However, little is known about malnutrition or underweight and acute pancreatitis. Alcohol abuse is a part of the aetiology of acute pancreatitis, and it can cause also malnutrition. Also, various chronic diseases, such as diabetes mellitus and chronic obstructive pulmonary disease, as comorbidities to acute pancreatitis, can be associated with risk of body composition alterations. It seems that underweight also predict the more severe pancreatitis and higher mortality risk (Taguchi *et al*., 2014), anyway no data is found about impact of sarcopenia (involuntary loss of skeletal muscle mass and/or strength) or sarcopenic adiposity in acute pancreatitis course.

The aim of our study was to analyse body composition (muscle mass, adipose tissue distribution), measured by CT scans, in acute pancreatitis patients, and determine its impact on disease severity.

## MATERIALS AND METHODS

A total of 100 patients were included in the study prospectively from January 2015 till April 2016. Patient inclusion criteria were: 1) ≥ 18 years old; 2) approved participation in the study; 3) diagnosis of acute pancreatitis, and 4) underwent abdominal CT. Acute pancreatitis was diagnosed based on two criteria of three as follows: the presence of typical abdominal pain (the cardinal symptom of acute pancreatitis), serum amylase or lipase levels threefold or more above the upper normal limit, abdominal CT scan findings compatible with acute pancreatitis (Banks *et al*., 2013). Patients were excluded if consent of participation in the study was not given or if they had not had a CT. We recorded data about patient age, gender, height, and body weight at admission, pancreatitis aetiology, severity of acute pancreatitis, hospitalisation days, and mortality. The study protocol was approved by the Ethics Committee of Pauls Stradiņš Clinical University Hospital.

Patients were stratified by body-mass index (BMI, kg/m²) according to the WHO classification (Anonymous, 1995) with cut-offs being 18.5, 23, 25, 27.5, 30, 32.5, 35, 37.5, and 40 $kg \cdot m^{-2}$.

Computed tomography scan was used in the study to assess body composition and measure adipose tissue and muscles areas. The software ImageJ v1.42q (National Institutes of Health Bethesda, Maryland, USA) was used for CT image analysis. The third lumbar vertebra was selected for the standard landmark measurements. Muscles were assessed based on their anatomical characteristics and structure, using a Hounsfielda unit (HU) range from (–29) to 150. The muscle cross-sectional area ($cm^2$) was measured for each patient. The HU thresholds used for adipose tissues were (–190) to (–30). Tissue boundaries were manually corrected as needed. Cross-sectional areas ($cm^2$) were calculated automatically by summing tissue pixels and multiplying by pixel surface area. The skeletal muscle index L3 ($cm^2 \cdot m^{-2}$) was estimated as the ratio between area of skeletal muscle at L3 vertebra level and the patient's height squared ($m^2$). Sarcopenia was recorded in cases when the ratio for men was under 52.4 $cm^2 \cdot m^{-2}$ and for women under 38.5 $cm^2 \cdot m^{-2}$ (Prado *et al*., 2008). Adipose tissue distribution (visceral fat, subcutaneous and intramuscular fat areas) was measured and the adipose tissue index was calculated as for the skeletal muscle index. The impacts of these factors on pancreatitis course were analysed.

The severity of AP was defined in accordance with the Atlanta Criteria: mild acute pancreatitis with no organ failure, local or systemic complications; moderately severe acute pancreatitis defined by the presence of transient organ failure, local complications or exacerbation of co-morbid disease; and severe acute pancreatitis defined by persistent organ failure, that is, organ failure >48 h. Local complications included in the analysis were peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst and walled-off necrosis (sterile or infected) (Banks *et al*., 2012).

Statistical analysis was performed with IBM SPSS Statistics 23. The Chi square test, t-test and general linear model were used. The significance level was set as $\alpha = 0.05$. When $p \leq 0.05$, the difference was considered statistically significant.

## RESULTS

Of the included 100 patients, 42 (42%) were females and 58 (58%) were males. Mean age was 51 (range 18–92).

Aetiologic factors were: biliary pancreatitis — 23 (23%), alcohol — 58 (58%), post-ERCP — 4 (4%), hypertriglyceridemia — 4 (4%), and idiopathic — 12 (12%). Most of patients received conservative treatment (78 cases; 78%), endoscopical treatment was applied in 8 (8%) cases, and drainage surgery in 14 (14%). Moderately severe acute pancreatitis occurred in 83% (83 patients) cases and severe pancreatitis in 17% (17 patients), no mild pancreatitis cases were included. Mortality was 6% (6 patients). Mean hospital time was 13 days (range 3 till 139) (Table 1).

