

УДК 616.37-002-036.11

DOI:10.24061/2413-0737/XXI.2.82.1.2017.15

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**FACTORS ASSOCIATED WITH OUTCOME OF ACUTE
NECROTIZING PANCREATITIS**

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Abstract. Prospective cohort study of 113 patients with necrotizing pancreatitis who were admitted to single intensive care department has been performed. Persistent organ failure was diagnosed in 50 (44 %) and transient – in 63 (56 %) cases. Death occurred in 31 (27,4 %) patients: 28 (56 %) with persistent and 3 (4,8 %) with transient organ failure and system complications. Respiratory failure (67 %) dominated in the mortality structure, cardio-vascular

(59 %), renal (56 %) and intestinal (54 %) failures occurred with an equal frequency. Bedside Index for Severity in Acute Pancreatitis (BISAP) score allowed making a high probability prognosis of organ failure and mortality in patients with acute necrotizing pancreatitis at admission.

Key words: acute necrotizing pancreatitis, hospital mortality, organ failure.

Introduction. An increasing incidence of acute pancreatitis has been reported recently, with an estimated 21000 new cases per year in the United States [4]. On the one hand, most of these cases are a mild form of pancreatitis, without severe gland injury and characterized with complete recovery. On the other hand, acute necrotizing pancreatitis is associated with increased morbidity and mortality. Assessment of the severity of the attack and predicting the course of the disease are important when determining the allocation of care for these patients or the need for transfer to a higher level care early in the disease process. Recent researches have established that the presence of multiorgan failure alongside with pancreatic infection are major determinants of mortality during acute necrotizing pancreatitis [8, 11]. The mortality rates in the absence of organ failure, in the presence of one organ failure, and in patients with multi-organ failure are 0 %, 3 %, and 47 %, respectively [2]. Different extents of pancreatic necrosis and its subsequent complications may contribute to the occurrence of organ failure and mortality during the admission period [9]. Therefore, the initial determination of severity in acute necrotizing pancreatitis to evaluate organ failure and the complications of pancreatic necrosis as soon as possible is critical for the appropriate management and risk assessment in a clinical setting.

Objective – to determine the incidence of multiorgan failure during acute necrotizing pancreatitis and to estimate the influence of different organ failure on the disease severity and mortality.

Material and methods. We performed a prospective observational cohort study of 113 patients with acute necrotizing pancreatitis who were admitted to single intensive care department of the emergency regional hospital, Chernivtsi, Ukraine, between March 2010 and September 2015. The study was conducted in accordance with the principles of the Declaration of Helsinki. The ethics review board of each participating hospital approved the study. The patients or their legal representatives had given their written informed consent. Patients were included in the current prospective study if they fulfilled the inclusion criteria of signs of pancreatic

necrosis on contrast-enhanced computed tomography (CECT). Necrosis was diagnosed by lack of pancreas enhancement on CECT, which was a sign of impaired or absent tissue perfusion. Patients with pancreatic necrosis and/or peripancreatic necrosis were selected. Severity of acute necrotizing pancreatitis was determined according to the recently revised Atlanta Classification [6]. Organ failure was defined for respiratory, cardiovascular, and renal system by modified Marshall scoring system. Besides above organs function of neurological system, the liver and the intestines were estimated as well. Neurological failure was established by Glasgow coma score. Hepatic function was evaluated according to Child-Pugh classification [10], grade B or C were criteria for diagnosis of liver failure. Intestinal failure was estimated by modified gastrointestinal failure score [7]. Three level of severity were defined: 1st - intolerance of enteral feeding more than 3 days, depressed intestinal peristalsis, preserved intestinal gas evacuation ability; 2nd - clinical and roentgenological signs of distended intestine with intraabdominal pressure 12-20 mm Hg, suppressed gas evacuation; 3rd - clinic of paralytic intestinal obstruction with intraabdominal hypertension over 20 mm Hg, acute gastric and duodenal erosions with hemorrhage. Intraabdominal pressure was measured via the bladder, with patients in the supine position, using the closed loop system repeated measurements technique [9]. Additionally, venous blood citrulline concentration was determined as an indicator of intestinal epitheliocytes functional activity [3].

The following parameters were collected for each episode of acute necrotizing pancreatitis: length of hospital stay, in-hospital mortality, presence of organ failure, and local complications such as acute peritoneal fluid collection, pseudocyst, acute necrotic collection and walled-off pancreatic necrosis. Acute Physiology and Chronic Health Evaluation (APACHE)-II [9], Bedside Index for Severity in Acute Pancreatitis (BISAP) [1] scores and presence of features of systemic inflammatory response syndrome (SIRS) were calculated using data from the first 24 h after admission. Continuous variables were expressed as mean with standard deviation and com-

pared using Student's t- test or Mann – Whitney test. Categorical variables were expressed as absolute numbers and proportions. Pearson's χ^2 test or Fisher's exact test was used for comparison of categorical variables. Logistic regression models were created to analyze the independent effects of APACHE II scores and the number of organ failures on mortality. To define predisposing factors, the odds ratio and its 95 % confidence interval were used as a binary parameter. Discrimination of the BISAP score for predicting the mortality was evaluated by receiver operating curve (ROC) analyze with calculation of the area under the curve (AUC). A p value of <0,05 was considered statistically significant.

