

Analysis of the Results of Complex Treatment of Patients with Pancronecrosis Complicated with Sepsis

Tokhir Musoev

Bukhara Branch of the Republican Scientific Center for Emergency Medical Care, Bukhara State Medical University, Uzbekistan

Abstract A retrospective cohort study of the results of a comprehensive examination and treatment of 97 patients with pancreatic necrosis was carried out. Analysis of the results of traditional methods of treatment of pancreatic necrosis complicated by sepsis showed a high level of complications of the disease of 38.1% and mortality of 30.9% due to the lack of objective criteria for predicting the development of pancreatogenic sepsis and multiple organ dysfunction syndrome, which requires detailed studies of the pathogenetic mechanisms of this formidable disease.

Keywords Pancreatic necrosis, Systemic inflammatory response syndrome, Sepsis as a complication of pancreatic necrosis, Conservative treatment, Surgical treatment, Immediate and long-term results

1. Introduction

There are many factors that determine the choice of treatment for pancreatic necrosis, among them the most significant are the speed and area of development of the necrobiotic process, both in the pancreas itself and around it [1,2,6,9]. Meanwhile, one of the current priority approaches in choosing tactics for treating pancreatic necrosis is taking into account the phases of the inflammatory process. Based on this approach, the following principles for choosing treatment tactics have taken root in modern pancreatology: use purely conservative therapy as a priority; conservative therapy with active wait-and-see tactics and use surgical treatment according to strict indications (uncertainty in diagnosis, the presence of progressive peritonitis and/or shock, progressive jaundice); actively use the surgical method of treatment, considering conservative therapy only a period of preoperative preparation [3,10,29,30]. An analysis of the literature over the past 10 years has shown that there are more and more supporters of conservative treatment of pancreatic necrosis with active expectant management. To increase the effectiveness of diagnostic and treatment tactics, proponents of this approach offer complexes of algorithms based on: combating pain and problems with bile outflow; suppression of secretory activity of both the pancreas itself and the stomach; complex anti-enzyme, anti-inflammatory and detoxification therapy; prevention of infection of the pancreas and correction of vascular changes in this organ [1,3,6,7,9,10,13,14].

The basis of the leitmotif of using a surgical method for treating pancreatic necrosis is to prevent the death of the patient. Proponents of active wait-and-see tactics, using the entire available arsenal of conservative therapy, begin to use surgical techniques in patients with pancreatic necrosis with only one goal - to prevent further rapid progression of pancreatic necrosis. In this regard, many issues related to the indications and timing of surgical interventions in patients with pancreatic necrosis remain far from resolved and sometimes even controversial [4,6,9]. The absolute indication for surgical treatment of pancreatic necrosis is its purulent-necrotic complication. On this issue, most surgeons are of the same opinion. However, in the matter of surgical treatment of sterile pancreatic necrosis, many aspects related to the timing and volume of surgical intervention still remain scattered. And this is one of the main issues that are discussed at specialized conferences and congresses on pancreatology. Is surgical intervention necessary for a sterile form of pancreatic necrosis?

Complications of the disease such as infection, abscess formation, and biliary pancreatic necrosis that is not amenable to endoscopic intervention are considered generally accepted direct indications for the use of surgical treatment methods. However, the options for complications of pancreatic necrosis in the form of a progressive deterioration of the patient's condition, the development of multiple organ failure, progressive necrosis of the pancreas, as well as with its total damage with focal infection remain controversial [11]. Other authors prioritize general changes in the body and believe that direct indications for surgical treatment should be the presence of purulent peritonitis, progressive multiple organ failure syndrome, ineffectiveness of conservative therapy, and even the possible development of sepsis syndrome [12]. But there is also a group of third

* Corresponding author:

mtokhir-1979@mail.ru (Tokhir Musoev)

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opinions, when indications for surgical treatment methods should be individual cases that go beyond the general rules of limitation. As an example, we can cite the opinion of researchers regarding the indications for surgery in the development of a clinical picture of peritonitis, even with only infiltrative changes in the pancreas [9].

Such versatility of modern information prompted us to conduct a study to evaluate the immediate and long-term results of complex traditional treatment of patients with pancreatic necrosis complicated by sepsis.

