Vladimirs Fokins

CONVENTIONAL AND ULTRASOUND-ASSISTED FOCUSED OPEN NECROSECTOMY IN THE TREATMENT OF NECROTIZING PANCREATITIS

COMPARISON OF TWO METHODS

Summary of the Doctoral Thesis for obtaining the degree of a Doctor of Medicine

Speciality – Surgery

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TABLE OF CONTENTS

ABBREVIATIONS ........................................................................................................ 4
INTRODUCTION ........................................................................................................ 5
Topicality (actuality) of the thesis .............................................................................. 5
Scope of the research ................................................................................................. 6
Objectives of the research ......................................................................................... 6
Research hypothesis ................................................................................................. 6
Scientific novelty of the treatment outcome .............................................................. 7
Practical value of the research and implementation of research results ................. 7
1. MATERIAL AND METHODS .............................................................................. 8
   1.1. Principles of forming a study group and a control group ......................... 8
   1.2. Types of data acquisition ........................................................................... 10
   1.3. Statistical analysis of the research data ..................................................... 13
   1.4. Decision of the Ethic Committee ............................................................... 14
2. ULTRASOUND-ASSISTED FOCUSED OPEN NECROSECTOMY .... 15
3. RESEARCH RESULTS ....................................................................................... 20
   3.1. Analysis of the research findings ............................................................... 20
      3.1.1. Analysis of inflammatory response ................................................... 21
      3.1.2. Operating time .................................................................................. 23
      3.1.3. Necessity of repeated operation ......................................................... 24
      3.1.4. Number of repeated operations ......................................................... 25
      3.1.5. Duration of hospital stay .................................................................... 26
      3.1.6. Time spent in the intensive care unit ............................................... 27
      3.1.7. Complications ................................................................................... 28
      3.1.8. Patient mortality ................................................................................. 34
DISCUSSION ........................................................................................................... 37
CONCLUSIONS ....................................................................................................... 48
PRACTICAL RECOMMENDATIONS .................................................................... 49
BIBLIOGRAPHY ..................................................................................................... 50
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC</td>
<td>acute necrotic collection</td>
</tr>
<tr>
<td>APA</td>
<td>American Pancreatic Association</td>
</tr>
<tr>
<td>ARDS</td>
<td>Acute respiratory distress syndrome</td>
</tr>
<tr>
<td>ASA PS</td>
<td>American Society of Anaesthesiologists Physical Status</td>
</tr>
<tr>
<td>CON</td>
<td>Conventional open necrosectomy</td>
</tr>
<tr>
<td>CRO</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CTSI</td>
<td>CT severity index</td>
</tr>
<tr>
<td>DT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>ERHPG</td>
<td>endoscopic retrograde cholangiopancreatography</td>
</tr>
<tr>
<td>FNA</td>
<td>fine needle aspiration</td>
</tr>
<tr>
<td>FON</td>
<td>focus open necrosectomy</td>
</tr>
<tr>
<td>IOUSS</td>
<td>intraoperative ultrasonoscopy</td>
</tr>
<tr>
<td>LSC</td>
<td>a liquid-solid collection</td>
</tr>
<tr>
<td>MODS</td>
<td>multiple organ dysfunction syndrome</td>
</tr>
<tr>
<td>MRT</td>
<td>magnetic resonance tomography</td>
</tr>
<tr>
<td>PCD</td>
<td>percutaneous drainage</td>
</tr>
<tr>
<td>PCT</td>
<td>procalcitonin</td>
</tr>
<tr>
<td>RAKUS</td>
<td>Riga East Clinical University Hospital</td>
</tr>
<tr>
<td>SIRS</td>
<td>systemic inflammatory response syndrome</td>
</tr>
<tr>
<td>SOFA scale</td>
<td>Sequential Organ Failure Assessment score</td>
</tr>
<tr>
<td>USAS</td>
<td>ultrasound-assisted operation</td>
</tr>
<tr>
<td>USS</td>
<td>ultrasonoscopy</td>
</tr>
<tr>
<td>VAC</td>
<td>vacuum-assisted closure system</td>
</tr>
<tr>
<td>VMS</td>
<td>v. mesenterica superior</td>
</tr>
<tr>
<td>VV</td>
<td>Wirsung duct</td>
</tr>
<tr>
<td>WON</td>
<td>walled-off necrosis</td>
</tr>
</tbody>
</table>
INTRODUCTION

Topicality (actuality) of the thesis

Acute pancreatitis is a relatively common disease, with a morbidity rate of 5 to 80 cases per 100,000 people. Data may vary slightly depending on the region and country of the world, but there is a steady increase in the number of newly diagnosed people (Gullo et al., 2002). The clinical course of acute pancreatitis in the majority of cases is mild and responsive to conservative therapy. Severe forms of acute pancreatitis develop in 10–20% of patients when the clinical course is complicated with organ failure, development of pancreatic and peripancreatic necrosis and inflammatory fluid collections and infection, reaching a high mortality rate between 27% and 40% (Howard et al., 2007; Connor et al., 2005; Wroński et al., 2014; Castellanos et al., 2005).

Surgical treatment of acute necrotizing pancreatitis is complicated and associated with a rather aggressive surgical intervention when the open surgical approach is used, since it involves a large laparotomy incision and a wide exploration of the retroperitoneal space.

Less aggressive approaches have been implemented to ensure effective control of septic source complex debridement and drainage. Several authors offer various types of minimally invasive operations, such as endoscopic transgastric necrosectomy, video-assisted retroperitoneal necrosectomy using endoscopes or a nephroscope, and laparoscopic necrosectomy.

Despite the fact that world literature offers several highly effective, minimally invasive methods, none of them have been able to become the new gold standard in the surgical treatment of acute necrotizing pancreatitis until now.
**Scope of the research**

Conduct a comparative study of the focused open necrosectomy (FON) approach, evaluating the efficacy, safety and compliance of sepsis control with the principles of modern minimally invasive surgery in the treatment of acute necrotic pancreatitis.

**Objectives of the research**

Conduct a comparative study of the innovative FON approach and the conventional open surgical approach according to the following criteria:

- Analysis of the inflammatory response dynamics,
- Duration of surgery,
- Duration of hospitalization,
- Need for reoperation,
- Number of repetitive operations,
- Duration of treatment in the intensive care unit,
- Complication rate,
- Mortality in patient groups that underwent surgery.