Normal weight according to BMI occurred in 38% (38 patients), overweight in 33% (33 patients), and obesity in 28% (28 patients) cases; one patient was underweight. Mean values of soft tissue areas by CT measurements are showed in Table 2.

Table 1

DISTRIBUTION OF PATIENT GROUPS

| | | | | |
|---|---|---|---|---|
| Age | Mean (years) | 51 | | |
| | Range (years) | 18–92 | | |
| Gender | Men (years) | 58 | | |
| | Women (years) | 42 | | |
| Body mass index | Mean (kg·m$^{-2}$) | 27.54 | | |
| | Underweight (<18.5 kg·m$^{-2}$) | Mean (kg·m$^{-2}$) | 15.24 | |
| | | Patients (n) | 1 | |
| | Normal weight (18.5–24.9 kg·m$^{-2}$) | Mean (kg·m$^{-2}$) | 22.87 | |
| | | Patients (n) | 38 | 38% |
| | Overweight (25–29.9 kg·m$^{-2}$) | Mean (kg·m$^{-2}$) | 27.48 | |
| | | Patients (n) | 33 | 33% |
| | Obesity (>30 kg·m$^{-2}$) | Mean (kg·m$^{-2}$) | 34.29 | |
| | | Patients (n) | 28 | 28% |
| Aetiology | Biliary (n) | 23 | 23% | |
| | Alcohol (n) | 57 | 57% | |
| | Post-ERHP (n) | 4 | 4% | |
| | Hypertriglyceridemia (n) | 4 | 4% | |
| | Idiopathic (n) | 12 | 12% | |
| Severity, (revised Atlanta classification, 2012) | Moderately severe | 83 | 83% | |
| | Sever | 17 | 17% | |
| Therapy | Conservative (n) | 78 | 78% | |
| | Surgery (n) | 14 | 14% | |
| | Endoscopy (n) | 8 | 8% | |
| Hospitalisation days | Mean (days) | 12.8 | | |
| | Range (days) | 3–139 | | |
| Mortality | Patients (n) | 6 | 6% | |

Table 2

COMPUTER TOMOGRAPHY SCAN MEASUREMENTS

| | | |
|---|---|---|
| Skeletal muscle area, cm$^2$ | Males | 165 |
| | Females | 114 |
| Skeletal muscle index, cm$^2$/m$^2$ | Males | 51 |
| | Females | 40 |
| Visceral fat area, cm$^2$ | 173.6 | |
| Subcutaneous fat area, cm$^2$ | 199.83 | |
| Intramuscular fat area, cm$^2$ | 11 | |
| Total fat area, cm$^2$ | 384 | |

Table 3

COMPUTER TOMOGRAPHY SCAN MEASUREMENTS AND SEVERITY OF ACUTE PANCREATITIS

| | Moderately severe pancreatitis | Severe pancreatitis | *p* |
|---|---|---|---|
| Skeletal muscle area, cm$^2$ | 138.11 | 151.67 | |
| Skeletal muscle index, cm$^{2}$·m$^{-2}$ | 45.14 | 57 | |
| Visceral fat area, cm$^2$ | 168.14 | 199.97 | |
| Visceral fat index, cm$^{2}$·m$^{-2}$ | 56.67 | 64 | 0.245 |
| Subcutaneous fat area, cm$^2$ | 199.68 | 202.55 | |
| Subcutaneous fat index, cm$^{2}$·m$^{-2}$ | 67.76 | 65 | 0.891 |
| Intramuscular fat area, cm$^2$ | 10.00 | 15.81 | 0.022 |
| Total fat area, cm$^2$ | 382.94 | 418.32 | |
| Total fat index, cm$^{2}$·m$^{-2}$ | 127.38 | 135 | 0.468 |
| Sarcopenia | 25 | 6 | 0.064 |
| Sarcopenic adiposity | 21 | 4 | 0.574 |
| Obesity | 17 | 11 | 0.026 |

Overall sarcopenia was detected in 51 patients (51%). According to BMI, sarcopenia was detected in one underweight patient, in 25 patients (67%) with normal weight, in 16 patients (47%) who were overweight, and in 9 obese patients (32%) (Table 3).

