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Original Article

Metabolic syndrome and acute pancreatitis

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ABSTRACT

Aim: The aim of our study was to investigate the influence of metabolic syndrome on the course of acute pancreatitis determined by disease severity, the presence of local and systemic complications and survival rate.
Patients and methods: 609 patients admitted to our hospital in the period from January 1, 2008 up to June 31, 2015 with the diagnosis of acute pancreatitis were analyzed. The diagnosis and the severity of acute pancreatitis were made according to the revised Atlanta classification criteria from 2012.
Results: Of 609 patients with acute pancreatitis, 110 fulfilled the criteria for metabolic syndrome. Patients with metabolic syndrome had statistically significantly higher incidence of moderately severe (38.2% vs. 28.5%; $p = 0.05$) and severe (22.7% vs. 12.8%; $p = 0.01$) acute pancreatitis in comparison to those without metabolic syndrome, while patients without metabolic syndrome had higher incidence of mild acute pancreatitis in comparison to those patients with metabolic syndrome (58.7% vs. 39.1%; $p < 0.001$). Patients with metabolic syndrome had a higher number of local and systemic complications, and higher APACHE II score in comparison to patients without metabolic syndrome. In multivariable logistic regression analysis, the presence of metabolic syndrome was independently associated with moderately severe and severe acute pancreatitis. Comparing survival rates, patients suffering from metabolic syndrome had a higher death rate compared to patients without metabolic syndrome (16% vs. 4.5%; $p < 0.001$).
Conclusion: The presence of metabolic syndrome at admission portends a higher risk of moderately severe and severe acute pancreatitis, as well as higher mortality rate.

1. Introduction

Acute pancreatitis is an inflammatory disorder of the pancreas. Due to the risk of developing local and systemic complications, these patients are admitted to internal medicine or surgical wards for further monitoring and treatment. The most common etiologies of acute pancreatitis are biliary and alcoholic [1]. The course of acute pancreatitis depends on the level of severity and can be, according to the revised Atlanta classification from 2012, divided into mild, moderate, or severe, with severe acute pancreatitis carrying a significant mortality risk of up to 40% seen in patients suffering from infected pancreatic necrosis [2]. Mild acute pancreatitis, the most common form, has no organ failure, local or systemic complications and usually resolves in the first week. Moderately severe acute pancreatitis is defined by the presence of transient organ failure, local complications or exacerbation of co-morbid disease(s). Severe acute pancreatitis is defined by persistent organ failure, lasting longer than 48 h. Local complications of acute pancreatitis are peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocysts and walled-off necrosis (sterile or infected) [3]. Due to high mortality and limited treatment options in the management of acute pancreatitis, potential modifiable risk factors, as well as new scoring systems for early identification of high-risk patients are still being investigated.

Metabolic syndrome is a combination of factors that increases the risk of cardiovascular diseases and includes diabetes mellitus type 2 (T2DM), dyslipidemia, arterial hypertension and abdominal obesity. It has been shown that metabolic syndrome is associated with a variety of other diseases and that obesity, as a vital component of the metabolic syndrome, correlates with the increased occurrence and severity of acute pancreatitis [4]. However, there is a lack of data regarding the association between severity of acute pancreatitis and the presence of metabolic syndrome. A small number of studies have shown conflicting data regarding the presence of metabolic syndrome and the course of acute pancreatitis [4]. Most of the studies have investigated the association between obesity and course of acute pancreatitis and majority of these studies have shown that the presence of obesity has a negative impact on the course of AP [4–10].

Therefore, the aim of our study was to investigate the influence of metabolic syndome on the severity of acute pancreatitis, on the presence of local and systemic complications, as well as on the survival rate.

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2. Patients and methods

In this retrospective study we analyzed 700 patients diagnosed with acute pancreatitis and admitted to our hospital in the period from January 1, 2008 to June 31, 2015. Acute pancreatitis was defined as the onset of typical upper abdominal pain (nausea and/or vomiting) within 48 h prior to admission and the elevation of serum amylase and/or lipase activity at least 3 times above the upper limit of normal. Only the patients having the first attack of acute pancreatitis were included in the study. Patients with a relapse of acute pancreatitis or an exacerbation of chronic pancreatitis were excluded. The diagnosis of acute pancreatitis was additionally confirmed with imaging methods (abdominal ultrasound and/or computed tomography scan). Patients suffering from active malignant diseases, patients younger than 18 years and those with incomplete medical data were excluded from the analysis. Following the rule, 91 patients were excluded, leaving 609 patients for the final analysis. Anthropometric data including gender, age, weight (in kg), height (in m) and waist circumference (in cm), as well as the presence of concomitant diseases (type 2 diabetes mellitus, arterial hypertension, dyslipidemia, obesity, coronary heart disease and chronic kidney disease) and medication use were noted at admission. Initial patient data at admission included full and differential blood count, biochemistry and arterial blood gasses.

Biliary etiology was defined as the presence of gallstones determined by at least one of the imaging methods (abdominal ultrasound, multislice computed tomography, magnetic resonance cholangiopancreatography or endoscopic ultrasound) and the elevation of cholestatic enzymes (alkaline phosphatase, γ-glutamyl transferase). Alcoholic etiology was considered in patients with confirmed excessive alcohol consumption (defined as more than 14 drinks/week in women, and more than 21 drinks/week in men, respectively) without biliary disease, metabolic disorders (hypertriglyceridemia, hypercalcemia) or other possible causes of acute pancreatitis (trauma, drugs, etc.)