**Research hypothesis**

The application of the ultrasound-assisted FON approach improves the accuracy of perioperative diagnostics, reduces the risk of operation, enables the use of the step-up approach in high-risk patients with severe sepsis, thus reducing the duration of treatment in the intensive care unit, the total number of complications, and mortality.
Scientific novelty of the treatment outcome

FON is an original method for a surgical treatment of acute necrotizing pancreatitis developed in our clinic. Intraoperative ultrasound navigation enables the surgeon to perform a relatively small incision subcostally and/or a minilumbotomy incision, thus providing access to the bursa omentalis for the peripancreatic, retroperitoneal, and paranephral space. This approach provides for the delimitation of the inflammatory process mainly in the retroperitoneum, preserving the contamination of the free abdominal cavity below the colon transversum in a way that the intestinal tract is not directly involved in the surgical intervention. Thus bowel and peritoneal homeostasis is maintained. The ability to visualize the layers of the abdominal wall by means of intraoperative ultrasonoscopy (IOUSS), the localisation of the necrotic debris when choosing the optimal incision and the visualisation of the large blood vessels and other significant anatomical elements intraabdominally in the operation area are some of the advantages of ultrasound-assisted necrosectomy that significantly reduce the risk of iatrogenic damage (intestinal or vascular traumatism).

Practical value of the research and implementation of research results

Thanks to the large collective effort including the development of the technical aspects of the method, drafting of the protocol, the collection, systematization, and analysis of the clinical and laboratory data, the ultrasound-assisted targeted FON method has been introduced into everyday practice.
1. MATERIAL AND METHODS

1.1. Principles of forming a study group and a control group

The study prospectively included 182 patients with severe acute necrotizing pancreatitis who received conservative treatment in the early phase of the disease combined with minimally invasive treatment when indicated later, and surgical treatment (necrosectomy and drainage) during the late phase of treatment. All patients were treated at Surgical Departments No. 10 and No. 13 of the Riga East University Hospital Gailezers from January 2004 to 2017.

All patients included in the study were divided into two groups: a control group and a study group.

In the study group, surgical tactics were applied, respecting the principles of ultrasound-assisted operation, and ultrasound-assisted focused open necrosectomy was performed. This group was also called the FON group. The principles of ultrasound-assisted surgery and surgical tactics are described in Chapters 3 of this thesis.

In the control group, conventional surgical tactics were applied and conventional open necrosectomy (CON) was performed, which was also called the CON group. See Figure 1.1 for the allocation of patients into groups.
The study included all patients with severe acute necrotizing pancreatitis who had undergone surgical treatment during the study period. No patient was excluded from the study.

Conventional open necrosectomy (CON) was used from 2004 to 2013, and the results were studied mainly through historical analysis. FON was used from 2008 to 2017, and the results were analysed prospectively (See Figure 1.2). As the diagram shows, from 2008 to 2013 FON and CON were carried out simultaneously, this time being referred to as the transitional period.
In 2013, a HPB Unit was established in our clinic, and since then only the FON method has been used for surgical treatment.

Randomization was not carried out to avoid any ethical violations.

Primary indications for surgical intervention:
1. Presence of a large necrotizing focus affecting the adjacent organs and anatomical structures, like a space occupying lesion before 4 weeks.
2. Infection with advanced inflammation.
3. Development of sepsis.

1.2. Types of data acquisition

The patient treatment results and all medical data evaluated statistically were obtained by analysing the patients’ medical history and medical records.
The variables for statistical analysis included the course of inflammation, results of laboratory and instrumental examination methods, as well as the protocols of invasive manipulation and operation.

The critical etiological factors that cause acute pancreatitis are alcohol abuse and the migration of gallstones in bile ducts, whereas other etiological factors are relatively rare. Consequently, three major groups of etiological factors were identified:

1. Gallstones (biliary).
2. Alcohol abuse.
3. Other factors.

Etiological factors were determined by analysing the anamneses of the patients. Acute pancreatitis that developed after alcohol abuse was considered a pancreatitis of alcoholic aetiology. Biliary aetiology (gallstone) pancreatitis was considered acute pancreatitis that developed due to gallstone migration. Other factors included acute pancreatitis, developed following endoscopic retrograde cholangiopancreatography with papillotomy. The group of other etiological factors included patients with dyslipidaemia and patients in whom the clarification of the etiological factor failed.

Computed tomography was performed in all patients in the preoperative period with intravenous contrast media to clarify the extent and distribution of pancreatic necrosis, and peripancreatic adipose tissue necrosis. The extent of pancreatic necrosis was calculated using the CT severity index (CTSI) (Enver Zerem, 2014; Balthazar et al., 1990; Balthazar, 2002):

- Less than 30% necrosis,
- 30–50% necrosis,
- Necrosis above 50%.

Radiological examination data was processed, and measurements were taken digitally by using the Centricity PACS-IW software and local Intranet.
Mathematical measurement scales were used for further processing of the obtained data.

An anaesthesiologist assessed and recorded the severity of preoperative general health condition of the patient by using the American Society of Anaesthesiologists Physical Status Classification System grade (ASA PS) (Cuvillon et al., 2011; Mak et al., 2002).

In the patients with acute necrotizing pancreatitis undergoing treatment in the intensive care unit, the Sequential Organ Failure Assessment (SOFA) score was analysed.

Sepsis was defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection (Mervyn Singer et al., 2016).

Organ dysfunction can be identified as a sudden change in the SOFA score (total score more than 2) indicating the host response to infection (Mervyn Singer et al., 2016).

A positive bacteriological inoculation from the biological material taken during percutaneous drainage and/or operation and CT confirmed signs of the presence of gas bubbles in the ANC and bacterial infestation of the necrotic tissue.

Levels of C-reactive protein (CRP) were defined as a biochemical marker of inflammation, and procalcitonin (PCT) was defined as a marker of sepsis. The results of both biochemical markers were analysed before the operation, as well as in dynamics on days 3 and 7 after the operation.

The patient groups were comparable, as there was no statistically significant difference in patient demographics, age, co-morbidity, the aetiology of pancreatitis, and the extent of pancreatic necrosis.