2. Material and Methods

A retrospective cohort study of the results of a comprehensive examination and treatment of 97 patients with pancreatic necrosis was conducted. All patients were treated and examined at the Bukhara regional branch of the Republican Scientific and Practical Medical Center for Emergency Medical Care from 2013 to 2017. In 38 (39.18%) cases, pancreatic necrosis was pregnant, and in the remaining 59 (60.82%) cases, it was infected. Moreover, among patients with infected pancreatic necrosis, in 20.62% of cases, infected pancreatic necrosis occurred against the background of severe sepsis, and in 4.12% of cases - septic shock. Thus, the patients were divided into 3 subgroups: Subgroup I – patients with sterile pancreatic necrosis (38 patients; 39.18%), Subgroup II – patients with infected pancreatic necrosis (35 patients; 36.08%), Subgroup III – patients with infected pancreatic necrosis, complicated by sepsis (24 patients; 24.74%). There were 62.9% male patients and 37.1% female patients. The base contingent consisted of patients of the most working age. Alcohol etiology of the disease accounted for 28.9% of patients. In 43 (44.3%) patients, the cause of pancreatic necrosis was cholelithiasis. The gastrogenic origin of the disease was identified in 25 (25.8%) patients. In 1 patient (1.03%), the etiological cause of pancreatic necrosis could not be determined. Patient visits to the clinic from the onset of the disease were not unambiguous, but there was a certain pattern among subgroups. In the group of patients, active surgical tactics were predominantly used, consisting of early laparotomies, despite the phase (sterile or infected) of the pathological process and the form (fine-focal, large-focal, subtotal, total) of the necrotic lesion. The main indications for surgical operations were negative dynamics of the disease despite conservative therapy and/or the presence of signs of peritonitis.

If laparotomy was performed during the sterile phase of pancreatic necrosis, at the first stage an inspection of the abdominal organs was performed. If the development of pancreatic necrosis was suspected, the omental bursa was opened and a visual inspection was performed. The operation was completed with sanitation and drainage of the omental bursa and abdominal cavity with several drains. In the case of the presence of dead areas of the pancreas, necrotic tissue was removed using blunt and sharp means. This procedure was sometimes very dangerous due to the

possible development of erosive bleeding or the formation of digestive fistulas. In case of biliary origin of pancreatic necrosis, interventions were performed on the gallbladder and bile ducts. In case of infected pancreatic necrosis, the main purpose of laparotomy was the timely and complete implementation of necrosectomy, drainage of purulent cavities of parapancreatic tissue for subsequent sanitation. The omental bursa and all possible cavities formed, which are filled with pus, were opened. Necrotic tissue of the pancreas and retroperitoneal space was removed using blunt and sharp methods. The latter was necessarily subjected to a thorough digital revision. Drainage was performed in the retroperitoneal space, omental bursa, and abdominal cavity.

To assess the condition of a patient with acute infected pancreatic necrosis complicated by sepsis, a gradation scale was used, consisting of the following criteria: dynamics and frequency of development of multiple organ dysfunction syndrome; frequency and severity of purulent complications in the general structure of treatment measures. The immediate results of treatment of patients with pancreatic necrosis were assessed according to four standard groups of results: excellent, good, satisfactory and unsatisfactory. An excellent result was characterized by the preservation of the anatomical integrity and functional usefulness of the pancreas in the absence of any inflammatory phenomena. A good result was characterized by a violation of the anatomical integrity of the pancreas in the presence of compensated functional activity, which did not require drug correction. There are no inflammatory phenomena. A satisfactory result was characterized by a violation of the anatomical integrity of the pancreas, the presence of local complications that do not require special surgical interventions and tend to heal independently or scar in the short term. The functional activity of the pancreas is preserved or compensated by medication. Temporary local inflammatory phenomena associated with the course of the above complications are possible. The unsatisfactory result was characterized by a violation of the anatomical integrity of the pancreas. The presence of local complications requiring repeated surgical interventions, the presence of erosive bleeding requiring special intervention. The functional activity of the pancreas is impaired with no prospect of recovery. Long-term drug compensatory (replacement) therapy is required. Inflammatory phenomena associated with ongoing necrosis of the pancreatic parenchyma persist, but with a tendency to be limited. The death of the patient as a criterion for the outcome of treatment could be classified as unsatisfactory, however, given the high frequency of this outcome in the treatment of patients with pancreatic necrosis, we highlighted this point separately.

