Morphological and functional consequences and quality of life following severe acute pancreatitis

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Dorota Koziel*, Edyta Suliga*, Urszula Grabowska*/**, Stanislaw Gluszek*/**

**Faculty of Medicine and Health Sciences, Jan Kochanowski University, Kielce, Poland*
***Clinical Department of General, Oncological and Endocrine Surgery, Regional Polyclinical Hospital, Kielce, Poland*

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In this study, we evaluated pancreatic morphology and function as well as nutritional status and quality of life among patients who experienced severe acute pancreatitis (SAP).
MATERIALS AND METHODS: *We enrolled 99 patients with SAP and 51 with mild acute pancreatitis (MAP). Computed tomography was performed one year following the disease. Endocrine function was evaluated by measuring hemoglobin A1c, insulin, and C peptide levels. Pancreatic exocrine insufficiency (PEI) was diagnosed by the concentration of fecal elastase-1. Nutritional status was assessed according to anthropometric parameters, albumin levels in blood serum, and the total number of lymphocytes. Quality of life was investigated using the Health Survey Questionnaire (SF-36).*
RESULTS: *PEI was observed in 17.2% of patients after SAP vs. 7.8% of patients after MAP ($p>0.05$). Endocrine insufficiency was noted in 18.6% of patients after AP vs. 4.3% of patients after MAP ($p<0.05$). We observed changes in pancreatic morphology in 52.5% of patients after SAP and 9.8% of patients after MAP ($p<0.0001$). A medium risk of malnutrition was observed in 16.2% of patients after AP vs. 2% of patients after MAP ($p=0.01$). Patients with SAP described their mental health in more negative terms than patients with MAP ($p<0.05$).*
CONCLUSIONS: *One year after SAP, patients exhibited changes in pancreatic morphology and carbohydrate metabolism disorders, and exocrine insufficiency occurred with a similar frequency. The majority of quality of life domains did not differ between patient groups.*

KEY WORDS: Acute pancreatitis, Pancreatic morphology, Pancreatic function

Introduction

Acute pancreatitis (AP) is currently an important clinical problem considering the systematic increase in the number of cases [1]. Epidemiological data concerning morbidity due to AP in Poland also indicate an upward tendency. This basic study was preceded by an epidemiological analysis of AP pertaining to morbidity. The incidence rate of AP is 99.96/100,000, and for first-time episodes, the morbidity is 79.7/10,000. The mortality rate due to AP is 3.9% [2]. This region of Poland ranks first among European countries and justifies the evaluation of AP.

It is believed that AP is a self-limiting process during which permanent changes in exocrine and endocrine pancreatic function do not develop following elimination of the etiological factor. However, studies focusing on this problem have been divergent. These differences could be associated with varying diagnostic methods and the proportions of examined patients regarding their etiological factor, disease, and differences in the tests applied [3]. Pancreatic function disorders frequently develop after severe inflammation and are correlated with the dimension of necrosis [4]. Other studies have also demonstrated frequent secretory function disorders among patients

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Correspondence to: Dorota Koziel, Jan Kochanowski University Zeromskiego 5, Poland (E-mail: dorota.koziel@wp.pl)

following severe acute pancreatitis (SAP) [5]. In our former studies, we observed that a more severe course of AP was associated with the N34S *SPINK1* mutation [6]. According to the present state of knowledge, recurrent AP (RAP) (especially when combined with hereditary pancreatitis, alcohol consumption, and tobacco smoking) can lead to chronic pancreatitis (CP) [7-9].

Endocrine function is most often evaluated via a glucose tolerance test and fasting glucose, glycated hemoglobin, insulin and C-peptide levels [4, 10-12]. Some researchers have also applied mathematical models to evaluate insulin resistance (Homeostasis Model Assessment HOMA-IR) and beta cell function (HOMA-beta) [13]. The evaluation of exocrine efficiency can be difficult, especially when non-invasive methods are applied [14]. Many functional tests are available to assess exocrine function. Evaluating human pancreatic elastase (pancreatic elastase-1) levels is easy to perform, does not require the discontinuation of enzyme supplementation and is specific for the pancreas. Studies conducted in the 1990s confirmed that the pancreatic elastase-1 concentration in the stool is equivalent to actual pancreatic secretion and is proportional to the levels of other enzymes present in the pancreatic juice: amylase, lipase, trypsin and chymotrypsin. The test applied is an immunoenzymatic ELISA with monoclonal antibodies [15]. The advantages of this test prompted us to use this instrument to evaluate pancreatic exocrine function. Pancreatic exocrine insufficiency (PEI) leads to malnutrition due to poor digestion and decreased nutrient absorption [16]. Malnutrition during the course of PEI can lead to cardiovascular complications, infections, and osteoporosis, and malnutrition frequently causes patients with CP to be hospitalized [16].