A detailed description of the study groups is presented in Table 1.1.
<table>
<thead>
<tr>
<th>Parameters</th>
<th>FON n=84</th>
<th>CON n=98</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male (%)</td>
<td>64 (76.2%)</td>
<td>71 (72.4%)</td>
<td>0.565</td>
</tr>
<tr>
<td>Age, years (IQR)</td>
<td>57.00 (47.00 – 65.00)</td>
<td>52.00 (46.00 – 61.00)</td>
<td>0.053</td>
</tr>
<tr>
<td>Aetiology:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Biliary</td>
<td>21 (25.0%)</td>
<td>23 (23.5%)</td>
<td>0.810</td>
</tr>
<tr>
<td>• Alcohol abuse</td>
<td>49 (58.3%)</td>
<td>59 (60.2%)</td>
<td>0.798</td>
</tr>
<tr>
<td>• Other</td>
<td>14 (16.7%)</td>
<td>16 (16.3%)</td>
<td>0.951</td>
</tr>
<tr>
<td>The extent of pancreatic necrosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt;30%</td>
<td>12 (14.3%)</td>
<td>23 (23.5%)</td>
<td>0.117</td>
</tr>
<tr>
<td>• 30%-50%</td>
<td>29 (34.5%)</td>
<td>33 (33.7%)</td>
<td>0.904</td>
</tr>
<tr>
<td>• &gt;50%</td>
<td>43 (51.2%)</td>
<td>42 (42.8%)</td>
<td>0.261</td>
</tr>
<tr>
<td>Preoperative ASA PS:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 2</td>
<td>30 (35.7%)</td>
<td>47 (48.0%)</td>
<td>0.096</td>
</tr>
<tr>
<td>• 3</td>
<td>47 (56.0%)</td>
<td>46 (46.9%)</td>
<td>0.225</td>
</tr>
<tr>
<td>• 4</td>
<td>7 (8.3%)</td>
<td>5 (5.1%)</td>
<td>0.381</td>
</tr>
<tr>
<td>Preoperative sepsis (%)</td>
<td>46 (54.8%)</td>
<td>57 (58.2%)</td>
<td>0.644</td>
</tr>
</tbody>
</table>

1.3. Statistical analysis of research data

The patient data from the study group and the control group were systematised using the Microsoft Excel data processing program. Statistical analysis of the clinical data was carried out using software SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Statistical data analysis was performed checking the normal distribution of quantitative data by the Kolmogorov-Smirnov test. The results were expressed in the arithmetic mean with standard deviation for the hospital stay of a patient; the remaining data were
presented in median values with interquartile range (IQR). A non-parametric test (Mann-Whitney U test) was used to compare quantitative data, whereas Student's T-test was used to compare parametric data. The analysis of the dynamics was performed with the Wilcoxon signed-rank test. For the qualitative data analysis, the Pearson Chi-square and Fisher’s exact test were applied. The results were considered statistically significant at the p-value of < 0.05 and confidence interval of 95%.

1.4. Decision of the Ethics Committee

No 10/A13 of the Ethics Committee of the RAKUS Support Fund for Medical and Biomedical Research of 12.09.2013 (See Annex).
2. ULTRASOUND-ASSISTED FOCUSED OPEN NECROSECTOMY (FON)

(Ultrasound-Assisted Focused Open Necrosectomy – FON)

In all patients, the operation is performed under general anesthesia with endotracheal intubation, positioned on the back.

If the patient has undergone transcutaneous drainage under ultrasonoscopy control at a previous phase of the treatment stage, mini-laparotomy is performed in the projection of the drain, and the drain is used as a guide for access to a necrotizing focus. If there has been no transcutaneous drainage carried out at a previous phase or if drainage has been evacuated, then it is imperative that the incision of the skin be made directly above the necrotizing focus or very close to that if the localisation of the necrotizing focus cannot be identified precisely. For the mapping of the incision, ultrasonoscopy with a convex probe of 2 to 6 MHz is performed. A longitudinal midline incision is made parallel to the left costal margin, but the size and projection of the incision can vary depending on the constitution of the patient, the localisation, and prevalence of the necrotizing focus, and repeated operations.

After treating the operative site with a disinfectant fluid and covering with a sterile drape, the sides of the patient should be freely accessible for mini lumbotomy.

An incision of 4–5 cm (mini-laparotomy) is made, slightly larger if the patient is adipose.

When opening the abdominal cavity, an intraoperative ultrasonoscopy is used to provide the most convenient access to the necrotizing focus. This usually occurs through lig. gastrocolicurn or along the lesser curvature of the stomach.

The avascular zone is selected when opening the focus by moving the intestinal loops and the omentum majus aside and clearing access for the tools,
but it should be noted that this stage is assisted by intraoperative ultrasound. Then a micro convex ultrasound probe of 5 to 13 MHz or a micro linear bar type probe of 5 to 18 MHz is used (See Figure 2.1).

![Ultrasound images](image)

Figure 2.1 **The IOUSS images using A – micro linear bar type probe, B – micro convex probe**

1 – stomach, 2 – necrotizing focus, 3 – the shadow of an instrument when opening LSC, 4 – avascular zone for opening the necrotizing focus bypassing the stomach wall. (Photos made by the author)

A necrotizing focus consists of a necrotizing mass of the pancreatic tissue and peripancreatic adipose tissue and *liquid-solid collection* (LSC). When opening that focus, the LSC is pumped out, but the necrotizing tissue is evacuated digitally or using atraumatic forceps (for example, Kalley sponge forceps).

The easily detachable tissue is only evacuated. After sanation of the focus, a repeated IOUSS is required to ensure that all necrotizing tissue and liquid-solid collections are evacuated and to check whether any residual foci are left. For this
purpose, only a micro convex probe is applied. If the ultrasound detects any additional focus, it is opened under ultrasound guidance by connecting it with the already sanated focus or through a separate access (See Figure 2.2).

![Additional collection in retroperitoneal space, IOUSS image with the micro convex probe](image)

Figure 2.2 Additional collection in retroperitoneal space, IOUSS image with the micro convex probe
1 – Retroperitoneal space tissue, 2 – additionally detected LSC.
(Photos made by the author)

Bacteriological sampling is made during the operation.

For adequate drainage of the focus, a contra-aperture is used through a minilumbotomy incision in retroperitoneal space on the left (most often) or the right side, or on both sides depending on the localisation of the focus. This step should be ultrasound-guided intraoperatively using a micro convex probe to avoid iatrogenic damage to the anatomical structures.

Iatrogenic damage can occur:

- On the left: great blood vessels and splenic angle of the colon,
- On the right: great blood vessels, retroperitoneal part of the duodenum and hepatic angle of the colon.
Drains are introduced via mini-laparotomy and/or minilumbotomy incision. After the drains are inserted, one must ensure that the drains interact with each other to ensure adequate source control (See Figure 2.3 and 2.4). Minilaparotomy and minilumbotomy incisions are stitched up as per layers of tissue, leaving the edges adjoining the drain free.