To study the long-term results of treatment and the quality of life of patients who suffered pancreatic necrosis, the following methods were used: questionnaires using the GIQLI questionnaire, clinical examination, ultrasound and computed tomography of the abdominal organs, magnetic resonance imaging.

3. Research Results and Discussion

According to archival material, acute pancreatitis was diagnosed only in 68 (71.1%) patients. In the remaining cases (28.9%), before hospitalization in our clinic, diagnoses of acute cholecystitis (15.5%), perforation of a gastroduodenal ulcer (7.2%), acute intestinal obstruction (4.1%) and acute appendicitis (3) were established., 1%). In the medical history at the time of hospitalization of the patients, 687 pathological signs were described. Of these, 26.6% were in patients of subgroup I, 39.7% in patients in subgroup II and 33.6% in patients in subgroup III. The distribution of these pathological signs showed that pain was predominant (it was noted in all 100% of cases). The pain was localized in the epigastrium, right or left hypochondrium; in most cases, the pain radiated to the left costovertebral angle, and then, in descending order, to the left shoulder, behind the sternum, between the shoulder blades. Pain was the flagship among the pathological manifestations of the disease in all analyzed subgroups. Dyspeptic disorders are a constant companion of destructive pancreatitis. They were in second place in terms of frequency of registration after pain syndrome and accounted for 93.8%. Among the types of dyspeptic disorders, nausea, indomitable vomiting that did not bring relief, constipation, flatulence and bloating prevailed. Moreover, in subgroups II and III, this symptom complex was noted in all patients, while in patients of subgroup I they bothered patients only in 84.2% of cases.

Local symptoms of acute pancreatitis were positive in 90.7% of cases. Local symptoms characteristic of acute pancreatitis occurred in all patients. Tension of the muscles of the anterior abdominal wall and symptoms of peritoneal irritation were noted in 100% of cases in patients of subgroups II and III, whereas among patients of subgroup I they occurred only in 29 (76.3%) patients. Almost half of the patients with destructive pancreatitis (43.3%) had icterus of the sclera and skin upon admission. Among patients of subgroup I there were 34.2% of them, among patients of subgroup II - in 40.0% of cases and among patients of subgroup III - in 62.5% of cases. Pathological signs of the cardiovascular system were in the form of tachycardia, recorded in 90.7% of cases, and a decrease in systolic blood pressure below 100 mm Hg. Art. in 68.0% of patients. Tachycardia was recorded in 100% of cases among patients of subgroups II and III, while in patients of subgroup I, increased heart rate was recorded only in 76.3% of cases. It should be noted that tachycardia and a decrease in systolic blood pressure were noted by us in the early stages of the development of destructive pancreatitis. An increase in body temperature above 37 °C was recorded in 75 (77.3%) cases. Moreover, among patients of subgroups II and III, as in the previous case, hyperthermia was noted in all cases, whereas in patients of subgroup I only in 16 (42.1%) cases. We noted disorders of the respiratory system in 70 (72.2%) patients. In subgroup I, patients with shortness of breath were 36.8%, in subgroup II – 91.4%, in subgroup III – in 100% of cases. The identified pathological manifestations of the genitourinary

system were presented in the form of hematuria, proteinuria, cylindruria or a combination thereof. In total, there were 37 (38.1%) patients with such disorders. There was only one patient in subgroup I, 12 (34.3%) patients in subgroup II, and all 24 patients in subgroup III. Mental and nervous system disorders upon admission were identified in 33 (34.0%) patients. They manifested themselves in 22 (22.7%) patients in the form of euphoria, anxiety and negativism. Psychomotor agitation and hallucinations were diagnosed in 9 (9.3%) patients. Severe mental depression, sometimes even to the point of coma, was diagnosed in 2 (2.1%) patients.