Results and discussion. All patients with acute necrotizing pancreatitis were divided into two groups. According to a recent revision of Atlanta classification [6] severe form (1st group) was established in 50 (44%) patients with persistent organ failure and local complications, moderate form (2nd group) was diagnosed in 63 (56 %) people with transient organ failures or local complications. APACHE-II and Marshall scores, hematocrit and creatinine level were significantly higher in patients of the 1st group (p<0,05). There were no differences between groups according to age and frequency of

local complications. Death occurred at 31 (27,4 %) cases from 113 patients. High hospital mortality was observed only among persons with severe form of acute necrotizing pancreatitis. Persistent organ failure occurred in 50 patients from the 1st group; 28 (56 %) of them died (table 1). Transient organ dysfunction appeared in 33 patients from the 2nd group, there were 3 (4,76 %) lethal cases. Intensive therapy, which included rigorous fluids resuscitation, hemodynamic and respiratory support, was ineffective in 17 patients, who died at the early phase of acute necrotizing pancreatitis (during the first or second week of disease) due to pancreatic shock caused by multiple organ failure. During the late phase of acute necrotizing pancreatitis (after two weeks from the onset) there were 14 lethal cases as result of infection of pancreatic necrosis with development of sepsis and multiple organ failure. The number of organs with dysfunction was significantly higher in deceased patients compared to those survived ($3,48 \pm 0,81$ and $1,33 \pm 0,44$, respectively, p<0,05) as well as APACHE II score, age, hematocrit and creatinine level. Multivariate logistic regression analysis revealed that the number of organs in multiple organ failure was the main prognostic factor of death in patients with acute necrotizing pancreatitis (p<0,01), wherein each organ failure development

Table 1

Influence of organs failure on survival of patients with acute necrotizing pancreatitis

	Deceased (n=31)	Survived (n=82)	Mortality (overall=27,4%)
Persistent organ failure, n (%)	28 (90,4 %)*	22 (42 %)	28 (56 %)
Respiratory failure, n (%)	28 (90 %)*	14 (17 %)	28 (67 %)
Cardio-vascular failure, n (%)	23 (74 %)*	16 (19 %)	23 (59 %)
Neurological failure, n (%)	11 (35 %)	24 (29 %)	11 (31 %)
Renal failure, n (%)	20 (64 %)*	16 (19,5 %)	20 (56 %)
Liver failure, n (%)	6 (19 %)	10 (12 %)	6 (37 %)
Intestinal failure, n (%)	21 (67 %)*	18 (22 %)	21 (54 %)
Amount of failed organs	$3,48 \pm 0,81$ *	$1,33 \pm 0,48$	
APACHE II score	$21,4 \pm 1,2$ *	$13,6 \pm 1,6$	
Hematocrit, %	$51,8 \pm 0,9$ *	$45,3 \pm 1,2$	
Citrulline, $\mu\text{mol/l}$	$10,31 \pm 0,42$ *	$16,64 \pm 0,68$	

Note. * p<0,05 in comparison with survival patients

Table 2

Impact of BISAP Score on Mortality and Organ Failure Development

	BISAP score, n (%)		Total
	<3 points	≥ 3 points	
Amount of patients	67 (59 %)	46 (41 %)	113
Mortality	3 (4,5 %)	28 (61 %)*	31 (27,4 %)
Persistent Organ Failure	12 (17,9 %)	38 (82 %)*	50 (44 %)
Extent of Pancreatic Necrosis:			
<30%	33 (49,3 %)	13 (28,3 %)	46 (40,7 %)
30-50%	30 (44,8 %)	25 (54,3 %)	55 (48,7 %)
>50%	4 (5,9 %)	8 (17,4 %)	12 (10,6 %)

Note. * p<0,05 in comparison with patients which BISAP score is <3 points

significantly worsened the outcome too. Respiratory failure dominated in mortality structure. Isolated respiratory failure was identified in 8 cases, 2 (25 %) of them resulted in death. In patients with respiratory failure accompanied by other organ failure the mortality rate increased by 66,7-85,6 %. Cardio-vascular (59 %), renal (56 %) and intestinal (54 %) failures occurred with equal frequency. Neurological and liver failures did not influence the patients' survival. Intestinal failure of the 3rd level were diagnosed in 21 (75 %) among 28 deceased patients of the 1st group, lasted more than 5 days and was presented by signs of paralytic ileus, intraabdominal compartment syndrome, acute gastric erosions and ulcers with bleeding. There venous citrulline concentration fell to $10,31 \pm 0,42 \mu\text{mol/l}$ during 48 hours after admission and was significantly lower ($p < 0,001$) than in the survived persons. In control group citrulline venous concentration was $36,8 \pm 0,43 \mu\text{mol/l}$, in patients with moderate acute necrotizing pancreatitis it decreased up to $20,7 \pm 0,67 \mu\text{mol/l}$ and in persons with severe acute necrotizing pancreatitis – fell almost three times ($p < 0,001$). There was a significantly inverse correlation ($r = -0,643$, $p < 0,05$) between gastrointestinal dysfunction score and citrulline concentration.