Figure 2.3 **CT image shows the drain position in the necrotizing focus**
(Photos made by the author)
Figure 3.4 Options for drain positioning:
A – Drains are placed through minilaparotomy, and minilumbotomy incisions on the left side, B – Two drains are located via minilaparotomy incisions, and one drain is positioned via minilumbotomy on the right side, C – A patient after repeated operations with incisions in several locations. All surgical interventions were performed in two attempts with interval of four days starting from the left side where the larger purulent collections and tissue debris was localised.

(Photos made by the author)
3. RESEARCH RESULTS

3.1 Analysis of the research findings

The research findings were evaluated according to the following criteria: dynamics of the inflammatory response in the postoperative period (See Table 3.2), duration of the operation, necessity for repeated operations and number thereof, duration of hospital stay, time spent in the intensive care unit, total number of complications, and mortality rate (See Table 3.1). A separate in-depth analysis was carried out on complications and their variations, as well as mortality.

### Table 3.1

**Analysis of the research findings**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>FON n = 84</th>
<th>CON n = 98</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of operation, min (IQR)</td>
<td>60 (45–75)</td>
<td>120 (98–146)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hospital stay, days (IQR)</td>
<td>48 (32–59)</td>
<td>69 (60–76)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Need for repeated operation</td>
<td>33 (39.3%)</td>
<td>64 (65.3%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of repetitive operations (SD)</td>
<td>2.76 (1.347)</td>
<td>3.31 (1.308)</td>
<td>0.053</td>
</tr>
<tr>
<td>Time spent in ICU, days (IQR)</td>
<td>12 (3–16)</td>
<td>21 (16–29)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of patients with complications</td>
<td>19 (22.6%)</td>
<td>29 (29.6%)</td>
<td>0.287</td>
</tr>
<tr>
<td>Number of patients died during the study</td>
<td>5 (6.0%)</td>
<td>9 (9.2%)</td>
<td>0.415</td>
</tr>
</tbody>
</table>
3.1.1 Analysis of inflammatory response

Reduction of the inflammatory response in the immediate postoperative period is one of the most important criteria for the efficiency of an operation. For the analysis of inflammatory response in the postoperative period, the dynamics of C-reactive protein (CRP) and procalcitonin (PCT) preoperatively, on days 3 and 7 after the operation were selected. A detailed analysis of the inflammatory response is presented in Table 3.2.

Table 3.2

<table>
<thead>
<tr>
<th>Parameters</th>
<th>FON n = 84</th>
<th>CON n = 98</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative CRP, mg/L (IQR)</td>
<td>229 (168–312)</td>
<td>213 (176–290)</td>
<td>0.447</td>
</tr>
<tr>
<td>CRP on postoperative day 3, mg/L (IQR)</td>
<td>126 (91–200)</td>
<td>200 (153–232)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CRP on postoperative day 7, mg/L (IQR)</td>
<td>49 (26–75)</td>
<td>120 (85–164)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Preoperative PCT, ng/mL (IQR)</td>
<td>3.62 (0.86–7.12)</td>
<td>3.83 (0.98–6.40)</td>
<td>0.821</td>
</tr>
<tr>
<td>PCT on postoperative day 3, ng/mL (IQR)</td>
<td>1.07 (0.22–3.15)</td>
<td>3.01 (1.40–5.36)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PCT on postoperative day 7, ng/mL (IQR)</td>
<td>0.20 (0.05–0.51)</td>
<td>1.20 (0.30–2.20)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

On analysing the dynamics of CRP, it was found that the CRP level in the patients from the FON group decreased more rapidly in the postoperative period if compared with the patients from the CON group. That was especially evident on the third postoperative day when the level decreased insignificantly in the patients from the CON group (See Figure 3.1).
When analysing the PCT level in the blood after the postoperative period, a convincing reduction in PCT levels on both day 3 and day 7 after the operation was found. This trend was more pronounced in the FON group (See Figure 3.2).
3.1.2 Operating time

It was proved with statistical reliability that minimally invasive operations are performed much faster than conventional open operations (See Table 3.1 and Figure 3.3). Ultrasound-assisted FON as a kind of minimally invasive surgical intervention was a less aggressive method, with less tissue traumatism and a shorter operating time.
3.1.3 Necessity of repeated operation

Often, a patient required a repeated operation to sanate the residual necrotizing foci.
The findings show that there were much fewer repeated operations in the study (FON) group because it is possible to visualise the additional collections and deeply enclosed necrotizing foci thanks to intraoperative ultrasound-guidance during the first operation, which can be overlooked during an open operation (See Table 3.1 and Figure 3.4).

### 3.1.4 Number of repeated operations

Having analysed the obtained results, less frequent repeated surgical interventions were observed in the FON group compared to the control (CON) group. However, it was not proved to be statistically significant (See Table 3.1).
3.1.5 Duration of hospital stay

Patients with severe acute necrotizing pancreatitis undergo long-term treatment in hospital.

The results demonstrate with statistical significance that the patients recovered faster in the study (FON) group than in the control (CON) group (See Table 3.1 and Figure 3.5).

Figure 3.5. Statistical data on duration of hospital stay
3.1.6 Time spent in the intensive care unit

All patients with severe acute necrotizing pancreatitis were treated in the intensive care unit (ICU). The results are shown in Figure 3.6.

With a statistical significance observed, the patients from the FON group spent much fewer days in the ICU than the patients from the control (CON) group did.

![Statistical data on time spent in the intensive care unit](image)

Figure 3.6 Statistical data on time spent in the intensive care unit
3.1.7 Complications

Surgical treatment of acute necrotizing pancreatitis is a technically complicated manipulation that can result in complications.

Although there were fewer complications in the FON group, there was no statistically significant difference. Results shown in Figure 3.7 and Table 3.1.

![Figure 3.7 Statistical data on complications](image)

In the study, there were three significant complications identified: prolonged, persistent pancreatic cutaneous fistula, bleeding, and intestinal fistula.
• **Prolonged persistent pancreatic cutaneous fistula**

It occurs when the pancreatic necrotizing process affects the pancreatic outflow channel of a large diameter resulting in the pancreatic juice entering the peripancreatic space and into the external environment along with a fistula. In the study (FON) group and the control (CON) group, the incidence of this complication practically did not differ (See Figure 3.8).

![Figure 3.8 Statistical data on pancreatic cutaneous fistula](image)

• **Bleeding**

Typically, severe intraoperative bleeding occurs when a blood vessel of a relatively large diameter is damaged during necrosectomy that might also be eroded due to a necrotizing process.

