

## Original Research Article

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# Comparison of open pancreatic necrosectomy with step-up minimally invasive approach as surgical treatment of patients with acute necrotizing pancreatitis

Ihor V. Khomiak<sup>1</sup>, Oleksandr V. Rotar<sup>2\*</sup>, Ivan S. Tereshkevych<sup>1</sup>, Vasyl I. Rotar<sup>2</sup>,  
Andrii I. Khomiak<sup>1</sup>, Krishna Taneja<sup>2</sup>

<sup>1</sup>Department of Pancreas Surgery and Bile Ducts Reconstruction Surgery, O.O. Shalimov National Institute of Surgery and Transplantology, Kyiv, Ukraine

<sup>2</sup>Department of General Surgery, Bukovinian State Medical University, Chernivtsi, Ukraine

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**\*Correspondence:**

Dr. Oleksandr V. Rotar,

E-mail: oleksandr.rotar@gmail.com

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## ABSTRACT

**Background:** Recent experimental and clinical researches improves our understanding of natural course of acute necrotizing pancreatitis and mechanisms of its complications development. Today there are no disagreements on the issue of timing and main indications for surgery of ANP, but different surgical approaches still exist.

**Methods:** The analysis of treatment of 226 patients with acute necrotizing pancreatitis has been performed. The study group included 116 patients in whom consequently diapeutic methods, endoscopic and lumbotomic video-controlled pancreatic necrosectomy, minilaparo and lumbotomy, in case of their insufficiency- "open" interventions on pancreas were applied. In 110 persons of the control group traditional surgical tactic with application of laparotomic procedures was used.

**Results:** Sequential (step-up) implementation of mini-invasive surgery allowed to reduce the number of open wide operations by 3.4 times ( $p < 0.05$ ) and to postpone their performance: 85% of operations in the study group were performed after 4 weeks of the disease onset, in the control group only 33% ( $p < 0.05$ ). Compared with the control group the level of the first diagnosed OF after the surgery was significantly lower in patients undergoing preliminary mini-invasive surgery (12.5% versus 28.2%,  $p < 0.05$ ), the number of patients requiring prolonged intensive care after the surgery was significantly lower (17.5% versus 38.2%,  $p < 0.05$ ). 4 patients of the study group died (versus 26 in the control group  $p < 0.05$ ).

**Conclusions:** Application of step-up individualized approach in patients with acute necrotizing pancreatitis ensures a decrease in the number of laparotomic pancreatic necrosectomies and allows to postpone "open" operations for the period after the 4<sup>th</sup> week of disease onset which is accompanied by reduction of the incidence of postoperative organ failure and mortality.

**Keywords:** Acute necrotizing pancreatitis, Minimally invasive procedures, Surgical treatment

## INTRODUCTION

Acute necrotizing pancreatitis (ANP) is a surgical disease caused by primary aseptic necrosis of the pancreatic

tissues, accompanied by the development of systemic inflammatory response syndrome in both aseptic and infected necrosis.<sup>1</sup> In recent years there has been a significant increase in the number of patients with

infected forms of ANP and the development of puruloseptic complications, whose mortality reaches 17-70%.<sup>2</sup> The secondary infection of pancreatic necrosis belongs to the major risk factors for the lethal consequences of ANP, therefore, infected pancreatic necrosis is an absolute indication for the surgery.<sup>3-6</sup> The traditional approach, or "gold standard" for surgery with infected necrotizing pancreatitis is pancreatic necrsequestration followed by closed (semi-closed, open) lavage, routine relaparotomy or laparostomy, which is accompanied by frequent complications and lethality.<sup>7</sup>

In recent years, medical management of the ANP has undergone significant changes. In the treatment of local complications of ANP, as an alternative to conventional techniques, the modern surgery is based on the widespread implementation of minimally invasive technologies: the puncture and drainage under the control of ultrasound (US) or computed tomography (CT) as well as the techniques for sanitation of purulent necrotic lesions using minimal accesses.<sup>8</sup> Minimally invasive approach is used as an independent method of surgical treatment of pancreatic abscesses and infected pseudocysts or as a preparation stage for necrsequestration (step-up approach), which corresponds to the basic principles of international recommendations IAP / APA on ANP.<sup>9-11</sup> At the same time, the place and role of minimally invasive surgery in the surgical treatment of ANP complications, primarily of infected pancreatic necrosis requires further clarification.

There are many factors that make it impossible to compare the efficacy of minimally invasive surgery used by different authors: a small number of observations in the experimental groups, no clear clinical and prognostic criteria for their use, different diagnostic approaches as well as insufficient number of clinical studies, where its efficacy was compared to open necrsequestration.<sup>14</sup> So aim of current study was to compare the effectiveness of individualized step-up approach to minimally invasive surgery with the initial "open" (laparotomy) surgeries while treating ANP.