Diagnostic laparoscopy was performed in 48 (49.5%) patients. On the 1st day of hospitalization it was used in 19 patients, on the 2nd day – in 10 patients, on the 3rd day – in 8 patients, on the 4th day – in 7 patients and on the 5th day – in 4 patients. The average duration of this intervention was 3.1 ± 1.1 days. Clinical and morphological parallels revealed a predominance of patients with total (32.0%) and subtotal (26.8%) necrotic lesions of the pancreas. With subtotal damage, the head and body of the pancreas were predominantly affected. In 40 (41.2%) patients, necrotic lesions of the pancreas were focal. Moreover, in 21.6% of cases there is a large-focal lesion, and in 19.6% of cases there is a small-focal lesion. A comparative analysis between sterile and infected forms of pancreatic necrosis revealed that in the first case, focal (13.9 times) prevailed, and in the second case, widespread (46.6 times) necrotic lesions of the pancreas prevailed. The average severity of damage by acute pancreatic necrosis was 8.4 ± 1.1 points.

The dispersion of the average value decreased from 10.1 ± 0.9 points for total pancreatic necrosis to 6.8 ± 2.9 points for small-focal pancreatic necrosis ($p < 0.05$). In the infected form of pancreatic necrosis, the lesion severity index was 1.9 ± 0.3 points higher than in patients with a sterile form of pancreatic necrosis ($p < 0.05$).

As can be seen from the description of the course of surgical interventions, there were several types per patient. In total, according to the operation protocols, 451 surgical interventions were performed. At the same time, an average of 4.6 ± 1.1 technical stages were performed for each patient. The leaders in these stages were drainage interventions (215), which amounted to 47.6%. At the same time, in 23.9% of cases, the omental bursa was drained and in 23.7% of cases, the abdominal cavity was drained. It should be noted that drainage of the abdominal cavity was performed without drainage of the omental bursa. But drainage of the omental bursa was carried out repeatedly, which causes the difference in values. Necrosectomy was performed in 13.7% of cases (62 times). Omentobursostomy and marsupialization of the omental bursa was performed in 13.5% of cases (61 times). Parapancreatic cage drainage was performed 48 times (10.6%). Interventions for cholelithiasis were limited to cholecystostomy (1.3%) and cholecystectomy with drainage of the bile ducts (8.2%). In 22 (4.9%) cases, the suppurating pancreatic cyst was opened and drained. The volume and nature of surgical interventions performed in the context of the pancreatic necrosis phase showed a 4.4-fold

prevalence in patients with infected pancreatic necrosis. In the phase of sterile pancreatic necrosis, there was an average of 2.2 ± 1.0 types of surgical intervention per patient, and in the infection phase this value was 2.8 times higher.

An analysis of the distribution of surgical interventions performed in the sterile phase of pancreatic necrosis depending on the morphostructural nature of the pancreatic lesion showed that drainage surgical interventions prevailed in small-focal and large-focal pancreatic necrosis. In case of subtotal damage to the pancreas, the volume of surgical interventions was distributed evenly between drainage of the abdominal cavity, drainage of the omental bursa, cholecystostomy, cholecystectomy with drainage of the ducts, and omentobursostomy with marsupialization of the omental bursa. In patients with small focal necrosis of the pancreas in the sterile phase of pancreatic necrosis, an average of 1.8 ± 0.3 types of surgical interventions were performed. For large-focal lesions this value was 2.2 ± 1.2 , and for subtotal lesions of the pancreas - 5.0 ± 1.1 stages of surgical intervention. Cholecystectomy with drainage of the bile ducts prevailed among patients with small focal pancreatic necrosis in the sterile phase of the disease. This nature of the surgical intervention is due to those cases where the operation was performed for acute calculous cholecystitis, but intraoperative findings revealed small-focal pancreatic necrosis. In such cases, after cholecystectomy, it was mandatory to drain the bile ducts and drain the omental bursa, followed by targeted conservative therapy for pancreatitis. In the infected phase of pancreatic necrosis in patients with large-focal lesions of the pancreas, there were an average of 5.8 ± 1.5 surgical stages of the operation per 1 patient, with subtotal lesions - 5.9 ± 1.0 , and with total lesions - $6.6 \pm 2, 1$. The variety of surgical techniques performed in the infected phase of pancreatic necrosis was more diverse than in the sterile phase. Most patients (up to 82.3%) were operated on within the first week, while 45.9% of patients were operated on within the first 2 days from the onset of the disease; in this group of patients, the tactics of early operations for pancreatic necrosis were predominant. The cohort retrospective study was based on data defining the final verification diagnosis. In a number of patients, during relaparotomy, performed 2-3 weeks after the first operation, there were pathomorphological manifestations of an already infected form of pancreatic necrosis. These patients had formed necrotic sequestra and abscesses of the omental bursa. Therefore, during the analysis, we took as a basis the final version of the diagnosis verification. In total, 58 patients underwent relaparotomy. Moreover, in 8 they were performed twice, and in 4 – three times. In one patient, relaparotomy was performed 4 times.