Prospective studies evaluating the quality of life of patients who have experienced severe pancreatitis have been scarce. There has also been a lack of assessments regarding quality of life changes after contracting the disease. Some studies have indicated a relatively good quality of life. However, various evaluation instruments have been used during various observation periods, which hinders the possibility of comparing results [17, 18].

The objective of the present study was to evaluate the functional and morphological consequences of severe acute pancreatitis. We also evaluated the perceived quality of life at the one year follow up.

Materials and methods

First, we created a registry of patients who were hospitalized due to AP in one region of Poland during 2011-2012. Diagnosis was based on the fulfilment of 2/3 criteria in accordance with the most recent Atlanta classification. We performed prospective patient observations. The registry of patients was utilized for further control studies. One year following the last episode of SAP, invitations were mailed to all patients who were diagnosed with severe AP. Patients with a history of mild AP (MAP) constituted the control group. Invitations were also mailed to patients who were diagnosed with MAP (without a severe course of AP according to their medical history). The criteria for study exclusion were a moderate

TABLE I - *Characteristics of patients with AP: causes, surgical procedures and recurrence.*

	Severe AP N=99	Mild AP N=51	P value	OR
Sex				
Male	67 (67.7%)	27 (52.9%)	p<0.05	3.62
Female	32 (32.3%)	24 (47.1%)	p<0.05	0.28
Age (years)/SD (mean ± SD)	52±17.3	56.7 ±16.2	NS	-
Cause				
Gallstones	42 (42.4%)	22 (43.1%)	NS	0.971
Alcohol	36(36.4%)	10 (19.6%)	p<0.05	2.33
Other causes	3 (3%)	1 (2%)	NS	1.589
Unexplained causes	18 (18.2%)	18 (35.3%)	p<0.05	2.44
Surgical procedure				
Necrosectomy	3 (3%)	0	-	-
Laparoscopy pseudocyst drainage	8 (8.1%	0	-	-
Cholecystectomy	18(18.2%)	15(29.4%)	-	-
Percutaneous pseudocyst drainage	7 (7.1%)	0	-	-
Recurrent AP	33 (33.3%)	11 (21.5%)	0.0948	1.9799
Gallstones	12 (36.4%)	3 (27.3%)	1	1.3817
Alcohol	13 (39.4%)	3 (27.3%)	0.4865	1.9713
Unexplained causes	8 (24.2%)	5 (45.4%)	0.2479	0.3647

Data are n (%) unless otherwise indicated.
AP- acute pancreatitis; OR- odds ratio; SD- standard deviation; NS- not statistically significant.

course of AP and a diagnosis of chronic pancreatitis before the disease.
This study was conducted in one center. To obtain coherent and comparable results, computed tomography was performed on all of the patients, using the same apparatus, by one physician who was unaware of the patients' clinical details. Laboratory tests involving biological materials were performed by one laboratory.
The results from the individual tests were compared and analyzed according to the severity of the disease.
A total of 99 patients with SAP (32.3% female and 67.7% male) and 51 patients with MAP (47.5% female and 52.9% male) were enrolled in the study. The mean age of the patients who were diagnosed with SAP was 52 years old, and the mean age of patients who were diagnosed with MAP was 56 years old. In total, 41 patients diagnosed with SAP, for various reasons, did not respond to the invitation (Table I).

Assessment of exocrine pancreatic function

An enzyme-linked immunosorbent assay (ELISA) immunoenzymatic test was utilized.
The examined material was a single stool sample (approx. 75-100 mg). The following concentrations were applied as reference values: normal, when the amount of elastase exceeded 200 μg/g stool; decreased, if the values remained within the range of 151-200 μg/g stool, which is equivalent to light pancreatic exocrine insufficiency (LPEI); considerably decreased, if the value was 100-150 μg/g stool, indicating moderately severe pancreatic exocrine insufficiency (MSPEI); and less than 100 μg/g, which indicated severe pancreatic exocrine insufficiency (SPEI).