## METHODS

The results of treatment of 226 patients with ANP have been analyzed. Among the patients there were 100 women (44.2%) and 126 (55.8%) men aged 18 to 78 years (the mean age was  $48 \pm 1$  year). The core group included 116 patients with ANP treated in O.O. Shalimov national institute of surgery and transplantology, Kyiv, Ukraine, who underwent surgical treatment with the predominance of minimally invasive technologies in 2014-2016. 110 patients with ANP (control group) who were treated in the regional communal establishment (emergency hospital) of Chernivtsi in 2004-2013 underwent the conventional surgery with the use of open laparotomy. ANP was diagnosed is based on medical history, clinical presentation, laboratory findings (blood amylase and urine diastase) and instrumental methods

(ultrasound and contrast enhanced computed tomography).

The severity of ANP was assessed according to the recommendations of the group on the revision of classification of acute pancreatitis (Atlanta, 1992), an international consensus in 2012 in the presence of transient or permanent organ failure (OF) and a scale APACHE II (acute physiology and chronic health evaluation II).<sup>8</sup> To diagnose the OF, we evaluated the functions of respiratory and cardiovascular systems as well as those of kidneys by Marshall modified scale while the neurological failure was determined by the Glasgow coma scale. The infection of pancreatic foci was diagnosed on the grounds of systemic inflammatory response, according to CT findings, those of the bacteriological research and positive procalcitonin test. 70 patients in group I were tested for presepsin in their blood to diagnose the infection and monitor the effectiveness of antibiotic therapy.<sup>14</sup> All the patients underwent individually tailored conservative therapy that considered the severity and features of pancreatitis flow including: pain relief, correction of disorders in the water-salt metabolism and in hemodynamics, the respiratory support, early enteral nutrition, inhibition of secretory activity of the pancreas, adequate protein and energy supply, prevention of stress ulcers and detoxification. On admission of the patients with severe course of ANP and suspected infectious complications they were empirically prescribed broad-spectrum antibiotics that penetrate well into the devitalized pancreatic tissues (mainly carbapenems).

According to the main demographic indices (age, gender, body mass index, etiology), to the severity of pancreatitis factors (organ failure, scores on APACHE II scale, creatinine and C-reactive protein rates) and morphological characteristics according to CT findings (prevalence of pancreatic necrosis, local complications) the patient groups were representative. To compare the efficacy of surgical treatment of the ANP we used: first detected postoperative organ failure, duration of the intensive care after the surgery as well as the postoperative infectious complications and postoperative mortality.

## RESULTS

In the control group 110 patients underwent open laparotomic (lumbotomic) necrsequectomies and drainage of pathological foci. The indications for surgery were: progression of peritonitis (11), the progression of biliary necrotizing pancreatitis in the presence of destructive calculous cholecystitis, jaundice, choledocholithiasis (19), deterioration of the patient's condition despite the intensive therapy (9), increased infiltration of the pancreas or peripancreatic fiber (PPF) in case of the failure of conservative treatment (15), infection of aseptic necrosis foci (20), bleeding foci of necrosis (3). On admission OF was diagnosed in 50

(39.7%) patients, it was transient in 19 (15.2%) individuals and permanent - in 39 (32.5%, Table 1). The severity of patients' condition according to the APACHE II scale averaged  $12.13 \pm 0.47$  points. For instance, the number of patients with OF after the surgery increased almost two-fold ( $p < 0.05$ ), 31 (28.2%) patients after surgery were first diagnosed with OF lasting more than 48 hours, 42 (38.1%) patients underwent prolonged postoperative intensive care. Postoperative complications developed in 7 (4.5%) patients: 3 patients had erosive bleeding and 4 individuals had pancreatic and colonic

fistulae. Relaparotomies, including the programmed ones were conducted in 13 (11.8%) patients. After the surgery, 22 patients died: 17 (21.8%) out of 78 patients who were operated in the initial stages, 5 (15.6%) out of 32 individuals who were operated in the later stages of the disease. The univariate regression analysis revealed the dependence of patients' mortality on OF both before operations ( $\chi^2 = 35.75$ ,  $p < 0.001$ ), and after the surgery ( $\chi^2 = 26.3$ ,  $p < 0.001$ ), on pancreonecrosis prevalence ( $\chi^2 = 9.94$ ,  $p < 0.001$ ) and infection in the pathological foci after surgery ( $\chi^2 = 4.101$ ,  $p < 0.043$ ).

**Table 1: Patients characteristics.**

	Study group (n=116)	Control group (n=110)
<b>Severity at admission</b>		
moderate	70 (60.3)	85 (77.3)
severe	46 (39.7)	25 (22.7)
APACHEII, points	11.3±0.33	12.1±0.47
<b>Spread of pancreatic necrosis, n (%)</b>		
less than 30%	33 (28.4)	48 (43.6)
30-50%	59 (50.9)	50 (45.5)
more than 50%	24 (20.7)	12 (10.9)
<b>Local complications</b>		
acute necrotic collections	49 (42.2)*	73 (66.4)
walled-off necrosis	67 (57.8)*	37 (34.6)
Pancreatic infection complications	84 (73)	79 (71.8)
<b>Duration of treatment before surgery</b>		
less than 4 weeks, n (%)	6 (15)*	78 (70.3)
more than 4 weeks, n (%)	34 (85)*	32 (29.7)
<b>Organ failures during postoperative period</b>		
transient, n (%)	6 (6)*	25 (22.7)
persistent, n (%)	26 (24.3)*	56 (44.5)
First-time diagnosed organ failure during postoperative period, n (%)	5 (12.5)*	31 (28.2)
<b>Mortality, n (%)</b>		
	4 (3.4)*	26 (20.6)

\* –  $p < 0.05$  in comparison with control group.