With the statistical significance of $p = 0.002$, one can state that severe bleeding was much less frequent during necrosectomy in the patients from the
FON group, because intraoperative ultrasonoscopy enabled vascular visualisation, thus reducing the risk of bleeding (See Figure 3.9), opposite to the case of conventional necrosectomy, which requires a large amount of tissue mobilization and, consequently, more tissue traumatism.

![Bleeding](image)

Figure 3.9 **Statistical data on bleeding**

- **Intestinal fistula**

  Intestinal fistulas are usually formed due to an ischemic intestinal wall as a result of the inflammatory process and the spread of pancreatic necrosis about thrombosis of small blood vessels.

  Iatrogenic damage to the intestinal wall was detected once in a patient from the study group, but it should be noted that this complication was observed during the approbation of the method. Although the results were slightly better
in the study group, there was no statistically significant difference. The results are shown in Figure 3.10.

The analysis of complications shows that the formation of pancreatic cutaneous fistula and intestinal fistula are less affected by the surgical method, but are associated with morphological changes in the tissue caused by the inflammation. Bleeding is associated with severe tissue damage and an increased risk of bleeding, but a minimally invasive operation reduces such risk of bleeding.

The development of several complications simultaneously in one patient was observed. The results are shown in Figure 3.11 and Table 3.3.
The following variations of combined complications were observed in the patients: pancreatic cutaneous fistula and bleeding; bleeding and intestinal fistula; pancreatic cutaneous fistula and intestinal fistula; pancreatic cutaneous fistula and bleeding, as well as intestinal fistula.

Patients with different combined complications in the study (FON) group were less common than in the control (CON) group ($p = 0.057$). However, there was no statistically significant difference. The results are presented in Table 3.3.
### Table 3.3

**Statistical data on combined complications**

<table>
<thead>
<tr>
<th>Number of patients with pancreatic cutaneous fistula</th>
<th>FON n = 84</th>
<th>CON n = 98</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with bleeding</td>
<td>6 (7.1%)</td>
<td>24 (24.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Number of patients with intestinal fistula</td>
<td>9 (10.7%)</td>
<td>16 (16.3%)</td>
<td>0.273</td>
</tr>
<tr>
<td>Number of patients with combined complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic cutaneous fistula and bleeding</td>
<td>1 (1.2%)</td>
<td>3 (3.1%)</td>
<td>0.625*</td>
</tr>
<tr>
<td>Bleeding and intestinal fistula</td>
<td>2 (2.4%)</td>
<td>9 (9.2%)</td>
<td>0.066*</td>
</tr>
<tr>
<td>Pancreatic cutaneous fistula and intestinal fistula</td>
<td>2 (2.4%)</td>
<td>0 (0.0%)</td>
<td>0.212*</td>
</tr>
<tr>
<td>Pancreatic cutaneous fistula, bleeding, and intestinal fistula</td>
<td>0 (0.0%)</td>
<td>3 (3.1%)</td>
<td>0.250*</td>
</tr>
<tr>
<td>Total</td>
<td>5 (6.0%)</td>
<td>15 (15.3%)</td>
<td>0.057*</td>
</tr>
</tbody>
</table>

* p-value was calculated by using the Fischer’s exact test.

### 3.1.8 Patient mortality

The number of patients who died during the study in the FON group was smaller than in the CON group (See Figure 3.12 and Table 3.1).
The number of patients who died during the study was relatively small, but the following trends were observed in the in-depth analysis of the statistical data on mortality:

- Among all patients included in the study, the highest mortality rate was detected in the patients with alcohol-induced pancreatitis, see Table 3.4.

**Table 3.4**

### Statistical data on patient mortality depending on the aetiology of acute necrotizing pancreatitis

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Total number of patients</th>
<th>Number of patients who died during the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary</td>
<td>44</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>108</td>
<td>10 (9.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>30</td>
<td>2 (6.7%)</td>
</tr>
</tbody>
</table>

- When analysing patient mortality depending on the extent of pancreatic necrosis, it was found that the number of patients who died during the study
was proportional to the extent of pancreatic necrosis. The more significant the extent of the pancreatic necrosis was, the higher was the number of deceased patients (See Table 3.5).

Table 3.5

**Statistical data on patient mortality depending on the extent of pancreatic necrosis**

<table>
<thead>
<tr>
<th>Extent of pancreatic necrosis</th>
<th>Total number of patients</th>
<th>Number of patients who died during the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>35</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>30–50%</td>
<td>62</td>
<td>4 (6.5%)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>85</td>
<td>8 (9.4%)</td>
</tr>
</tbody>
</table>

- In the patients who died during the study period, the overall health status according to the ASA PS was evaluated before the operation, and it was found that the poorer the general health condition as of the operation was, the higher was the mortality rate, see Table 3.6.

Table 3.6

**Statistical data on patient mortality depending on patient’s general health condition before the operation**

<table>
<thead>
<tr>
<th>Preoperative ASA PS</th>
<th>Total number of patients</th>
<th>Number of the patients who died during the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>77</td>
<td>2 (2.6%)</td>
</tr>
<tr>
<td>3</td>
<td>93</td>
<td>10 (10.8%)</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>2 (16.7%)</td>
</tr>
</tbody>
</table>

Although the primary indication for surgical intervention on patients with necrotizing pancreatitis is a necrotic infection, it follows from Table 3.7 that the mortality risk increases rapidly if the operation is performed on patients with sepsis.
When analysing the statistical data on mortality, a higher mortality rate among patients requiring a repeated operation was observed, as shown in Table 3.8.

### Table 3.8

**Statistical data on patient mortality depending on the necessity of repeated operation**

<table>
<thead>
<tr>
<th>Repeated operation required</th>
<th>Total number of patients</th>
<th>Number of patients who died during the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>97</td>
<td>12 (12.4%)</td>
</tr>
<tr>
<td>No</td>
<td>85</td>
<td>2 (2.4%)</td>
</tr>
</tbody>
</table>
DISCUSSION

The surgical treatment of acute necrotizing pancreatitis is very complicated and involves a large number of intraoperative and postoperative complications as well as patient mortality.

This thesis presents a prospective analysis and comparison of two surgical approaches when the treatment of acute necrotizing pancreatitis required surgical intervention, that is, focused open necrosectomy and conventional open necrosectomy.