Effective prognosis of organ failure development and mortality risk may improve strategy of patients with acute necrotizing pancreatitis management. The BISAP score is a new scoring system first described in 2008 [1]. The BISAP uses five points: urea nitrogen more than 25 mg/dl, impaired mental status by evidence of disorientation or disturbance in mental status, presence of SIRS, age above 60 years, and pleural effusions [9]. The number of patients with BISAP score of 0-5 was 4 (3,5 %), 19 (16,8 %), 44 (38,9 %), 14 (12,4 %), 14 (12,4 %) and 18 (15,9 %) and their mortality rates were 0 %, 0 %, 6,7 %, 35,7 %, 64,3 % and 77,8 %, respectively. There was significantly an increased risk of death with increasing BISAP score ($p < 0,0001$): AUC for mortality by BISAP score was 0,893 (95 % confidence interval 0,829 to 0,957, $p < 0,0001$), and ROC analyze demonstrated a BISAP score of 3 as the optimal sensitivity (81 %) and specificity (84 %) threshold for mortality. On evaluating outcomes according to BISAP score of 3 as the cut-off value, we found that patients with BISAP score 3 and more had a 4,6 times higher risk of developing persistent organ failure after 24 h of admission ($p < 0,001$) and more fre-

quent occurrence of extended pancreatic necrosis ($p = 0,033$, table 2).

Conclusions

Multiple organ failure is a leading cause of mortality cases both during the early and the late phases of acute necrotizing pancreatitis. Respiratory failure (67 %) dominates in mortality structure of acute pancreatitis, cardio-vascular (59 %), renal (56 %) and intestinal (54 %) failures occur with equal frequency. Serum citrulline concentration is an easy and objective marker of intestinal failure in patients with acute necrotizing pancreatitis. BISAP score over 3 points during 24 hours after admission has high reliable power for organ failure and mortality prognosis in patients with acute necrotizing pancreatitis.

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ФАКТОРЫ, ОКАЗЫВАЮЩИЕ ВЛИЯНИЕ НА РЕЗУЛЬТАТЫ ЛЕЧЕНИЯ ОСТРОГО НЕКРОТИЧЕСКОГО ПАНКРЕАТИТА

А.В. Ротарь

Резюме. Проведено проспективное когортное исследование 113 больных острым некротическим панкреатитом, которые были госпитализированы в одно отделение интенсивной терапии. Постоянная органная недостаточность выявлена в 50 (44 %) и транзиторная – в 63 (56 %) наблюдениях. Умерли 31 (27,4 %) пациент: 28 (56 %) из 50 человек с постоянной и 3 (4,76 %) больных с транзиторной органной недостаточностью и системными осложнениями. В структуре летальности преобладала дыхательная (67 %), почти с одинаковой частотой встречалась серде-

чно-сосудистая (59 %), почечная (56 %) и кишечная (54 %) недостаточность. Шкала BISAP позволяет с высокой вероятностью прогнозировать развитие органной недостаточности и летальности у больных острым некротический панкреатит при их госпитализации.

Ключевые слова: острый некротический панкреатит, госпитальная летальность, органная недостаточность.

ФАКТОРИ, ЩО ВПЛИВАЮТЬ НА РЕЗУЛЬТАТИ ЛІКУВАННЯ ГОСТРОГО НЕКРОТИЧНОГО ПАНКРЕАТИТУ

О.В. Ротар

Резюме. Проведено проспективне когортне дослідження 113 хворих на гострий некротичний панкреатит, які були госпіталізовані в одне відділення інтенсивної терапії. Постійна органна недостатність виявлена в 50 (44 %) і транзиторна – у 63 (56 %) спостереженнях. Померли 31 (27,4 %) пацієнт: 28 (56 %) із 50 осіб із постійною і 3 (4,76 %) хворих із транзиторною органною недостатністю і системними ускладненнями. У структурі летальності переважала дихальна (67 %), майже з однаковою частотою траплялася серцево-судинна (59 %), ниркова (56 %) і кишкова (54 %) недостатності. Шкала BISAP дозволяє з високою вірогідністю прогнозувати розвиток органної недостатності і летальності у хворих на гострий некротичний панкреатит при їх госпіталізації.

Ключові слова: гострий некротичний панкреатит, госпітальна летальність, органна недостатність.

Вищий державний навчальний заклад України
«Буковинський державний медичний університет», м. Чернівці

Рецензент – д.мед.н. В.В. Максим'юк

Buk. Med. Herald. – 2017. – Vol. 21, № 2 (82), part 1. – P. 67-70

Надійшла до редакції 04.04.2017 року