In most cases, pancreatic necrosis occurred with various complications, which were often combined and thus could manifest in several ways in the same patient. It is they who determine the urgency of surgical intervention and tactics for pancreatic necrosis. Peritonitis was detected in 49 (55.5%) patients. Local peritonitis was diagnosed in 16.3% of patients, diffuse - in 22.4% and diffuse - in 61.2% of patients. The serous nature of the effusion was noted in 18.4% of

patients, hemorrhagic - in 32.6%, purulent - in 14.3% and fibrinous-purulent - in 34.7% of patients.

Of course, it should be taken into account that peritonitis in patients was an indication for surgical intervention. However, given the fact that if the exudate was serous or hemorrhagic, minimally invasive interventions would have been very effective, nevertheless, during that period of medical care, the more complex and traumatic laparotomy remained the main surgical technique. And laparoscopy was performed only for diagnostic purposes and verification of the final diagnosis of the disease. Moreover, exactly half of the deceased patients had peritonitis. And here it should be noted that peritonitis was one of the frequent complications of pancreatic necrosis. Phlegmon of the retroperitoneal space was in 2nd place (34.0%) after peritonitis. This type of complication of pancreatic necrosis was detected at various times from the onset of the disease, on average 7.2 ± 3.8 days. Damage to the right half of the retroperitoneal space was noted by us in 24.2% of patients, the left half - in 63.6% of patients, and total - in 12.1% of patients. Moreover, in 28.9% of patients, lesions of the retroperitoneal space were determined only by infiltration without signs of suppuration at the time of intraoperative verification. However, during repeated surgery, pancreatic abscesses were diagnosed in 11.3% of patients. The nature of complications characterizing the generalization of the purulent-inflammatory process in patients with different phases of pancreatic necrosis was unusual (Table 1).

Table 1. The nature of the frequency of registration of generalization of the inflammatory process

PROCESS TYPE	Pancreonecrosis				TOTAL	
	Sterile		Infected			
	N	%	n	%	n	%
Systemic inflammatory response syndrome	15	100	0	0	15	20,3
Sepsis syndrome	0	0	35	59,3	35	47,3
Severe sepsis	0	0	20	33,9	20	27,0
Septic shock	0	0	4	6,8	4	5,4
TOTAL	15	20,3	59	79,7	74	76,3

Pancreatogenic sepsis in patients with the sterile phase of pancreatic necrosis (subgroup I) was diagnosed in 39.5% of cases. Whereas among patients with the infected phase of pancreatic necrosis, it was diagnosed in 100% of cases. I would like to remind you that the III subgroup of patients was formed by patients with severe sepsis and septic shock. Accordingly, patients of subgroup II, who also had a generalized form of complication of a purulent-destructive process, were represented by the presence of sepsis syndrome or only the syndrome of a systemic inflammatory response of the body.

Pancreatogenic sepsis was diagnosed in 74 (76.3%) patients on the day of hospitalization. Of these, almost half of the patients (47.3%) were diagnosed with sepsis syndrome, represented by patients with the infected phase of pancreatic necrosis. Patients who formed the III research subgroup

(with the presence of severe sepsis and septic shock) amounting to 32.4% had an exclusively infected form of pancreatic necrosis. Moreover, if there were 27.0% of patients with severe sepsis, then there were 5.4% of patients with septic shock. Despite the ranking of patients with systemic inflammatory response syndrome by the presence of organ dysfunction or septic shock, nevertheless, there were quite an impressive number of patients with sepsis syndrome on the day of hospitalization (59.3%). Systemic inflammatory response syndrome was diagnosed in the absence of a purulent focus and organ dysfunction in 20.3% of patients, and all of them were patients with the sterile phase of pancreatic necrosis (Table 2). The distribution of patients depending on the number of signs of systemic inflammatory response syndrome showed that the most were 4 clinical and laboratory signs (27.8%). There were only one less number of patients with 3 clinical and laboratory signs. There were 21.6% of patients with 2 clinical and laboratory signs, and 23.7% of patients with 1 clinical and laboratory sign. It is the latter category of the nature of the manifestation of systemic inflammatory response syndrome that was represented in more than half by patients with the sterile phase of pancreatic necrosis (60.5%).