The prevention of systemic error is crucial for the comparison of any treatment methods. As it is known, randomization provides it best, which eliminates both patient allocation into groups and errors in evaluating the results. However, randomization is difficult to achieve in surgical studies (Carmen Paradis, 2008). The most frequently mentioned reason is the ethical factor, expressed moral discomfort, and the inability to separate the role of a researcher from the role of a doctor. The aspect of the patient's rights emerges here. As Taylor and his colleagues say, only 27% of the 91 surveyed surgeons could hardly organise randomized groups in their studies, as it was associated with concerns about the patient and the awareness that the new method would bring more benefits and recovery chances and comparing it with the old method would not be correct (Taylor et al., 1984).

In our study, we did not apply randomization due to ethical considerations, since the experience with the introduction of ultrasound-assisted surgery allowed us to improve diagnostic accuracy and use ultrasound for intraoperative navigation, thereby significantly reducing the degree of tissue traumatism and avoiding damage to adjacent tissues and blood vessels that was impossible in the case of conventional open necrosectomy.
As noted in Chapter 1.1, we compared the study FON group in our research, which was analysed prospectively, with the historical control group CON. As several authors have already mentioned, this study has its own disadvantages (Carmen Paradis, 2008), where the major one is the time (chronological) factor.

The time period analysed in our study is more than ten years. During this period, both the experience of doctors, the conditions of treatment, and diagnostic resources as well as the patient monitoring have improved. All of the above affects the outcome of the treatment. We cannot avoid the time factor. We can try to analyse the extent to which this time factor affects the outcome of the treatment, relative to the effect of the chosen method of surgery.

Comparing the results throughout the study period, when the time factor could have influenced them, with the results during a transitional period, when there was no time factor, we observe that they differ only slightly. Consequently, we can conclude that the influence of the time factor on the results in our study is not decisive.

The study included all patients treated for acute necrotizing pancreatitis at RECUH Gailezers from 2014 to 2017 who needed surgical treatment. No patient was excluded from the study. The groups were as close as possible to the real clinical practice scene, no additional exclusion criteria were used.

The study groups did not differ in terms of gender, age, and comorbidities, as well as in other parameters characterizing the preoperative period, suggesting that both patient groups were statistically credibly comparable.

Consequently, it can be argued that the method of surgery is a key factor influencing the results of the research.

The time when an operation is carried out is of great importance in the treatment of acute necrotizing pancreatitis. The specialised literature indicates that early operations are associated with a high number of complications and high mortality (Besselink et al., 2009; Wroński et al., 2014; Mier et al., 1997).
A modern treatment approach involves a conservative treatment strategy at an early phase of the disease, but surgical intervention should be made as late as possible when a necrotizing focus has formed, and the necrotizing tissue is well detachable. The Atlanta classification reflects the stages of necrotizing focus formation very well (Banks et al., 2013). The optimal surgical tactic must be in line with the so-called 3D principle (Enver Zerem, 2014):

**Delay** – conservative tactics,

**Drain** – USS-guided percutaneous drainage of symptomatic collections at the ANC phase,

**Debride** – operational tactics at the WON phase (4 weeks after the onset of the disease).

The preoperative treatment period of acute necrotizing pancreatitis is very long (approximately 4 weeks), and predominantly conservative surgical treatment tactics have a significant effect on the future recovery. In order to evaluate the results of surgical treatment, surgical intervention methods were statistically analysed. The preoperative health condition of the patients was analysed as per several criteria like age, gender, and etiologic factors, and the physiological condition defined by the anaesthesiologists regarding comorbidities, using the ASA SP scale. We also analysed the dynamics of inflammation, the presence of septic conditions, the extent of pancreatic necrosis, and the morphological condition of the necrotizing focus associated with the surrounding tissue and the degree of isolation based on ultrasound and computed tomography. Other authors have also used these criteria in similar studies (Working Group, I.A.P.A.P.A.A.P.G., 2013; van Santvoort et al., 2010; Freeman et al., 2012; Karakayali, 2014).

Several authors have noted in their studies that the most frequent patients diagnosed with acute necrotizing pancreatitis are between 50 and 65 years of age on average and that women tend to be slightly older than men, and men develop this disease about two times more often than women (Carter, McKay and Imrie,
Horvath et al., 2001; Raraty et al., 2010; Horvath et al., 2010; Voermans et al., 2007; Seifert et al., 2009; Gambiez et al., 1998; Connor et al., 2005; Castellanos et al., 2005; van Santvoort et al., 2007; Bucher et al., 2008; Sileikis et al., 2010; Lakshmanan et al., 2010; Tang et al., 2010; Ahmad et al., 2011; Papachristou et al., 2007; Seewald et al., 2005; Charnley et al., 2006; Schrover et al., 2008; Mathew et al., 2008; Escourrou et al., 2008; Coelho et al., 2008; Jurgensen et al., 2011). The above data relating to the patient’s age and gender were also confirmed in our study.

The etiological factors of acute pancreatitis in the literature vary across regions and countries. In European countries, for example, in Germany, biliary aetiology is 34.9% and alcohol-induced aetiology is 37.9%, with similar results in France of 24.6% and 38.5% respectively. Alcohol-induced aetiology is prevalent in Hungary in 60.7% of cases, while biliary genesis is prevalent only in 24.0% of cases. In Greece, biliary aetiology dominates in 71.4% of patients, while alcohol-induced aetiology constitutes only 6%. A similar trend also prevails in Italy, where 60.3% of pancreatitis are induced by gallstone migration, and 13.2% of pancreatitis are alcohol-induced (Gullo et al., 2002).

Our research data showed (taking into account all 182 patients included in the study) that alcohol caused acute pancreatitis in 59.3% of patients and gallstone migration induced it in 24.2% of patients. It should be noted that alcohol was predominantly a cause of pancreatitis among men (alcohol-induced in 66.7% and biliary aetiology in 20.7% of patients), while gallstone-induced pancreatitis was almost equally frequent in women as alcohol-induced pancreatitis (alcohol-induced in 38.3% and biliary aetiology in 34% of patients).

Several authors come to the conclusion that alcohol-induced pancreatitis is associated with a more severe course of the disease and a higher mortality rate (Gullo et al., 2002; Rashidi et al., 2016; Cho et al., 2015). It was also confirmed in our study.
Most authors emphasise that an effective treatment of sepsis plays an essential role in acute necrotizing pancreatitis. Currently, the so-called *step-up* principle in the treatment is dominant (Van Santvoort et al., 2010; Mier et al., 1997; Freeny et al., 1998; Freeman et al., 2012). The primary objective in the early (ANC) phase is to carry out USS-guided transcutaneous drainage and to evacuate the liquid infected part of the necrotizing focus, which improves the patient’s condition and allows delaying the operation until necrosis fully forms (WON phase). In its turn, the primary objective of surgical treatment is to perform necrosectomy, as well as to ensure adequate drainage of the infected focus and subsequent control.

