

## THE DEVELOPMENT OF EARLY ORGAN FAILURE IN NECROTISING ACUTE PANCREATITIS

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### Aims

The study was aimed at the correlation of the development of early organ failure with the necrotising lesion of the pancreas and the prevalence of peripancreatic infiltration.

### Materials and methods

The treatment data of 1,550 patients with acute pancreatitis were analysed. The pancreatic lesion characteristics were evaluated by dynamic ultrasound and CT angiography in the third week of the disease. The conclusion on the presence of signs of organ failure was based on the international guidelines (more than 2 points on the SOFA scale).

### Results

In 85.61%, acute pancreatitis was not accompanied by the development of necrotic lesion of the pancreas. In 88.99% of cases of interstitial oedema of the pancreas, there was no peripancreatic infiltration. The formation of peripancreatic infiltration in the absence of symptoms of necrotising lesion of the pancreas is a poor prognostic sign. A microfocal lesion was observed in 7.48% of patients, in these, infiltration of up to 3 regions of the retroperitoneal cellular tissue was detected in 42.25% of cases, and of 4 to 6 regions – in 27.59%. Macrofocal necrosis was noted in 5.74% of them, and in 40.44% of cases, was accompanied by involvement of 4 to 6 regions of the cellular tissue in the pathological process. Subtotal lesion in less than 1% of cases was accompanied by a massive infiltration of the cellular tissue, 7 or more anatomical regions in 46.15%. Most often, complications on the part of cardiovascular system developed in phase I – 28.08% of severe acute pancreatitis. The development of multiple organ failure accompanies 48.82% of patients with severe course of the disease. The development of organ failure was not detected in interstitial oedema of the pancreas. Microfocal lesion was accompanied by complications in 41.38% of cases, while macrofocal – in 92.13%, and pancreatic damage with more than 50% of the volume always caused organ dysfunction.

### Conclusions

The risk of early organ failure in phase I of severe acute pancreatitis increases with a lesion of greater volume of the pancreas involving more than 3 areas of retroperitoneal cellular tissue in the pathological process.

**Keywords:** acute pancreatitis, organ failure.

## INTRODUCTION

Early organ failure in patients with necrotizing pancreatitis is an acute issue not only in urgent surgery but also in resuscitation science. Phase I of severe acute pancreatitis (SAP) is characterized by a “mediator hurricane” and is often associated with severe general complications that require complex treatment in the conditions of the intensive care department [1-3]. Patients with SAP have a high rate of lethality. It should be highlighted that 40% of lethal outcomes result from the development of early organ failure [4-6].

The clinical development of acute pancreatitis reflects the pathological process in the pancreas and retroperitoneum [7-9]. Thus, the evaluation of the extent and depth of the pancreas damage is the primary task in the diagnostics of acute necrotizing pancreatitis as one of the most severe forms of the disease.

**The aim of the study** was to evaluate the association between the development of early organ failure and the character of the necrotizing process in the pancreas and the extent of peripancreatic infiltrate.

## MATERIALS AND METHODS

The prospective clinical observation included 1550 patients with acute pancreatitis that were treated in the clinical facilities of the Department of General Surgery named after Prof. M.I. Gulman at the Krasnoyarsk State Medical University named after Prof. V.F. Voino-Yasenetskiy of the Ministry of Healthcare of the Russian federation in 2010-2015. All the patients were diagnosed with acute pancreatitis based on the clinical picture, which was verified by the results of laboratory and instrumental studies performed according to the accepted clinical recommendations.

The identification of the form and stage of the pathological process was based on the Atlanta international classification of acute pancreatitis (Atlanta, 1992), in its modification (Kochin, 2012) approved by the International Association of Pancreatologists and the Working Group on the classification of acute pancreatitis of the International Association of Pancreatologists/American Pancreatic Association (2013) and the Russian Association of Surgeons (2014).

The study entry criteria were patients from 18 years old of any sex that were delivered to the inpatient facility by the ambulance service with the diagnosis of acute pancreatitis phase I. The criteria of exclusion were patients with diabetes mellitus and other endocrine, autoimmune, infectious, and oncologic diseases, comorbid cardiovascular pathology, cardiac insufficiency 2A and higher, 2 and higher (functional classification by NYHA), allergic reactions and intolerance to contrasting agents in the anamnesis, pregnancy. The criterion for withdrawal was the patient's refusal from participation in the study.

The evaluation of the condition of the pancreas and retroperitoneum was performed with a screening ultrasonic study with Aloka SSD 3500, 3.5 MHz transducer rate. The study was performed at the admission and in the dynamics on Days 7, 14 and 21.