Evaluation of pancreatic endocrine function

Venous blood was collected from patients after fasting. The levels of glucose, insulin, and C-peptide were determined in serum.
To determine the glycated hemoglobin (HbA1c) levels, blood was collected with EDTA. The measurements were performed based on immuno-inhibition testing. The levels of glycated hemoglobin (HbA1c) and glucose were investigated via Beckman Coulter kits and the biochemical analyzer AU 680. Glucose was measured via the hexokinase method. Insulin was measured via the immunoenzymatic method using the Beckman Coulter UniCel DxI 600 Access. C-peptide levels were measured by the chemiluminescence method using a Roche Elecsys 2010 analyzer.
We utilized the following reference values to interpret the results: HbA1c 4.6-6.5%; insulin 1.9-23 μU/ml; and Cs-peptide 1.1-4.4 ng/ml. Patients with a history of diabetes were excluded from the evaluation of endocrinal function. Insulin resistance was assessed using the HOMA-IR indicator (fasting insulinemia [mU/ml] x fasting glycaemia [mmol/l] / 22.5). The value of the indicator HOMA-IR >3 was considered severe insulin resistance.

Evaluation of pancreatic morphology

Computed tomography (CT) of the abdominal cavity is commonly considered a reference method that provides reliable information regarding the morphological evaluation of this on-going process.

Evaluation of nutritional status

The *subjective global assessment* (SGA) combines nutritional surveys and anthropometric examinations. Based on the self-reported amount and intensity of the reported symptoms, the patients were classified into the following groups: good nutrition (Group A), moderate nutrition (Group B), and intensified malnutrition (Group C).
Anthropometric examinations (measurements of body weight, height, arms, waist, hip circumference, and the measurement of skinfold thickness) were used to calculate the body mass index (BMI) and arm muscle circumference (AMC).
The protein–calorie nutritional status was determined by measuring the serum albumin levels. To determine the weakening of resistance that accompanies malnutrition, the total number of lymphocytes (TNL) was determined by using the following formula:

TNL = (% of lymphocytes x number of lymphocytes)/100

Evaluation of quality of life

The Short Form-36 Health Survey Questionnaire (SF-36) is designed for self-reported health. The SF-11 consists of 11 items containing 36 statements, which allow for the determination of 8 elements: physical functioning, limitations due to physical health, pain sensation, perceived general health, vitality, social functioning, emotional functioning, and mental health. The indicator of quality of life is the sum of the evaluation scores of all 8 quality of life scales, which enables a general assessment of the state of health. In the present study, we utilized the Polish version of the SF-36v2 questionnaire [19].

Ethics

Consent for conducting the study was obtained from the Bioethical Commission (No. 1/2012), Faculty of Health

Sciences, Jan Kochanowski University, Kielce. All of the patients expressed their consent to participate in the study.

Statistical methods

The differences regarding the proportions of patients with specific causes and recurrences among patients with severe or mild AP were assessed with Fisher's exact test. The data sets were displayed in the form of 2x2 contingency tables. Fisher's test was adequate because some of the cell numbers in the tables were small, and there were rather large differences between cell numbers. Fisher's test was also used to analyze the associations between the course of AP (SAP or MAP) and several indicators of exocrine pancreatic efficiency, carbohydrate metabolism or malnutrition status. Odds ratios (ORs) were used to compare the odds of specific event occurrences in the MAP and SAP groups. Comparisons regarding quality of life domains after MAP or SAP were performed using the two-sample t-test or unequal variance t-test to determine whether the two population means were significantly different.

Results

Among the majority of patients, gallstones (SAP 42.4%; MAP 43.1%), alcohol (SAP 36.4%; MAP 19.6%), and other causes (SAP 3%; MAP 2%) were the main causes of this disease. The cause was not explained in 18.2% of patients after SAP and 35.3% after MAP. The cause of the disease did not exert any effect on the severity of SAP (p>0.05). In the SAP group, 3 patients underwent necrosectomy, 8 patients underwent laparoscopic drainage for pancreatic cysts, and 7 patients underwent percutaneous drainage (Table I). During the observation period, gallstone removal was performed among 18 of 42 patients after SAP (42.9%) and 15 of 22 patients after MAP (68.2%). Recurrent AP more frequently affected patients after SAP: 33 (33.3%) vs. 11 (21.6% MAP). However, no significant relationships were observed (p=0.09; OR 1.9).

The median time to perform a follow-up examination after severe AP was 13 months (mean 13.9 ±3.8), which was comparable to the control group in which the median was 14.8 (mean 15±3.6) months (Table I).

Evaluation of exocrine pancreatic function

PEI was more frequently observed among patients with SAP than MAP - 17.2% vs. 7.8%. However, the difference was not significant (p=0.14) (Table II).

PEI was noted in 15.2% of patients who experienced severe recurrent AP compared to no patients with mild recurrent AP (p=0.31). PEI was registered jointly (SAP and MAP) in 5 of 44 (11.4%) patients with recurrent AP vs. 16 of 106 (15.1%) patients without recurrence. We observed low elastase 1 values in the stool in 6 of 46 (13%) patients after alcohol-related AP (4 after SAP and 2 after MAP), 7 of 42 (16.7%) patients after gallstone-related SAP, 0 after MAP, and 8 of 36 (22%) patients in whom the cause of the disease was not explained (6 after SAP and 2 after MAP): p>0.05.

Among all of the patients with SAP and PEI, we observed various changes in pancreatic morphology. However, the differences were insignificant (p=0.35). Patients who experienced MAP and PEI had no concomitant pancreatic morphological changes. PEI was more frequently observed in patients after surgical interventions for SAP. However, the relationship was insignificant (p>0.05) (Table II).

Evaluation of endocrine pancreatic function

Among the patients with severe AP, 3.2% had a medical history of type 2 diabetes prior to the disease, and 2 had histories of type 1 diabetes (total 13/99). Among patients with mild AP, type 2 diabetes was noted for 7.8%. This group of patients was excluded from further analyses of exocrine pancreatic efficiency.

TABLE II - *Parameters of exocrine pancreatic efficiency after acute pancreatitis.*

Intensity of PEI	SAP n=99	MAP n=51	P value	OR	RSAP n=33	RMAP n=11
All PEI	17 (17.2%)	4 (7.8%)	p=0.41	2.42	5 (15.2%)	0
Light PEI*	5 (5.1%)	-	p=0.17	inf.		
Moderate PEI**	3 (3%)	1 (2%)	p=1	1.56	1 (3%)	0
Severe PEI***	9 (9.1%)	3 (5.8%)	p=0.75	1.59	4 (12.1%)	0

*Light PEI - elastase 1=150-200 μg/g stool; **Moderate PEI elastase 1=100-150 μg/g stool; ***Severe PEI- elastase 1<100 μg/g stool. Data are n (%) unless otherwise indicated; PEI -pancreatic exocrine insufficiency; SAP – severe acute pancreatitis; MAP- mild acute pancreatitis; RSAP- recurrent severe acute pancreatitis; RMAP- recurrent mild acute pancreatitis OR- odds ratio.

TABLE III - *Carbohydrate metabolism among patients after severe and mild AP.*

	SAP n=86	MAP n=47	P value	OR
HOMA–IR >3	22 (25.6%)	7 (14.9%)	0.19	1.955
HbA1c > 6.5%	16 (18.6%)	2 (4.3%)	0.031	5.1
C-peptide <1.1 ng/ml	7 (8.1%)	1 (2.1%)	0,259	4.04
C-peptide >4.4 ng/ml	9 (10.5%)	3 (6.4%)	0.538	1.71

HOMA -Homeostasis Model Assessment; HbA1c- glycated hemoglobin SAP – severe acute pancreatitis; MAP- mild acute pancreatitis; OR- odds ratio.