In the study group 62 (63.9%) patients were treated by percutaneous US-controlled intervention, 35 (33.7%)-through the wall of the stomach or duodenum under endoscopic US (EUS) control, in 21 patients combined transcutaneous and endoscopic access was applied. In 62 out of 97 patients (63.9%) the US-guided interventions allowed to interrupt the chain of pancreatitis phase course and patients recovered without the open surgery. In 35 cases, the such procedures together with the conservative therapy allowed to stabilize the patients' condition and became a stage in preparing for the further surgical treatment. Among them video-assisted retroperitoneal debridements through the nephroscope were applied in 12 patients and endoscopically trans gastric debridements- in 5 patients.

Due to ineffectiveness of the transcutaneous interventions or impossibility of their use, we performed the next stage

of the treatment -low-traumatic operations: mini-laparotomy in 6, and mini-lumbotomy in 4 patients. Open laparotomies with pancreatic necrosectomy were performed in 31 (28.2%) patients: in 20 persons after preliminary mini-invasive procedures and in 11 people as a first step of the surgical treatment.

Mini-invasive interventions were not used in 6 patients who were operated in the initial stages of the disease in other hospitals in the presence of diffuse peritonitis (4) and destructive cholecystitis (2). In 5 cases mini-invasive interventions were not performed due to anatomical features of localization of pathological foci (interposition of the intestine or blood vessels on the way of possible puncture) and the presence of sepsis. First diagnosed OF during postoperative period developed in 5 (12.5%) patients of study group, there were 4 lethal cases (mortality rate -3.44%).

## DISCUSSION

In both groups, surgical treatment of ANP was chosen differentially, individually, according to the phases and features of the disease course. In control patients most of operations (70.3%, Table 1) observed were performed in the initial stages, up to 4 weeks from the onset of the disease that directly affected the outcomes. In the study group the surgical treatment was performed sequentially, starting with the least invasive methods according to recent guidelines recommendations.<sup>10,11,15,16</sup> First-line methods were US-guided procedures, which included transcutaneous and endoscopically performed punctures and drains.<sup>17,18</sup> While performing the treatment puncture, we removed the content of the pathological foci at most, repeatedly washed the cavities with antiseptic solutions, including ozonized isotonic and povidone-iodine solutions. If the pathological focus contained a lot of detritus, it was drained using the Seldinger technique by installing large diameter silicone drains. While performing the external drainage of the lesser sac, we introduced two drain tubes under control of US, which enabled to create a flushing-aspiration system. As the drain installed under control of US was not efficient enough, 9 patients with infected foci of pancreonecrosis underwent the dilatation of the existing canals by means of probes as well as necrsequestration under a visual control through a nephroscope. If it was impossible to perform the ultrasound-controlled interventions, 3 patients underwent the selective trans lumbar video-controlled retroperitoneal sanitation of the pathological focus using a nephroscope as the first stage of surgical treatment. 5 patients with infected separated pancreatic necrosis underwent pancreatic necrsequestration performed through the stomach wall using an echo video endoscope through an installed metal stent.

Selective mini-laparomy or mini-lumbotomy was indicated by separated localized infected fluid aggregations, foci of infected pancreatic necrosis, infected necrotic caries of the pancreas and parapancreatic cellular tissue, abscesses of the pancreas and retroperitoneal space. Mini-laparotomy was performed in the left and right subcostal areas using the transrectal and adrectal accesses along the median line in the epigastric region. Mini-lumbotomy was mainly performed along the front and middle axillary lines.

Sequential (step-up) implementation of mini-invasive surgery allowed to reduce the number of open wide operations by 3.4 times ( $p < 0.05$ ) and to postpone their performance: 85% of operations in the study group were performed after 4 weeks of the disease onset, in the control group only 33% ( $p < 0.05$ ).

Compared with the control group the level of the first diagnosed OF after the surgery was significantly lower in patients undergoing preliminary mini-invasive surgery (12.5% versus 28.2%,  $p < 0.05$ ), the number of patients requiring prolonged intensive care after the surgery was

significantly lower (17.5% versus 38.2%,  $p < 0.05$ ). 4 patients of the study group died (versus 26 in the control group  $p < 0.05$ ), including 3 patients after the operations that were previously carried out in other hospitals in the early stages of the disease. In the study and control groups there was a tendency to increased mortality of patients undergoing surgery in the initial stages of infection ( $p = 0.114$ ), age of patients ( $p = 0.096$ ) and BMI ( $p = 0.107$ ).

## CONCLUSION

Study concluded that application of step-up individualized approach in patients with acute necrotizing pancreatitis ensures a decrease in the number of laparotomic pancreatic necrosectomies and allows to postpone "open" operations for the period after the 4<sup>th</sup> week of disease onset which is accompanied by reduction of the incidence of postoperative organ failure and mortality.

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