For detailed visualization, patients with suspected acute necrotizing pancreatitis underwent computed angiography with bolus abdominal contrasting with a multi-spiral 4-layer computed tomographic scanner LightSpeed (General Electric, USA). Computed angiography was performed for all patients who had a verified diagnosis of severe acute pancreatitis (211 patients).

The medical conclusion on the extent of the pathological process and formation of peripancreatic infiltrate was made on Week 3 (Days 14-21). The description of the extent of the peripancreatic process was made by the classification proposed by Titova (1989).

In cases when the results of CT angiography did not agree with the results of the ultrasonic study, the results of CT scanning were used taking into account the clinical picture of the disease and changes in the results of the laboratory tests. In the early period (72 hours from the disease onset), the impairment of tissue perfusion revealed by CT angiography with bolus contrasting

indicates a formation of necrotic foci in the pancreas. In the later period, the areas of necrosis do not accumulate the contrasting agent and cannot be revealed by CT scanning. The verification was performed by the Balthazar–Ranson scale.

An increase in the threshold by 2 points by the SOFA scale indicates a dysfunction of the organ system.

In the present study, the general lethality rate was 2.58% (40 patients). In 24 patients (60%), the lethal outcome resulted from purulo-necrotic complications. In 16 cases (40%), the lethal outcomes occurred during phase I of acute necrotizing pancreatitis and were caused by severe systemic complications: pancreatogenic shock in 10 cases and development and progressing of early organ failure in 6 cases.

The statistical processing of the data was performed with the software package Statistica 6.1. The obtained results are presented in absolute and relative values. The conclusion on the association between certain symptoms is based on the single-factor correlation analysis of Spearman, Gamma and Kendall's tau coefficients.

The study protocol followed guidelines for experimental investigation with human subjects in accordance with the Declaration of Helsinki and was approved by the ethics committee. Written informed consent was obtained from each patient (or official representative) before the study.

## RESULTS

In 85.61% (1327) of patients, acute pancreatitis was not associated with the development of necrotic damage of the pancreas. The visualization showed that the image in the pancreas corresponded to interstitial edema. In 88.99% (1181) of cases, there was no peripancreatic infiltrate revealed in patients with the development of interstitial edematous pancreatitis. In 11.01% of cases, interstitial edematous pancreatitis was associated with the presence of retroperitoneal infiltrate. The formation of peripancreatic infiltrate in patients without the signs of necrotizing damage of the pancreas is a prognostically unfavorable sign. The evaluation of the extent of the infiltrate showed that in 10.03% of cases, up to 3 anatomical areas were involved in the pathological process. Only in 0.69% (9) of cases, the infiltrate extended to 4-6 areas and, in single cases (4), to 7 and more areas.

Fine-focal damage of the pancreas was observed in 7.48% of cases (116 patients): in 42.25% (49) of cases, the infiltrate extended to 3 areas of the retroperitoneal fat, in 27.59% (32) of cases – from 4 to 6 areas. Macrofocal necrosis was revealed in 5.74% (89) of cases and, in 40.44% of cases, it was associated with the involvement of 4 to 6 areas of fat tissue in the pathological process. Subtotal damage of the pancreas was diagnosed in 0.84% (13) of cases and, in 46.15% of cases; it was associated with peripancreatic infiltrate extending to 7 and more anatomic areas. Total damage of the pancreas was observed in 0.32% (5) of cases. The involvement of the retroperitoneum fat in the pathological process was revealed in 100% of cases (Table 1).

The evaluation of the extent of pancreas damage revealed a high direct correlation with the volume of peripancreatic infiltrate ( $rS=0.78$ ;  $p=0.001$ ).

Cardiovascular complications in patients with phase I of SAE were registered in 28.08% (89) of cases. Acute kidney failure was diagnosed in 30.81% (65) of patients. The development of the signs of acute kidney failure is a predictor of early organ failure. In 28.91% (61) of patients with SAE, intoxication consciousness disorders developed. Respiratory failure was observed in 20.85% (44) of cases. The progressing of acute respiratory failure, including in patients on APV, was registered in senior and senile patients. Hepatic failure was observed in 18.01% of patients (Table 2).

Table 1

Dependence between the extent of the disease and the formation of retroperitoneum infiltrate

Extent of pancreas damage	Total number of patients	Formation of retroperitoneum infiltrate			
		No	Up to 3 areas	4 to 6 areas	7 and more areas
Interstitial edematous pancreatitis	1327 (85.61%)	1181 (88.99%)	133 (10.03%)	9 (0.68%)	4 (0.30%)
Fine-focal pancreonecrosis (V < 30%)	116 (7.48%)	23 (19.82%)	49 (42.25%)	32 (27.59%)	12 (10.34%)
Macrofocal pancreonecrosis (V from 30 to 50%)	89 (5.74%)	3 (3.37%)	31 (34.83%)	36 (40.44%)	19 (21.35%)
Subtotal pancreonecrosis (V from 50 to 75%)	13 (0.84%)	0	3 (23.08%)	4 (30.77%)	6 (46.15%)
Total pancreonecrosis (V > 75%)	5 (0.32%)	0	0	1 (20.00%)	4 (80.00%)
Total:	1550 (100%)	1207 (77.87%)	216 (13.94%)	82 (5.29%)	45 (2.90%)