TABLE IV - *Relationship between HOMA-IR and BMI among patients after severe and mild acute pancreatitis.*

	BMI ≤ 20**		20<BMI ≤ 24,9		25 ≤ BMI ≤ 29,9		BMI ≥ 30	
HOMA -IR post-SAP*	0.84 ± 0.33	NS	1.74 ± 2.09	NS	3.71 ± 3.56	NS	3.71 ± 3.56	NS
HOMA-IR post-MAP*	1.09 ± 1.09		1.14 ± 0.49		2.12 ± 1.25		2.43 ± 2.13	

HOMA - Homeostasis Model Assessment; BMI - body mass index; SAP - severe acute pancreatitis; MAP- mild acute pancreatitis
*Values are presented as the mean ± SD
**BMI, kg/m^2

Endocrine pancreatic insufficiency was observed in 16 of 86 (18.6%) of the remaining patients after SAP vs. 2 of 47 (4.3%) patients after MAP (p<0.05; OR 5.1). Severe insulin resistance, expressed by the indicator HOMA-IR>3, was observed with a similar frequency among the groups after severe or mild AP (p>0.05) (Table III).

High values of HOMA-IR were associated with an increased BMI (Table IV). The multiple regression model was used to predict HOMA using 2 independent variables: BMI and SAP or MAP. The regression coefficient for BMI was highly significant (p<0.0001). For the SAP group, the HOMA value increased by 0.77 units (similar to the effect of BMI).

Exocrine and endocrine pancreatic function disorders were observed in 6 patients after SAP (6.1%). No relationship was confirmed between exocrine and endocrine pancreatic efficiency (p=0.41). Endocrine insufficiency more often occurred in patients after surgical interventions during the course of SAP (22.2% vs. 14.8%). However, the relationship was insignificant (p>0.05) (Table V).

Evaluation of pancreatic morphology

Changes in pancreatic morphology were noted in 52.5% of patients after SAP and in 9.8% after MAP (p<0.0001). Frequently, the changes were observed in the tail [16] and core of the pancreas [15]. Fig. 1 presents a detailed analysis of the changes. Changes in pancreatic morphology were most frequently related to biliary etiology (28.3%) followed by alcohol-related causes (14.1%), unexplained causes (9.1%), and other causes (1%) among patients with SAP.

Changes in pancreatic morphology were observed in 18 of 44 (40.9%) patients with recurrent AP, including one patient after recurrent MAP. No differences in the frequency of occurrence of morphologic changes were noted for patients with (18/44 patients; 41%) or without recurrent AP (39/106; 36.8%): p> 0.05. No relationship was confirmed between PEI and changes in pancreatic morphology (p=0.35). Changes in pancreatic morphology were significantly more common among patients who underwent surgical interventions during the course of SAP (77.8% vs. 48.1%; p<0.05) (Table V - Fig. 1).

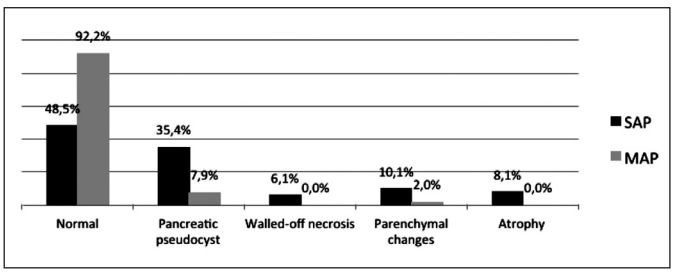

Fig. 1: Changes in pancreatic morphology following severe and mild AP

*Some patients experienced multiple changes; therefore, the results do not sum to 100%.

TABLE V - *Relationships among pancreatic morphology, exocrine and endocrine pancreatic function, and surgical interventions during the course of severe acute pancreatitis.*

	Pancreatic Exocrine Insufficiency N=17	P value	Endocrine insufficiency N=16	P value	Changes in pancreatic morphology N=53	P value
Surgical procedure N=18/99 (18.2%)	5/18 (27.8%)	p=0.30	4/18 (22.2%)	p=0.48	14/18 (77.8%)	p=0.04
Without surgical intervention N=81/99 (81.8%)	12/81 (14.8%)		12/81 (14.8%)		39/81 (48.1%)	
Necrosectomy N=3/99	1/3 (33.3%)	p=0.44	1/3 (33.3%)	p=0.41	2/3 (66.7%)	p=1
Without necrosectomy N=96/99	16/96 (16.7%)		15/96 (15.6%)		51/96 (53.1%)	
Laparoscopy pseudocyst drainage N=8/99	2/8 (25%)	p=0.62	1/8 (12.5%)	p=1	5/8 (62.5%)	p=0.72
Without Pseudocyst derivation N=91/99	15/91 (16.5%)		15/91 (16.5%)		48/91 (52.7%)	
Percutaneous pseudocyst drainage N=7/99	2/7 (28.6%)	p=0.34	2/7 (28.6%)	p=0.32	7/7 (100%)	p=0.01
Without Percutaneous pseudocyst drainage N=92/99	15/92 (16.3%)		14/92 (15.2%)		46/92 (50%)	