At the beginning of 2016, new so-called sepsis-3 criteria were published, a definition of the septic condition and septic shock was supplemented (Mervyn Singer et al., 2016), and we followed the new recommendations in our study (See Section 3.1.2). According to our data, the disease had a comorbid condition with sepsis in 103 patients (56.6%) out of all 182 operated patients.

The CRP was defined as an inflammatory biochemical marker and PCT was defined as a sepsis marker in the patients. In patients with sepsis, CRP level was > 150 mg/ml and PCT level was > 2.0 ng/ml. The results of both biochemical markers were analysed before the operation, as well as in the dynamics on days 3 and 7 after the operation. This analysis helped us assess the efficiency of the operation and decide on the necessity for a repeated operation.

We observed a more rapid decrease of CRP in the FON group, especially on postoperative day 3 showing a significant difference to the CON group. This finding might be explained with more efficient source control in the FON group and the following induction of anti-inflammatory mechanisms. It was achieved by the assistance of the IOUSS that allowed a more complete evacuation of necrotic tissue and ensured a well-functioning postoperative drainage.

PCT is a highly sensitive prognostic marker (Rau BM et al., 2007), which demonstrates the presence of infection, the relationship between the severity of
infection, the effectiveness of surgical treatment and the outcome of the disease very well. In our study, high levels of PCT prior to surgery and an objective reduction of PCT level in the postoperative period reflect the ability of the body to delimit the infection focus, which is more effectively seen in the FON group compared with the control group.

Intraoperative ultrasound navigation enables the surgeon to make a relatively small incision subcostally and/or minilumbotomy, thus providing access to the bursa omentalis for the peripancreatic, retroperitoneal, and paranephral space. This approach provides for the delimitation of the inflammatory process, because the free abdominal cavity below the colon transversum is not opened and the intestinal tract is not directly involved in the inflammation process, thus maintaining peritoneal homeostasis.

Operating time was among the criteria we analysed. This criterion is very variable and depends on several factors such as the extent and prevalence of necrosis, number of foci, body mass index, and experience of the operating surgeon.

As we noted earlier, several patients underwent ultrasound-assisted percutaneous drainage of symptomatic inflammatory exudate collections in the ANC stage using pig-tail catheters. The drain can also serve as a guide during an operation for easier access to a necrotic focus. This significantly facilitates and speeds up the operation. This surgical approach using a drainage catheter inserted in a necrotic focus has been used for the minimally invasive methods described above, such as MARPN or minimal access retroperitoneal pancreatic necrosectomy and VARD or video-assisted retroperitoneal debridement (Carter, McKay and Imrie, 2000; Connor et al., 2003; Horvath et al., 2010).

The operating time can be much longer in the event of intraoperative complications, especially bleeding. Despite this, there is a trend suggesting that
ultrasound-assisted focused open necrosectomy can be almost twice as short as conventional open necrosectomy.

Treatment of acute necrotizing pancreatitis, as well as treatment of any other purulent focus often requires surgical revision. Repeated operations are characteristic of both open (conventional) necrosectomy and other minimally invasive methods described in the literature. The need for a repeated operation is one of the analytical criteria used by other authors in similar studies (Carter, McKay and Imrie, 2000; Horvath et al., 2001; Bausch et al., 2012; Gardner et al., 2009).

The main reason for a repeated operation is the presence of contaminated residual collections with advanced sepsis. We often drain such collections transcutaneously under USS control, but it is not technically feasible in all cases, mainly due to the localization of those collections. Transcutaneous ultrasound visualisation of those collections is difficult because it often contains air and is covered with intestinal loops or stomach. In those cases, we evaluate the collection/topography of the collection by a repeated CT examination. On the other hand, intraoperative ultrasound-guided navigation is also very efficient in the event of repeated operation because the intermittent intestinal loop or stomach can be moved aside or squeezed so that their content would not interfere with sonography examination.

Another life-threatening situation is bleeding in the immediate postoperative period when an urgent repeated operation is required. In those cases, it is tough to find a bleeding site, and an operation must often end with tamponade, which is easy to perform if the operation approach is channel-shaped, which exactly is characteristic of the FON method.

In our study, we noticed a trend that the necessity for a repeated operation decreased after the FON type operations.

Some authors note the need for a repeated conventional open necrosectomy after minimally invasive surgical interventions. The frequency of
such operations is up to 32% of the cases (Bausch et al., 2012). This occurs more often after transgastric endoscopic necrosectomy. In the patients included in our study, conventional open necrosectomy after the FON type operation was not applied.

In our study, we also analysed some repeated operations. The average number of repeated operations described in the literature varies between 2 and 7 (Carter, McKay and Imrie, 2000; Horvath et al., 2001; Raraty et al., 2010; Horvath et al., 2010; Voermans et al., 2007; Seifert et al., 2009; Gambiez et al., 1998; Connor et al., 2005; Castellanos et al., 2005; Van Santvoort et al., 2007; Bucher et al., 2008; Sileikis et al., 2010; Lakshmanan et al., 2010; Tang et al., 2010; Ahmad et al., 2011; Papachristou et al., 2007; Seewald et al., 2005; Charnley et al., 2006; Schrover et al., 2008; Mathew et al., 2008; Escourrou et al., 2008; Coelho et al., 2008; Jurgensen et al., 2011). In our study, this number reached 3.65 after a conventional open necrosectomy and is slightly less after the FON-type operations (See Section 3.1.4).

Most of the patients included in our study were treated in the intensive care unit. A successful treatment of acute necrotizing pancreatitis mainly depends on the efficacy of this phase of the treatment. Pain management, rehydration, electrolyte imbalance compensation, adequate antibacterial therapy, timely enteral and parenteral nutrition, and management of the organ dysfunction and MODS are vital compounds of the treatment, and monitoring that can only be provided in the intensive care unit.

The time spent in the ICU also largely depends on the efficiency of surgical treatment. When analysing the average number of days that the patients spent in the intensive care unit, we found that the time spent in the ICU was significantly lower in the FON group (See Section 3.1.6). Not all authors use this criterion in the analysis of their performance. Some authors analyse only the need for treatment in an intensive care unit after operation (Carter, McKay and Imrie,
Other authors evaluate the time spent in the ICU (number of days) only after operation (Bausch et al., 2012).

Our findings are comparable with the findings reported by other authors, although there are reports that the time spent in the ICU and hospital stay practically do not differ between the patients treated with minimally invasive methods and conservative open necrosectomy (Senthil Kumar, Ravichandran and Jeswanth, 2012).