Sarcopenia was found in six patients (35%) with severe pancreatitis and in 45 patients (54%) with moderately severe pancreatitis.

Univariate analysis showed significant difference between groups of moderately severe and severe acute pancreatitis in intramuscular fat area ($p = 0.022$), and occurrence of obesity ($p = 0.026$) and nonsignificant for sarcopenia ($p = 0.064$).

A general linear model was used to estimate the occurrence of severe pancreatitis based on sarcopenia as a random factor and age as covariate. The model showed that none of the independent variables had a statistically significant effect on the occurrence of severe pancreatitis ($p = 0.095$ and 0.154, sarcopenia and age, respectively).

Also, the model was used to test whether obesity had a significant association with severe pancreatitis, taking patient's age into account (as a covariate). The model showed that obesity had a significant ($p = 0.026$) effect on the occurrence of severe pancreatitis while age was not a significant factor ($p = 0.208$).

A general linear model between sarcopenia, sarcopenic adiposity and visceral, subcutaneous, total fat indexes, and intramuscular fat area showed that only intramuscular fat area had a significant effect on the occurrence of severe pancreatitis ($p = 0.029$).

As mean values of intramuscular fat area were 10.00 cm$^2$ in moderately severe and 15.81 cm$^2$ in severe pancreatitis, it was proposed that higher value of intramuscular fat area increases risk of severe acute pancreatitis. An area under the ROC (receiver operating characteristic) curve was 0.689 and intramuscular fat area 11 cm$^2$ was considered as the threshold at which the probability of severe pancreatitis increases.

## DISCUSSION

The present study investigated association between body composition analysis by CT scan and acute pancreatitis severity. Our study results showed that obesity was a risk fac-

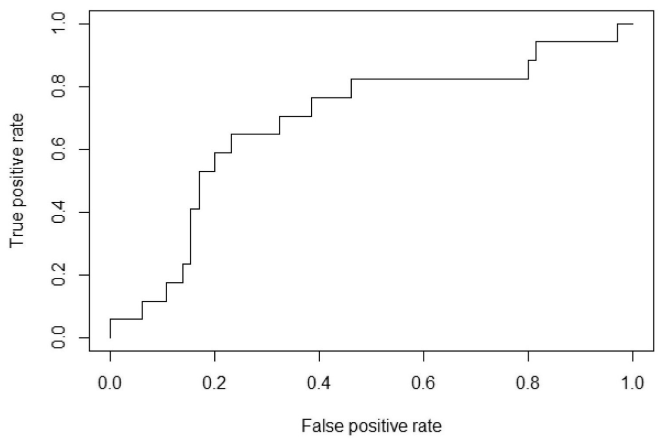


*Fig. 1.* Area under the ROC (receiver operating characteristic) curve of intramuscular fat area and severe acute pancreatitis.

tor of severe pancreatitis and that higher intramuscular fat area likely was another risk factor.

Obesity as a risk factor of severe acute pancreatitis is consistent with findings of other studies (De Waele *et al*., 2006: Martinez *et al*., 2006; Wang *et al*., 2011; O'Leary *et al*., 2012; Katuchova *et al*., 2014; Sawalhi *et al*., 2014; Thandassery *et al*., 2014, Hall *et al*., 2015).

Still, neither the sarcopenia, nor sacropenic adiposity, were observed to be associated with higher risk of severe pancreatitis in our study.

Analysis of abdominal fat distribution using computer software based on CT images has been addressed in many studies till now. Nevertheless, conflicting conclusions of different studies have been reported (Mery *et al*., 2002; O'Leary *et al*., 2012; Hall *et al*., 2015). Fat depots in the abdominal cavity or the liver have higher systemic levels of proinflammatory cytokines (Malavazos *et al*., 2007; Chalasani *et al*., 2012). Patel *et al.* observed that unsaturated fatty acids generated via lipolysis of visceral fat by pancreatic lipases are associated with severe acute pancreatitis, independently of pancreatic necrosis and the inflammatory response (Patel *et al*., 2015).

Several studies have suggested that intramuscular adipose tissue may release proinflammatory cytokines, which results in local inflammation (Zoico *et al*., 2010; Koster *et al*., 2011; Addison *et al*., 2015). Beasley *et al.* (2009) suggested that intramuscular adipose tissue may be related, also, to increased systemic body inflammation, and showed a relationship between the amount of intramuscular adipose tissue within the thigh and systemic measures of proinflammatory cytokines in the serum.

Our results did not show significant effect of visceral fat depots on severe acute pancreatitis; the subcutaneous fat amount also did not have significant effect. However, intramuscular fat area had significant effect on risk of severe acute pancreatitis ($p$ value = 0.029). However, the area under the ROC curve was 0.689, which suggests that increased intramuscular fat amount is associated with more severe acute pancreatitis, and the threshold was estimated to be 11 $cm^2$. However, a larger patient cohort is needed to provide a more precise estimation of the threshold. We could not find similar data in the literature about this association with the amount of intramuscular adipose tissue. We suggest that this threshold of area or some index could be defined as a pathologic state with substantial impact on health.

Various techniques like dual-energy X-ray absorptiometry, bioelectrical impedance analysis, CT and magnetic resonance imaging can be used to estimate body composition. CT is a diagnostic technique that is often used in patients with inflammatory diseases or in an area of oncology. CT has shown high accuracy in body composition evaluation (Mourtzakis *et al*., 2008; Gibson *et al*., 2015). Therefore, gaining additional information through body composition analysis from CT imaging data can provide an opportunity to integrate supportive care in nutrition or rehabilitation. This procedure can be done even for severely ill patients with poor overall status without any extra investigations (Brewster *et al*., 2014).

Also, measurement of body composition by CT scans gives more precise data about nutrition status than just BMI. In our patient group, only one patient was underweight by BMI and 51% had sarcopenia.

A limitation of this study was lack of patient with mild pancreatitis. CTs were done for patients with the need for recheck of diagnoses or because complications were suspected. Increase of patient cohort size might give more significant data about effect of fat distribution on severe pancreatitis risk, as a small number of patients were in the severe pancreatitis category.

In conclusion, body composition analysis can be done in moderately severe and severe acute pancreatitis patients by CT imagery. Body composition analysis showed that adiposity is a risk factor of severe acute pancreatitis, and likely higher intramuscular fat area is another risk factor.

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ĶERMEŅA UZBŪVES, KAS IZVĒRTĒTA, IZMANTOJOT DATORTOMOGRĀFIJAS PAPILDUS MĒRĪJUMUS, IETEKME UZ AKŪTA PANKREATĪTA GAITU

Smags akūts pankreatīts sastopams vidēji 15–25% no visiem akūta pankreatīta (AP) gadījumiem. Smagas gaitas riska faktoru atpazīšana dotu iespēju laicīgi uzsākt pacienta intensīvāku monitorēšanu un ārstēšanu. Pētījuma mērķis bija ķermeņa uzbūves izvērtēšana akūta pankreatīta pacientiem, izmantojot datortomogrāfijas (DT) izmeklējumus, nosakot ķermeņa uzbūves ietekmi uz slimības smagumu. Pētījums bija prospektīvs, tas tika veikts Paula Stradiņa klīniskajā universitātes slimnīcā laikā no 01.2015. līdz 04.2016. Pētījumā bija iekļauti 100 pacienti. Ķermeņa uzbūves mērījumus veica pēc DT izmeklējumiem, izmantojot *ImageJ v1.49q* standarta programmu. Izmantoja trešā jostas skriemeļa līmeņa attēlus, kuros veica mērījumus skeleta muskulatūras, viscerālo, zemādas un intramuskulāro taukaudu laukumiem. Attiecinot pret pacienta augumu, izrēķināja muskuļu un taukaudu indeksus ($cm^2 \cdot m^{-2}$). AP smagumu noteica, izmantojot Atlantas revidētos kritērijus (2012). No visiem iekļautajiem pacientiem vidēji smags AP bija 83% (83 pacienti), smags 17% (17 pacienti). Nosakot ķermeņa masas indeksu, normāls svars bija 38%, liekais svars 33%, aptaukošanās 28%. Tomēr sarkopēniju kopumā konstatēja 51%. Sarkopēniju atrada sešiem pacientiem (35%) ar smagu AP, 45 pacientiem (54%) ar vidēji smagu AP. Izmantojot vispārējo lineāro modeli — aptaukošanās ($p$ = 0,026) un intramuskulāro taukaudu laukums ($p$ = 0,029) parādīja ticamu ietekmi uz smagu AP kā riska faktori. Pēc iegūtajiem rezultātiem, aptaukošanās bija riska faktors smagam AP, kā arī intramuskulāro tauku laukums ir otrs rādītājs, kas norāda uz paaugstinātu risku smagam AP.