Assessment of nutritional status

None of the patients with SAP were classified as having a high risk for malnutrition (Category C) according to the SGA vs. one patient after MAP. Sixteen patients after SAP (16.2%) were classified as having a medium risk for malnutrition (Category B) vs. 1 after MAP (2%) (p=0.01). A relatively small group was classified as being at risk for malnutrition based on BMI <20 kg/m^2. In this group, 7.1% of patients experienced SAP and 4% experienced MAP. AMC values less than the adopted values (90% of the normal values: men 22.8 cm, women 20.9 cm) were observed in 14.1% patients after SAP and 19.6% patients after MAP. Malnutrition (albumin <3.5 g/dl) was observed in 10.1% of patients after SAP and 3.9% after MAP (Table IV).

Considerable impairment of resistance state and severe malnutrition (TNL<800) were noted in 4.1% patients after SAP and 0 patients after MAP. Moderate malnutrition (TNL of 800-1199) was observed in 4.1% of patients after SAP and 3.9% patients after MAP. Slight malnutrition (TNL 1200-1499) was observed in 18.2% of patients after SAP and 23.5% after MAP.

Among patients with PEI, a significant relationship was confirmed between low values of TNL (p=0.05) and SGA (p=0.05). No significant correlations were observed between low albumin values and anthropometric indicators, such as AMC and BMI, or exocrine pancreatic insufficiency based on the concentration of elastase 1.

Evaluation of quality of life

Patients with SAP evaluated their mental health in more negative terms than patients with MAP (p<0.05). However, both groups of patients similarly evaluated their physical health (p>0.05). Patients from both groups expressed very negative evaluations regarding their general health: (SAP 45.3 and MAP 46) (Table VII).

Discussion

Clinical studies have focused primarily on the direct complications of the disease, whereas less attention has been devoted to the chronic effects of AP. The efficiency of the pancreas after mild AP may remain unchanged. However, after experiencing severe AP, changes are usually observed in pancreatic function and morphology [5,14,20]. The strength of the present study compared with that of previously published studies is due to the enrollment of a homogenous patient group (only SAP vs. MAP). The patients were clas-

TABLE VI - *Malnutrition status among patients after severe acute pancreatitis compared to mild acute pancreatitis.*

	Normal nutritional status			Malnutrition		
	SAP N=99	MAP N=51	P value	SAP N=99	MAP N=51	P value
SGA	85 (83.8%)	49 (96.1%)	0.09	14 (14.1%)	2 (3.9%)	0,09
BMI<20 kg/m^2	92 (92.9%)	49 (96.1%)	0.72	7 (6.1%)	2 (3.9%)	0,72
Albumin<3.5 g/dl	89 (89.9.9%)	49 (96.1%)	0,22	10 (10.1%)	2 (3.9%)	0,22
TNL<1,200 in 1 mm^3 blood	91 (91.9%%)	49 (96.1%%)	0.50	8 (8.1%%)	2 (3.9%%)	0,50
AMC	86 (86.9%)	41 (80.4%)	0.34	14 (14.1%)	10 (19.6%)	0,34

SGA - Subjective Global Assessment; BMI - body mass index; TNL - total number of lymphocytes; AMC - arm muscle circumference

TABLE VII - *Quality of life domains in patients after MAP or SAP.*

Domains	MAP Mean	SD	SAP Mean	SD	P value
Physical functioning	58.4	7.3	57.6	8.0	0.54
Role physical	59.8	9.6	57.6	10.6	0.25
Body pain	52.1	11.2	49.9	12.5	0.43
General health	46.0	7.0	45.3	5.7	0.61
Vitality	58.7	13.9	57.2	18.7	0.62
Social functioning	71.9	17.7	63.9	22.5	0.04
Role emotional	58.8	7.6	54.7	9.8	0.03
Mental health	57.8	14.7	54.0	18.0	0.27
Physical Health	57.1	12.3	54.7	13.3	0.32
Mental Health	79.9	20.2	71.9	28.5	0.02