Table 2. Distribution of patients according to the number of signs of systemic inflammatory response syndrome

NUMBER OF SIGNS OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	PANCREONECROSIS				TOTAL	
	Sterile		Infected			
	N	%	n	%	n	%
SIRS ₀₋₁	23	60,5	0	0	15	23,7
SIRS ₂	7	18,4	14	23,7	35	21,6
SIRS ₃	5	13,2	21	35,6	20	26,8
SIRS ₄	3	7,9	24	40,7	4	27,8
TOTAL	38	39,2	59	60,8	97	51,1

It should be noted that the nature of the change in the curve of the numerical value of patients with systemic inflammatory response syndrome among patients with the sterile phase of pancreatic necrosis had an inverse correlation with the number of patients ($R = -0.847$). In other words, as the number of clinical and laboratory signs of systemic inflammatory response syndrome increased, there was a progressive decrease in the number of patients with pancreatic necrosis in the sterile phase. At the same time, among patients with the infected phase of pancreatic necrosis, the correlation significance between the number of clinical and laboratory signs of systemic inflammatory response syndrome and the number of patients had a close direct correlation ($R = 0.954$).

Thus, an analysis of the registration of the presence or absence of pancreatogenic sepsis at the time of hospitalization of patients revealed that pancreatic necrosis in the infected phase is characterized by the predominance of sepsis without dysfunction of vital organs (more than half of the patients). Moreover, among patients with the sterile phase of pancreatic necrosis, this type of inflammatory

complication manifested itself in only 1/3 of patients without dysfunction of vital organs. However, in the dynamics of the treatment, the picture regarding the manifestation of the development of generalization of the inflammatory process has changed radically. As can be seen from the diagram, the curve of changes in the frequency of registration of pancreatogenic sepsis over the course of 2 weeks of treatment only increased.

According to the medical history records, the presence of pancreatogenic sepsis was recorded 405 times. On average, there were 5.5 times per patient. Such a high registration rate for sepsis was probably due to the amount imposed on the deceased patients. However, when subtracting deaths among patients with pancreatogenic sepsis, this indicator decreased by only 0.4 times. The ratio between patients with the sterile phase of pancreatic necrosis and those with the infected phase was 2.1 times in favor of the latter.

Mortality among patients with acute pancreatic necrosis was 30.9% (30 cases) and in the dynamics of treatment was distributed as follows.

On the day of admission, 1 (3.3%) patient died, and by the end of the first day another 1 (3.3%) patient died. Subsequently, 2 (6.7%) patients died on days 2-3 of treatment, 7 (23.3%) patients died on days 3-7, 10 (33.3%) patients died on days 7-14, and in the long term (over 14 days and up to 3 months) another 9 (29.9%) patients died. Overall, 83.3% of patients died in the subgroup with acute infected pancreatic necrosis, and the remaining 16.7% died with acute sterile pancreatic necrosis.

Thus, the first 14 days turned out to be the most dangerous, during which 21 (70.1%) patients out of 30 died. When comparing the total amount of complications for various systems in the dead, it was found that, on average, for each death in days 1-7 there were 5.6-6.5 complications each, and on days 7-14 4.9-6.6 complications associated with organ dysfunction. Of these, 4.5 – 5.8 complications on days 1-7 of patients' admission were associated with disturbances in the functioning of vital organs. A combination of severe disorders of vital organs occurred in almost all patients who died in the first 3 days of observation - 3.6-3.8 such disorders per 1 patient, and subsequently this figure decreased slightly. The decrease in the frequency of septic shock in the first 3 days fully corresponds to the number of dead patients, which is associated with the initial severity of the admitted patients. Starting from the 3rd day, there was a persistence of cases of septic shock due to the deterioration of the patients' condition, inadequate treatment with the development of complications (primarily purulent-septic). The most common causes of death in pancreatic necrosis were generalization of infection (70.9%), peritonitis (59.6%), cardiovascular disorders (58.3%) and hepatorenal disorders (45.4%) and other complications. Arrosive bleeding was less common (6.7%). Such a high specific percentage of multiple organ "interest" prompted us to retrospectively study pathomorphological changes in patients with a comparative analysis of lethal outcomes. In 30 (30.9%) of the deceased, the data of pathomorphological examination of organs were studied. It

was found that fatty and granular degeneration of liver cells was observed in 29 (96.7%) cases, liver cirrhosis - 9 (30.0%), amyloidosis - in 4 (13.3%). Changes in the kidneys in 23 (76.7%) of the deceased were characterized by granular dystrophy of the convoluted tubule epithelium and in 2 (6.7%) - amyloidosis. Pathological changes in the heart muscle were found in 25 (83.3%) patients (no changes were found in 16.7%). These changes were characterized by granular dystrophy, combined in three patients with fragmentation of muscle fibers. Of the internal organs, the liver underwent the most profound changes, which, as is known, is exposed to purulent intoxication to a greater extent than other organs. The identified changes were characterized by granular degeneration of internal organs, combined in one patient with damage to several organs at once and the development of multiple organ failure.

Thus, the high mortality rate among patients who have had repeated relaparotomies indicates that it is necessary to delay their performance in case of infected pancreatic necrosis. They are acceptable when performed in conditions of delimitation of processes. The limited necrosis of the pancreas is lysed and sequestered. In such cases, the sanitizing and draining goals of surgical intervention are easily achievable. This is what allows surgical intervention to be performed in a more favorable background, since it will be less traumatic. The results of treatment of patients were assessed using our improved gradation scale: excellent, good, satisfactory and unsatisfactory (Table 3).

Table 3. Immediate results of treatment of patients with pancreatic necrosis

RESULTS	OF PANCRONECROSIS PHASE				TOTAL	
	Sterile		Infected			
	n	%	n	%	n	%
Excellent	3	7,9	0	0	3	3,1
Good	10	26,3	5	8,5	15	15,5
Satisfactory	6	15,8	6	10,2	12	12,4
Unsatisfactory	14	36,8	23	39,0	37	38,1
Mortality	5	13,2	25	42,4	30	30,9
TOTAL	38	39,2	59	60,8	97	51,1

Of the 97 patients, 3 (3.1%) achieved complete preservation of the anatomical integrity and functional activity of the pancreas based on the results of treatment. Good treatment results, in the form of a violation of the anatomical integrity of the pancreas, but in the presence of compensated functional activity, which did not require drug correction, were found in 15 (15.5%) patients. All of them were without any inflammatory phenomena. Among such patients, there were often cases with incorrect diagnosis. Among patients with a sterile form of pancreatic necrosis, this indicator was 3.1 times higher than in patients with an infected form of pancreatic necrosis. Treatment results that resulted in a violation of the anatomical integrity of the pancreas (10 patients), the presence of local complications that did not require special surgical interventions with a tendency to spontaneous healing or scarring in the short term

were achieved in 12 (12.4%) patients.

In 7 (7.2%) patients, the functional activity of the pancreas was preserved, but in 5 (5.2%) patients it was compensated by medication. 3 (3.1%) patients had temporary local inflammatory phenomena associated with the course of the above complications. In general, this treatment result was higher by 5.6% among patients with a sterile form of pancreatic necrosis than among patients with an infected form of pancreatic necrosis. In 15 (15.4%) patients, the anatomical integrity of the pancreas was impaired. However, 12 (80.0%) of them had local complications that required repeated surgical interventions. In 1 (1.03%) patient, the likelihood of developing erosive bleeding remained, which was stopped by repeated endoscopic interventions. The functional activity of the pancreas was impaired in 22 (22.7%) patients with no prospect of recovery. All of them acquired diabetes mellitus. Prolonged drug compensatory (replacement) therapy was necessary in 18 (18.6%) patients. In 3 (3.1%) patients, inflammatory phenomena associated with ongoing necrosis of the pancreatic parenchyma persisted, but all of them tended to be limited. This treatment outcome was higher among patients with an infected form of pancreatic necrosis by 2.2%. The average bed days out of the total number of patients was 49.1 ± 9.2 bed days. Here it should be taken into account that among patients with a sterile form of pancreatic necrosis there was no total damage to the pancreas, and among patients with an infected form of pancreatic necrosis there was no small focal damage. In this regard, the average value of bed days in patients with small focal pancreatic necrosis was 38.4 ± 4.2 bed days, while among patients with total pancreatic necrosis it was 1.7 times higher. The average number of bed days among patients with the sterile form of pancreatic necrosis was 42.9 ± 3.5 bed days, and with the infected form, patients were treated 12.5 days longer.