Note: V – extent of the pancreas damage

Table 2

The structure of the development of complications in patients with phase I of severe acute pancreatitis (SAP)

SAP I phase complications	Patients with complications	Total number of patients	Patients with SAP
Acute cardiovascular insufficiency	89	5.74%	42.18%
Acute kidney failure	65	4.19%	30.81%
Intoxication consciousness disorders	61	3.94%	28.91%
Gastrointestinal insufficiency	63	4.06%	29.86%
Acute respiratory failure, including in patients on artificial pulmonary ventilation	44	2.84%	20.85%
	15	0.97%	7.11%
Acute hepatic failure	38	2.45%	18.01%
Total (n)	148	1550	211

The development of early organ failure was observed in 48.82% (103) of patients with SAE and significantly aggravated the disease prognosis and the development of phase I of SAE. The complications in two organ systems were revealed in 58.11% (86) of patients, in more than 2 systems – in 11.49% (17) of cases with SAE. Early organ failure in SAE phase I caused lethal outcome in 18 cases, which was 8.53% of patients with SAE, 17.48% of cases of multiorgan failure, and 45% from the total lethality in the present study. The obtained results agree with the available published data [3; 4].

There were no cases of organ failure revealed in patients with interstitial edematous pancreatitis. Fine-focal damage of the pancreas was associated with complications in 41.38% of cases, macrofocal – in 92.13% of cases, and the extent of damage of more than 50% of the pancreas always caused the development of organ dysfunction (Table 3).

A high direct correlation ( $r_s=0.72$ ,  $p=0.001$ ) was revealed between the extent of the pancreas damage and the development of early organ failure in patients with SAE phase I.

The lack of peripancreatic infiltrate signs in patients with early organ failure was observed only in 3 cases (0.25%). When there were 3 and more areas involved in the pathological process, the share of complications was 14.35% (31). In patients with peripancreatic infiltrate, early organ failure developed in 89.02% (73) of cases. In patients with 7 and more damaged areas, early organ failure developed in 91.11% (41) of cases (Table 4). There was a direct correlation between the formation of peripancreatic infiltrate and the development of complications in patients with SAE phase I,  $r_s=0.64$  ( $p=0.001$ ).

The extent of necrotizing damage of the pancreas and the formation of peripancreatic infiltrate significantly influences the development of acute pancreatitis. There is a direct positive correlation between the development of necrotizing pancreatitis and the formation of peripancreatic infiltrate. In rare cases, the involvement of retroperitoneal fat in the pathological process was not associated with the damage of pancreatic parenchyma. There is a correlation between the volume of the pancreas and the development of early organ failure.

Table 3

Dependence between the extent of the pancreas damage and the development of early organ failure

Pancreas damage	n	Development of early organ failure
Interstitial edematous pancreatitis	1327	0
Fine-focal pancreonecrosis (V < 30%)	116	48(41.38%)
Macrofocal pancreonecrosis (V from 30 to 50%)	89	82 (92.13%)
Subtotal pancreonecrosis (V from 50 to 75%)	13	13 (100%)
Total pancreonecrosis (V > 75%)	5	5 (100%)

Table 4

Dependence between the volume of peripancreatic infiltrate and development of early organ failure

Volume of peripancreatic infiltrate	n	Early organ failure
Without a spread to fat tissue	1207	3 (0.25%)
Up to 3 areas affected	216	31 (14.35%)
4 to 6 areas affected	82	73 (89.02%)
7 and more areas affected	45	41 (91.11%)



A similar association exists between the development of early organ failure and the formation of peripancreatic infiltrate. The development of early organ failure in patients with SAE phase I is associated with the autotoxication caused by the outburst of numerous biologically active substances, proinflammatory mediators and under oxidized metabolites into the bloodstream after the tissue damage. The obtained data is valuable because patients with acute necrotizing pancreatitis often require urgent medical help in the intensive care unit, and the character of the extent of the pathological process to the pancreas and retroperitoneum fat significantly influences the development of severe systemic complications

and early organ failure, which is an acute surgical and intensive care issue [9].

### CONCLUSIONS

The risk of the development of early organ failure in patients with SAE phase I increases in cases of a greater extent of the pancreas damage and the involvement of more than 3 areas of retroperitoneum fat into the pathological process.

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### CONFLICTS OF INTEREST

The authors declare no conflict of interest

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