SAP - severe acute pancreatitis; MAP - mild acute pancreatitis.

sified according to disease severity in accordance with the most recent Atlanta classification, and the follow-up examination was performed within a narrow time interval of approximately one year after contracting AP. The requirement for only patients with SAP or MAP (without the moderately severe form) resulted in a relatively small number of available reports regarding SAP. A limitation in this study was the enrollment of patients with various disease etiologies and recurrent AP.

PEI occurred more frequently among patients after SAP vs. MAP (not significant). Many patients may develop long-term PEI after SAP or MAP (60.5% and 39.5%, respectively) [21]. In Andersson et al. [14], during the initial period, all of the patients exhibited preliminary PEI, which remitted in 80% of patients after 12 months [13]. The results from the present study are similar to results obtained in Turkey. Within 32 months after falling ill, PEI was observed in 17.9% of patients after SAP and 11.4% after MAP [22]. Exocrine inefficiency occurred equally often among patients with alcohol-related, biliary, and idiopathic etiologies, similar to the study by Xu [21]. Contrary to expectations, exocrine pancreatic function was disturbed not only in patients after recurrent SAP but also in the majority of other patients without recurrence (p>0.05). Therefore, even a single episode of SAP can damage pancreatic function, which (as shown by other studies) can lead to chronic pancreatitis (CP) [23]. PEI was more often observed among patients after necrosectomy. However, no significant difference was confirmed. A relationship between PEI and necrosectomy was reported by Chandrasekhar et al.[24] PEI was observed in 57.1% of patients after necrosectomy vs. 14.2% of patients who did not undergo surgery. Our analyses and other studies indicate that it is necessary to evaluate exocrine pancreatic function in patients susceptible to PEI because it leads to nutritional disorders and can increase the number of complications and mortality [25]. The frequency of clinical and anthropometric symptoms among patients with PEI is difficult to specify [16]. Classifying the state of malnutrition based only on actual body weight or BMI tends to underestimate this problem, and many patients have an increased risk of malnutrition after severe AP with EPI [26]. Additionally, in the present study, BMI and AMC were not sensitive markers for nutritional status. TNL<800 and albumin <3.5 g/dl might be useful for diagnosing patients who are at risk for an impaired state of resistance and severe malnutrition.

In recent years, it was noted that endocrine pancreatic function may be impaired after AP. This impairment is not limited only to patients with severe AP[5, 10, 11, 20]. The percentage of patients after SAP in whom endocrine pancreatic function disorders were observed ranges from 13% - 43% [4,20,22,27]. In the present study, patients after SAP experienced endocrine insufficiency significantly more often: 18.6% vs. 4.3% (p<0.050). In Vujasinovic et al.[11], 14% of all patients (100 patients) after AP developed endocrine insufficiency, which was more frequently noted in patients after SAP. The HOMA-IR test facilitated the diagnosis of insulin resistance in 21.9% of all patients. Gasparoto et al. [13], using the HOMA-IR model, diagnosed insulin resistance in 31.2% of patients after AP. None of the patients had a concentration of C-peptide less than 0.9 ng/ml. Among the patients in this

study, 3.5% of patients after SAP had C-peptide levels less than 0.9 ng/ml.

Intensification of exocrine pancreatic insufficiency is correlated with the extent of necrosis and simultaneous intensification of endocrine pancreatic insufficiency [4,28]. Gupta et al. [29] confirmed that 40% of patients developed simultaneous disorders of exocrine and endocrine secretion, especially during the first year after AP. The frequency of occurrence of these disorders decreased during the period of observation. In the present study, simultaneous disorders of exocrine and endocrine secretion of the pancreas were noted in 6.1% of patients after SAP and in none of the patients after MAP. Changes in pancreatic morphology were observed in all patients. However, no significant relationship was confirmed.

Patients with a mild course of the disease exhibited significantly fewer changes in the pancreas during the observation period ($p<0.05$). Changes in the pancreatic parenchyma were observed in more than half of the patients after SAP (most often of a biliary etiology). These changes were correlated with surgical procedures during SAP, especially percutaneous pseudocyst drainage ($p<0.05$). Chandrasekhar at al.[24] observed changes in the morphology of the pancreas in 88.5% of patients after SAP. The non-operative group had more patients with completely visualized MPD.

Changes in the pancreas are most frequently described in patients with recurrent AP [13]. However, in the present study, patients with recurrent AP constituted 33.3% of all patients with pancreatic changes after SAP. The remaining patients experienced only one episode of SAP, which suggests that even a single episode of AP may cause chronic morphological changes within a longer time period.

Patient quality of life after AP remains unclear. The results based on a meta-analysis of 16 prospective studies indicated more negative evaluations of the general health and vitality domains among patients with AP compared to healthy individuals. The researchers concluded that quality of life might be significantly weakened after AP. However, considering various interventions in this evaluation is necessary [18]. The results obtained by Hochman [30] suggested a worse quality of life for patients 24 and 36 months after AP, especially regarding physical functioning. Over time, quality of life can return to normal levels. Worse quality of life, as measured by the SF-36 questionnaire, was also observed in studies of British patients after acute necrotizing pancreatitis regarding all domains at 3, 6 and 12 months after disease onset [31]. In the present study, patients with severe AP, compared to mild AP, evaluated only the psychological domain in more negative terms. It would be interesting to determine which factors contribute to the negative evaluation of this domain. Some researchers have presented results according to Ranson's criteria, which can be a prognostic factor for decreased quality of life.

In the present study, we evaluated the consequences of AP in a homogenous group of patients after severe AP. All patients were evaluated at the same time point: one year after contracting the disease. Patients with severe AP experience a difficult convalescence period. Hence, unfavorable consequences should be properly monitored and treated to obtain recovery within the shortest time possible.

Conclusions

One year after severe AP, patients exhibited changes in pancreatic morphology and disorders in carbohydrate metabolism. Exocrine insufficiency occurred with equal frequency among patients with severe or mild AP. Patients with recurrent AP are particularly prone to exocrine function disorders and may develop severe AP. Although we observed no group differences regarding the majority of quality of life, it seems important to identify the causes of the more negative mental health status after SAP.

Riassunto

In questo studio abbiamo valutato la morfologia del pancreas, i dati funzionali e nutrizionali e la qualità di vita su un gruppo di pazienti precedentemente affetti da pancreatite acuta grave (SAP).

Per lo studio sono stati arruolati 99 pazienti in precedenza affetti da< SAP e 51 pazienti precedentemente colpiti da pancreatite acuta di media gravità (MAP). Il controllo TAC è stato eseguito un anno fopo il termine della malattia, e le funzioni endocrine sono stata valutate con la misurazione della Emoglobina A1c, del livello di insulina e del C peptide.

Il grado di insufficienza pancreatica esocrina (PEI) è stato diagnosticato dalla concentrazione della elastasi-1 fecale. Lo stato nutrizionale è stato determinato sui parametri antropometrici, sull'albuminemia sierica e sul numero totale di linfociti.

La determinazione della qualità di vita è stata indagata con l'uso dello Health Survey Questionnaire (SF-36).

Dallo studio è risultata una PEI nel 17,2% dei pazienti già affetti da SAP contro il 7,8% di quelli già affetti da MAP ($p>0.05$).

Una insufficienza endocrina è stata rilevata nel 18,6% dei pazienti già affetti da SAP contro il 4,3% di quelli già affetti da MAP ($p>0.05$).

La morfologia del pancreas è risultata alterata del 52% dei pazienti già affetti da SAP contro il 9,8% di quelli già affetti da MAP ($p>0.0001$). Un rischio moderato di malnutrizione è stato osservato nel 16,2% dopo SAP contro il 2% dopo MAP ($p=0.01$). I pazienti con SAP hanno descritto la loro salute mentale in termini maggiormente negative rispetto agli intervistati dopo MAP ($p<0.05$).

In conclusione un anno dopo SAP i pazienti hanno presentato cambiamenti della morfologia pancreatica, del

metabolismo dei carboidrati ed insufficienza esocrina con incidenza simile. La qualità di vita non è risultata nella maggioranza dei casi differente tra i due gruppi.

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