Analysis of bed days among patients without taking into account deceased patients changed the picture of values in favor of increasing the duration. For example, the average value of bed days in this statistical analysis was 7.6 ± 2.1 bed days more than in the general cohort of patients. The increase in the length of the inpatient treatment period for patients in the second cohort (excluding deceased patients) was higher in all gradations than in the first cohort (total number of patients). However, this increase was not proportional. So, for example, in the case of patients with small focal sterile pancreatic necrosis in the second cohort, the duration of bed days was only 1 bed day longer, while the comparative analysis between the first and second cohorts, as well as small focal and total lesions of the pancreas, was 2 times longer (38.4 ± 4.3 and 78.9 ± 5.8 bed days, respectively; $p < 0.05$).

Long-term results were assessed in 63 patients who suffered pancreatic necrosis. Moreover, in a hospital setting, long-term results were assessed in 118 patients. A survey of patients showed that the average GIQLI score was 117.9 ± 2.2 points. The division of the scoring structure was carried out depending on the subgroups of patients based on the immediate results of treatment. Thus, of the total value, the

maximum (136.9 ± 1.9 points) was in patients with excellent immediate treatment results. In the remaining patients, the decrease in the average score had a direct correlation with the immediate results of treatment. For example, the minimum score (105.6 ± 0.8 points) was observed in patients with unsatisfactory immediate treatment results. Analysis of quality of life indices of patients depending on the type of pancreatic necrosis suffered also had a significant difference ($p < 0.001$). In patients with the sterile phase of pancreatic necrosis, the average GIQLI score was 121.2 ± 1.2 points, while among patients who had an infected form it was 107.1 ± 2.1 points ($p < 0.001$).

Recurrence of acute pancreatitis was observed in 11 (33.3%) of 33 patients who suffered aseptic destructive complications, and in 9 (26.5%) of 34 patients who suffered infected destructive complications. The main reasons for the development of recurrent pancreatitis were factors such as alcohol intake (25.0%) and excessive consumption of fatty (25.0%) and fried foods (50.0%).

The assessment of functional pancreatic insufficiency in the long-term period was checked by the level of elastase-1 concentration in feces. The normal value was when the level of elastase-1 in feces was above 200 mg per 1 g of feces. In patients who suffered a sterile form of pancreatic necrosis, in half of the cases (51.2%), a normal value of this indicator was detected in the feces. A moderate variant of enzymatic deficiency was detected in 45.2% of patients, and in 3.6% of cases a severe form of exocrine insufficiency was diagnosed. In patients who suffered an infected form of pancreatic necrosis, in half of the cases (28.3%), a normal value of this indicator was detected in the feces. A moderate variant of enzymatic deficiency was detected in 66.9% of patients, and in 4.8% of cases a deficiency of elastase-1 activity in feces was diagnosed, which corresponded to a severe form of exocrine insufficiency. Diabetes mellitus developed in 32.9% of patients. At the same time, type I diabetes mellitus was diagnosed in 12 cases, and type II in 15 cases. Postoperative ventral hernia developed in 23 patients. In addition, among the morphological changes in the pancreas in the long-term postoperative period, pancreatic pseudocysts were identified in 12.8% of cases.

Thus, an analysis of long-term results of treatment of patients with pancreatic necrosis showed an excess of negative values among patients who suffered an infected form of pancreatic damage. All this allows us to conclude that when choosing the optimal treatment tactics for pancreatic necrosis, one should focus not only on the patient's condition and the course of the disease, but also take into account a possible decrease in the quality of life or the development of complications in the long term.

4. Conclusions

1. Analysis of the results of traditional methods of treating pancreatic necrosis complicated by sepsis showed a high level of disease complications of 38.1%

and mortality of 30.9%.

2. The high percentage of complications and mortality is due to the lack of objective criteria for predicting the development of pancreatogenic sepsis and multiple organ dysfunction syndrome, which requires detailed studies of the pathogenetic mechanisms of this terrible disease.

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