The severity of acute pancreatitis was classified according to the revised Atlanta classification from 2012 and was divided into: mild acute pancreatitis, with no organ failure, local or systemic complications; moderately severe acute pancreatitis, defined by the presence of transient organ failure (lasting shorter than 48 h), local complications and/or exacerbation of co-morbid diseases; and severe acute pancreatitis, defined by persistent organ failure (lasting longer than 48 h). Local complications of acute pancreatitis were divided into peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocysts and walled-off necrosis (sterile or infected) [3]. Initial assessment of predicted disease severity was performed by calculating the Acute Physiology and Chronic Health Evaluation II (APACHE II) score. The score includes 12 physiological measurements, age and chronic health points, which are translated into score points and summed, the total ranging from 0 to 71. Values equal or larger than 8 predict a more severe form of the disease. CT severity index was also calculated, based on the contrast-enhanced CT abdominal scan performed between the fifth and seventh day of hospital stay. CT severity index is calculated by determining the extent of pancreatic inflammation (named Balthasar score, ranges from zero to four) and pancreatic necrosis (ranges from zero to six). Total score ranges from zero to ten, with values less or equal than three indicating mild form, values between four and six indicating moderate form, and values equal or larger than seven indicating the severe form of acute pancreatitis.

Metabolic syndrome was defined according to the International Diabetes Federation criteria by the presence of waist circumference > 94 cm for men and >80 cm for women and at least two of the following metabolic abnormalities: blood pressure ≥ 130/85 mmHg or antihypertensive treatment; previously physician-diagnosed type 2 diabetes mellitus, or use of any hypoglycemic drugs or a fasting plasma glucose level ≥ 5.6 mmol/L; triglyceride levels >1.7 mmol/L; HDL-cholesterol <1.04 mmol/L for men and <1.29 mmol/L for women or lipid-lowering treatment [11].

The primary endpoint of this analysis was the relation between the presence of metabolic syndrome and the severity of acute pancreatitis.

Secondary endpoints were:

- the number of metabolic syndrome components in relation to the severity of acute pancreatitis according to the revised Atlanta classification from 2012;
- severity of acute pancreatitis with respect to the presence of metabolic syndrome according to the APACHE II score;
- -the number of local (peripancreatic fluid collections, pancreatic and peripancreatic necrosis and pseudocysts) and systemic complication of acute pancreatitis with respect to the presence of metabolic syndrome. The occurrence of walled-off necrosis was not investigated due to the small number of patients with this type of local complication;
- the duration of total hospital stay, hospital stay in high dependency unit and intensive care unit between patients with metabolic syndrome and those without metabolic syndrome;
- the survival rate with respect to the presence of metabolic syndrome.
- Statistical data analyses were performed using descriptive statistics (mean and SD). Differences between categorical variables were tested by χ^2 test or Fisher's exact test. Testing the importance of the difference between two independent groups was performed using Student's t-test or ANOVA, where appropriate.

Univariable and multivariable regression analyses were performed using the logistic regression analysis (and the results were expressed as regression coefficent B with its standard error and significance, odds ratio [OR] and 95% confidence intervals [CI]). $P < 0.05$ was considered to be statistically significant. Statistical analysis were made using MedCalc statistical software package, version 10 (MedCalc, Mariakerke, Belgium) and IBM SPSS v22.

3. Results

Of the 609 patients with acute pancreatitis, 110 fulfilled the criteria for metabolic syndrome. Table 1 shows demographic and clinical characteristics of our patients. The mean age of the analyzed patients was 63.2 ± 16.1 years, 55.5% of the patients were male. The most common etiologies of acute pancreatitis were biliary (66.2%) and alcoholic (13.8%). There was no statistically significant difference between the groups of patients with metabolic syndrome compared to those without metabolic syndrome with respect to gender, the presence of chronic kidney disease, as well as with respect to the etiology distribution of acute pancreatitis. However, patients with metabolic syndrome were older, had a higher incidence of coronary heart disease and had a higher

Table 1
Demographic and clinical data of investigated cases.

Characteristic	All patients (n = 609)	No-MetS (n = 499)	MetS (n = 110)	P
Age (y)	63.2 ± 16.1	62.4 ± 16.7	66 ± 14.2	0.03
Male, n(%)	338 (55.5%)	280 (56.1%)	58 (52.7%)	NS
T2DM, n(%)	86 (14.1%)	20 (4.01%)	66 (60%)	0.004
Arterial hypertension, n(%)	337 (55.3%)	236 (47.3%)	101 (91.8%)	<0.001
Dyslipidemia, n(%)	99 (16.3%)	30 (6%)	69 (62.7%)	<0.001
Obesity, n(%)	416 (68.3%)	258 (51.7%)	107 (97.3%)	<0.001
Coronary heart disease, n(%)	64 (10.5%)	44 (8.8%)	22 (20%)	0.001
Chronic kidney disease, n(%)	60 (9.9%)	18 (3.6%)	7 (6.4%)	NS
Etiology of AP				
Biliary, n(%)	403 (66.2%)	331 (66.3%)	72 (65.5%)	NS
Alcoholic, n(%)	84 (13.8%)	68 (13.6%)	16 (14.5%)	NS
Hypertriglyceridemia, n(%)	9 (1.5%)	7 (1.4%)	2 (1.8%)	NS

Diabetes mellitus type 2 (T2DM); metabolic syndrome (MetS); acute pancreatitis (AP); non-significant (NS).