In our study, the hospital stay was significantly shorter after the FON-type operation compared to CON.

The method of surgery significantly affects the duration of hospital stay. The FON type operation is associated with relatively small incisions and less tissue traumatism, so the postoperative rehabilitation period is significantly shorter. Patient begins to activate, walk and serve himself or herself more quickly. Reducing the inflammatory response, the need for re-operation and the number of complications are important factors for the recovery, and patients in the FON group recovered faster.

The duration of hospital stay also depends on outpatient care options. In cases where it is possible to ensure adequate surgical drain care and wound care in outpatient clinics and when the general health condition of a patient allows, the hospital stay might be shorter.

Complications are one of the most critical criteria that reflect the safety of an operation. Three major types of complications are reported after necrosectomy and drainage: pancreatic cutaneous fistula, intra-abdominal bleeding, and intestinal fistula.

In the current study we also followed the same classification and did not collect data on the development of late complications, like diabetes, the need for pancreatic enzymes, and the development of a post-operative hernia analysed by several authors (Van Santvoort et al., 2010; Bakker et al., 2012; Sorrento, Chiara and Mutignani, 2017). We analysed the complications inherent in a particular
surgical procedure. For example, gastrointestinal bleeding and gastric perforation with peritonitis are characteristic of endoscopic transgastric necrosectomy.

We observed a downward trend in the number of complications following the FON type operations. In particular, with a statistically significant difference, this trend was evident when analysing the incidence of intra-abdominal bleeding, since one of the advantages of the focused minimally invasive ultrasound-assisted necrosectomy is the ability, through the IOUSS, to visualize not only superficial foci, but also the foci localised deeply retroperitoneally. It is important to visualise large blood vessels and other significant anatomical elements in the surgery area, which significantly reduces the risk of iatrogenic damage. It is known that conventional open necrosectomy requires large tissue mobilization and more tissue traumatism, leading to increased risk of vascular damage.

The analysis of complications shows that the formation of pancreatocutaneous and intestinal fistula is less affected by the surgical method, but it is related to the morphological changes in the tissue caused by the disease and inflammation. The risk of bleeding increases with the use of high tissue mobilization in contrast to the minimally invasive surgical procedure that reduces that risk of bleeding.

Severe acute necrotizing pancreatitis is always associated with high mortality. An analysis of our study suggests that the number of dead patients has been higher among the patients with alcohol abuse-induced acute pancreatitis with the amount of pancreatic necrosis over 50% and severe comorbidities characterized by the ASA PS criteria. Higher mortality was observed among the patients with sepsis in need for a repeated surgery. According to the literature data, mortality is up to 40% in the event of conventional open necrosectomy (Howard et al., 2007; Connor et al., 2005; Wroński et al., 2014), whereas the mortality rate after minimally invasive surgical interventions constitutes up to
27% (Castellanos et al., 2005). The main reason is the MODS. The development of sepsis doubles the risk of poor treatment outcome (Trikudanathan et al. 2014; Sorrentino, Chiara and Mutignani, 2017; Werge, Novovic and Schmidt, 2016). According to our findings, the mortality rate was lower after the FON-type operations.

Existing literature data suggest that intraoperative ultrasound assistance was very rarely used in the case of necrotic pancreatitis (See the chapter of literature review). Mostly, IOUSS is used for diagnostic purposes, most commonly for verification of metastatic oncological diseases due to its high specificity and sensitivity. For example, according to Vazharov (2013), liver metastases were detected with IOUSS during an operation, which were not detected preoperatively with transabdominal ultrasound and CT.

When using intraoperative ultrasound assistance in FON operations, we often find the difference between the intraoperative site and the preoperative CT data. The use of IOUSS enables clarifying the prevalence of necrotic process and finding a necrotic focus which was not diagnosed with CT.

Ultrasound-assisted navigation made reaching the necrotic focus without extensive tissue preparation and traumatism, bypassing large blood vessels and other anatomical structures involved in inflammatory infiltration around necrosis. This significantly reduces the duration of surgery and a number of complications after FON operations compared to conventional open necrosectomy.

The advantages of intraoperative ultrasound-assistance and the results of the study allow us to assess the efficiency of the FON method and make it a part of our daily practice.
CONCLUSIONS

1. The use of ultrasound-assisted focused open necrosectomy enabled a significant reduction in tissue traumatism and operating time.
2. The ultrasound-assisted focused open necrosectomy is entirely consistent with the primary task of surgical treatment, that is, to perform necrosectomy, as well as adequate rehabilitation and drainage of the infected focus, which triggers progressive sepsis.
3. The method is associated with a significantly reduced postoperative inflammatory response.
4. FON compared to CON is associated with a reduced hospital stay, stay in the intensive care unit, the incidence of complications, and mortality.
5. Ultrasound-assisted FON is an efficient method; it fully complies with the patient’s safety and the principles of modern surgery in the treatment of acute necrotizing pancreatitis.
PRACTICAL RECOMMENDATIONS

1. Ultrasonoscopy is used in all phases of acute necrotizing pancreatitis treatment and provides an opportunity:
   - **In the preoperative period**, to evaluate the localization and prevalence of the necrotizing focus, to define the closest access to the pathological process, and to drain the transcutaneous symptomatic collections.
   - **In the intraoperative period**, to clarify the prevalence of necrotizing focus and its relationship with other abdominal cavity structures, to localise the access of surgical trajectory to the focus precisely, to conduct real-time examination parallel to a surgical intervention aimed at providing accurate access to the focus and evaluating the efficiency of the applied surgical procedure.
   - **In the postoperative period**, to monitor debrided and drained foci to assess the presence and prevalence of residual collections and to drain transcutaneous collections if necessary.

2. Intraoperative ultrasound navigation makes a relatively small subcostal and/or minilumbotomy incision possible, thus providing access to peripancreatic, retroperitoneal, and paranephral space without opening the abdominal cavity below the colon transversum and maintaining peritoneal homeostasis.

3. The optimal surgical tactic must be in line with the so-called 3D principle:
   - Delay – conservative tactics.
   - Drain – USS-guided percutaneous drainage of symptomatic collections at the ANC phase.
   - Debride – operational tactics at the WON phase (4 weeks after the onset of the disease).

   That can be provided by applying the FON tactics.
BIBLIOGRAPHY


PUBLICATIONS AND REPORTS ON THE SUBJECT OF THE RESEARCH

Publications on the subject of the research


Theses and presentations at international congresses:


