

INSTITUTE OF DOCTORAL STUDIES  
DOCTORAL FIELD: MEDICINE

DOCTORAL THESIS  
SUMMARY

**SURGICAL THERAPEUTIC WINDOW OF ACUTE  
PANCREATITIS**

PhD:

**MIHAI FAUR**

Doctoral Advisor:

**prof. univ. dr. DAN SABĂU**

SIBIU, 2021

## *MOTIVATION FOR CHOOSING THE RESEARCH TOPIC*

Dieulafoy's "great abdominal drama", called acute pancreatitis, is a complex pathology with multiple diagnostic difficulties, with a multifactorial etiology, the evolution of which provides functional repercussions on the whole organism and whose treatment does not have a clear protocol to follow.

In Romania the incidence of pancreatitis is 40-50 per 100.000 inhabitants per year, with a distribution of 25-30% in the Ardeal area and a mortality of 30-40%.

The physiopathological mechanisms leading to the onset of the pancreatic autodigestion process are still unclear, although advances in research into the etiopathogenesis of the disease have led to new therapeutic approaches with repercussions on the course of the disease.

Professor Dr. Dan Sabău proposed a new concept regarding etiopathogenesis of pancreatitis, namely the hyperpressure in the main bile duct which has direct repercussions on the channels of the pancreas, being directly proportional to the course of the disease.

The concept of surgical therapeutic window of acute pancreatitis is introduced, which aims to apply a complex treatment protocol involving lowering the biliopancreatic pressure both medicinally and surgically.

The incessant development of minimally invasive surgery and imaging explorations offers modern possibilities for treatment in acute pancreatitis by introducing new methods to address the pancreatic lodge.

Due to the increased frequency in our region, the fulminant evolution of the disease and the lack of a well-established protocol regarding the treatment of acute pancreatitis, I decided to choose the mentioned doctoral research topic.

I have structured the paper into two components, respecting the current requirements for the drafting of a doctoral thesis, the theoretical part in which the research framework is presented and the special part comprising a clinical study on the diagnosis and treatment of acute pancreatitis.

## INTRODUCTION

Research and discussions in recent years on the diagnosis and treatment of acute pancreatitis are focused on solving major problems, of which, a particular interest in the study carried out is the establishment of the indication and the optimal operative moment, the therapeutic strategy in severe forms and the evaluation of new therapeutic procedures: surgical, interventional radiology, endoscopic and associated.

The most significant progress in the last ten years is the decrease in mortality caused by this disease, 5-10% in mild acute pancreatitis and 10-20% in severe pancreatitis.

Treatment of acute pancreatitis requires a complex, multidisciplinary approach involving the surgeon, the gastroenterologist, the specialist in intensive care and anesthesia and the imaging specialist.

The research aims to identify the favorable moment in the diagnosis and treatment of patients with acute pancreatitis and the development of a diagnostic and therapeutic protocol. The study is focused on the analysis of clinical observation materials and paraclinical examinations, focusing on the diagnosis and minimally invasive treatment of acute pancreatitis.

To achieve this goal, an important role is played by the identification of acute pancreatitis based on laboratory investigations (the values for hemoglobin, hematocrit, leukocytes, amylasemia, creatinine and pancreatic ascites were monitored), as well as by imaging exploration methods.

In achieving the intended goal, it is essential to assess the severity in acute pancreatitis according to the score systems, which was made by comparative analysis of the Ranson and Apache II score.

The era of minimally invasive approach has brought new alternatives to the management of acute pancreatitis. The advantage of these laparoscopic techniques is to decrease the operator stress in patients with critical general condition, and their application has increased exponentially, methods of minimally invasive treatment have developed and have been applied to patients in an attempt to find the best access to necrosis areas in the retroperitoneum.

The main target of the research is the identification of the optimal surgical therapeutic window and the evaluation of minimally invasive biliopancreatic decompression in acute pancreatitis. The purpose of the study was to present an original approach to minimally invasive treatment in acute pancreatitis and to illustrate its advantages by exposing the results obtained in

a group of patients. Minimally invasive pathogenic therapeutic approach of acute pancreatitis has as its primary objective the interruption of the pathogenic chain by early biliopancreatic decompression by laparoscopic approach, in order to improve the evolution of acute pancreatitis. It also aims to cut the symptoms: pain, dyspeptic syndrome, vomiting, dynamic ileus and prevention of local and systemic complications. After the introduction of early biliopancreatic decompression, a decrease in the incidence of severe pancreatitis is observed in the total of acute pancreatitis. The study leads to conclusions suggesting that laparoscopic treatment of acute pancreatitis has many advantages. We can explore, irrigate, perform biliopancreatic tree decompression and drain pancreatic lodge, also we can perform postoperative lavage through drainage tubes. The advantages of decompression of the extrahepatic bile ducts performed regardless of the etiological form and severity (I applied it to all cases of edematous pancreatitis) allows the removal of bile stasis, it can avoid the development of acute enzymatic cholecystitis or ascending angiocholitis, it causes the reduction of pancreatic edema especially cerebrospinal edema, it prevents the progression to acute pancreatitis. The extension of the condition can be determined and so we can apply the right treatment. The laparoscopic technique creates less trauma in the early stages of acute pancreatitis. Postoperative lavage and drainage also remove the harmful, irritating autodigestive effect of pancreatic ascites and prevent toxic products from entering the systemic circulation. Drainage tubes also serve to introduce lavage fluid, which allows the elimination of necrotic strips and detritus or the introduction of lactic acid to cut the harmful effect of intraperitoneal extravasated pancreatic juice. The pancreatic abscess can be drained by transcutaneous approach under ultrasound or CT.

The presented cases demonstrate a significant extension of the limits of laparoscopy, with the increase of the indication and "aggressiveness" of the surgical act, with the appeal to the laparoscopic procedure and reintervention, none of the cases being solved with the help of open surgery.

Acute pancreatitis remains a condition with unpredictable evolution and of great severity, sometimes fatal. The optimal treatment is the one adapted to each case, with the mention of the accreditation of the ideas of "therapeutic window". Laparoscopic surgical treatment in acute pancreatitis may be the first and sometimes the only form of treatment of some cases (of acute pancreatitis), selected in dynamics.

## I. THEORETICAL PART - PRESENTATION OF THE RESEARCH

The first part of the paper consists of six chapters that address theoretical notions about the surgical anatomy of the pancreas and its polyetiological disease - acute pancreatitis, with reference to the etiopathogenesis, diagnosis, complications, prognostic evaluation and treatment.

**Chapter 1** entitled "**Introductory notions**" shows preliminary concepts related to the exposition of clinical terminology specific to acute pancreatitis and a rich review of the efforts made over the centuries by countless clinicians and researchers in determining the cause of genesis of this disease.

**Chapter 2** entitled **The etiopathogenesis of acute pancreatitis** lists the obstructive, metabolic, infectious, vascular and idiopathic mechanical factors that determine the etiology of acute pancreatitis. The epidemiology of acute pancreatitis is discussed based on published studies on the incidence and mortality of acute pancreatitis after 2000. A subchapter describes the preenzymatic stage, the enzymatic stage, the enzymatic and cytotoxic sepsis, and the postenzymatic stage that chronologically systematizes the pathophysiological processes of acute pancreatitis. The recent pathogenic theories are discussed At the end of the chapter, providing a prognosis in detecting the underlying causes of the pathology.

**Chapter 3, Complications of acute pancreatitis** describes the local complications of acute pathology (hemorrhage, pancreatic seizure, pancreatic abscess, postnecrotic pancreatic cyst) and general complications due to multiple visceral damage (metabolic, neuropsychic, myocardial, pleuropulmonary and renal).

**Chapter 4** discusses aspects related to the **Treatment of acute pancreatitis** with reference to conservative medical treatment as the treatment chosen in the early phase (first 12-14 days) and which has as primary objective the restoration of electrolyte volume and balance, nutritional support and prevention of systemic complications. It involves hydroelectrolytic rebalancing, electrolyte supplementation, blood transfusion if the hematocrit falls below 25%, pain treatment, antibiotic therapy effectively in preventing pancreatic and peripancreatic septic complications, using antibiotics with good penetrability in the pancreatic tissue and with effective local concentrations. Specific treatments aim at antagonizing the enzymatic autodigestion of the pancreas, controlling pancreatic secretion or neutralizing inflammation mediators, and the treatment of organic insufficiency (ARDS, acute renal failure, cardiovascular

insufficiency, disseminated intravascular coagulation, hepatic insufficiency or metabolic encephalopathy). Surgical treatment of acute pancreatitis is a central goal in this research. The paper presents the treatment of infected necrosis, the treatment of pancreatic abscess, minimally invasive methods and the treatment of pancreatic pseudocyst according to specialized studies, consensus conferences and diagnostic and treatment guidelines.

## **II. SPECIAL PART - CLINICAL STUDY ON THE DIAGNOSTIC AND TREATMENT OF THE ACUTE PANCREATITIS**

The special part presents a prospective study carried out during the research and elaboration of the thesis, comprising 118 patients diagnosed with acute pancreatitis, hospitalized and treated in the Surgery Clinic I and II of Sibiu County Emergency Clinical Hospital, between January 2016 and December 2020.

**Chapter 5** sets out the **Research Framework**, specifying the purpose, objectives and stages of the research.

*The aim of the paper* is to identify the favorable moment in the diagnosis and treatment of patients with acute pancreatitis. Given the analysis of this case study and the reporting of the results to the data from the specialized literature, I proposed the elaboration of a diagnostic and therapeutic protocol. The study focuses on the analysis of clinical observation materials and paraclinical examinations, focusing on the diagnosis and minimally invasive treatment of acute pancreatitis.

### *Research objectives*

1. identification and classification of acute pancreatitis from an imaging point of view;
2. application of the optimal surgical window in acute pancreatitis;
3. the value of early biliopancreatic decompression performed minimally invasive in acute pancreatitis;
4. comparison of the results of minimally invasive treatment with those of conservative and surgical treatment in the group of patients studied.

### *Stages of research*

1. establish the positive diagnosis and the clinical form of disease;
2. calculating the Ranson and Apache II scores and performing a comparative balance of the two scores in assessing the severity of acute pancreatitis;

3. application of the surgical therapeutic window protocol for the subjects of group B;
4. synthesis of lesion macroscopic morphology in the studied cases of acute necrotic pancreatitis;
5. clinical, biochemical and imaging monitoring of the evolution during the hospitalization.

**Chapter 6** details the conduct of the research and the interpretation of the results.

Initially, the characteristic of the clinical material is presented. The general group comprising the 118 patients was divided into three groups.

Group A consists of patients who received conservative treatment, a group of 28 patients (23.72%).

Group B composed of patients who benefited from the surgical therapeutic window protocol, group with a number of 60 patients (32.43%).

Group C includes patients undergoing surgical treatment of complications of acute pancreatitis, with a number of 30 patients (25.42%).

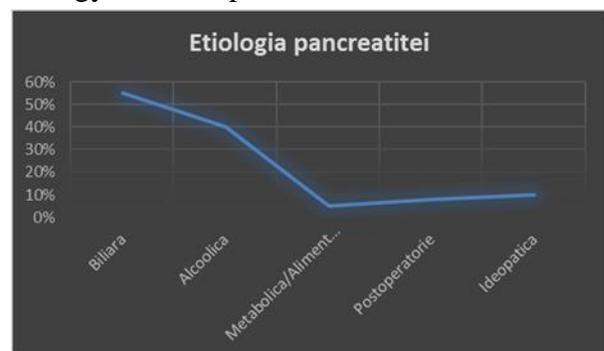
The classification of the general group was made according to the following criteria: gender, age, environment of origin, the degree of severity of acute pancreatitis in compliance with the Atlanta criteria.

Regarding the severity of pancreatitis, 86 pancreatitis were mild (72.88%) and 32 pancreatitis were severe (27.11%).

Patients studied were divided according to the etiology of acute pancreatitis as shown in the following diagram.

**Fig. 1 Etiology of acute pancreatitis**

Specialized literature indicates a frequency between 35-49% of acute pancreatitis of biliary etiology and a percentage of about 20% for pancreatitis of alcoholic origin. [46, 47, 48,



49, 224, 225] According to our study, the frequency of pancreatitis of biliary origin is 45% and the frequency of acute pancreatitis of alcoholic etiology is 30%, compared to data from the specialized literature, which explains a higher frequency of alcohol consumption in our country. As in the specialized literature, I found a significant percentage of acute pancreatitis of idiopathic origin of about 10% and 15% pancreatitis of other causes. The absence of a "gold standard" for

the diagnosis of this condition may explain the increased frequency of acute pancreatitis of unknown etiology and thus make it difficult to evaluate the tests proposed for diagnosis. [46, 47, 48, 225, 226, 227]

The information in the prospective study performed is from the observation sheets of the patients, namely:

- general information - age, gender, hereditary antecedents, associated diseases, way of onset of the disease, weight;
- clinical data - clinical signs and symptoms;
- laboratory data – at the moment of hospitalization, in the evolution of the disease, preoperatively and postoperatively;
- imaging investigations - ultrasound, lung radiography, abdominal radiography, computed tomography;
- data obtained intraoperatively - the extension of peripancreatic and pancreatic necrosis, the condition of the gallbladder and extrahepatic bile ducts, the existence of pathological fluids, with their collection for culture and antibiogram, associated visceral lesions;
- treatment - conservative, minimally invasive and open surgery;
- therapeutic results - healing, complications, recurrences, deaths.

The group was analyzed according to the etiological forms, the therapeutic decision and the treatment specific to the etiological form, the time interval between the admission and the day on which the patient underwent surgery (operative moment).

Minimally invasive/laparoscopic surgery proposed and performed on patients in group B was analyzed from several points of view: operative moment, location of necrosis in necrotic pancreatitis, length of hospitalization, reinterventions, postoperative complications, deaths. The collection of all this information shaped the value of laparoscopy in acute pancreatitis.

To identify and determine the severity we used the Atlanta criteria, namely:

- Glasgow score on admission  $\geq 3$
- Apache Score II  $\geq 8$
- presence of one or more organ dysfunctions (shock, acute respiratory distress syndrome, acute renal failure, upper digestive haemorrhage, disseminated intravascular coagulation)

- the presence of one or more local complications (pseudocyst, abscess or pancreatic necrosis)

We used the Balthazar criteria for the information provided by computed tomography.

The obtained data were processed by computer, with the application of the set of statistical programs Microsoft Excel and Medcalc-MedCalc trial version 11.6.0 (MedCalc Software, Mariakerke, Belgium). The data were presented in tables and diagrams for the demonstrative reflection of the obtained results.

Quantitative variables are presented with mean value and intervals ( $\pm$  limits). The Mann-Whitney test, the Student t test, was used for comparisons between groups of assays. The chi-square or  $\chi^2$  test was used to associate categorical values.

Predictive, specificity, sensitivity, accuracy or prognostic scores were established using the Statistical Operation Receptor Analysis (ROC) curve. Results with p value  $<0.05$  were considered statistically significant.

The zero point of the research is to establish the diagnosis of acute pancreatitis based on information provided by patients' symptoms at hospitalization, laboratory investigations, imaging methods of exploration and scoring systems.

The clinical data obtained from the objective clinical examination and the signs and symptoms of the patients allowed to raise the suspicion in most cases of a pancreatic pathology, and in the case of patients with severe general condition, investigations continued until the diagnosis of acute pancreatitis.

In order to assess the severity of the evolution, the anamnesis and the present accusations, the primary clinical inspection were taken into account and the following clinical parameters were examined:

- pain
- hemodynamic indices (pulse, blood pressure)
- frequency of breathing
- fever

The clinical picture of acute pancreatitis symptoms on admission is illustrated by the table below:

The laboratory study included the following clinical and biochemical examinations: blood count, urine summary examination, blood biochemical analysis: serum bilirubin, ASAT

(aspartate-aminotransferase), ALT (alanine - aminotransferase), alkaline phosphatase, GT range, prothrombin index, urea, creatinine, blood sugar, ionogram (K<sup>+</sup>, Na<sup>+</sup>, total Ca, ionizing Ca). Serum enzymes, amylase and pancreatic lipase were determined in the biochemical diagnosis, much more specific and with a longer half-life than amylases.

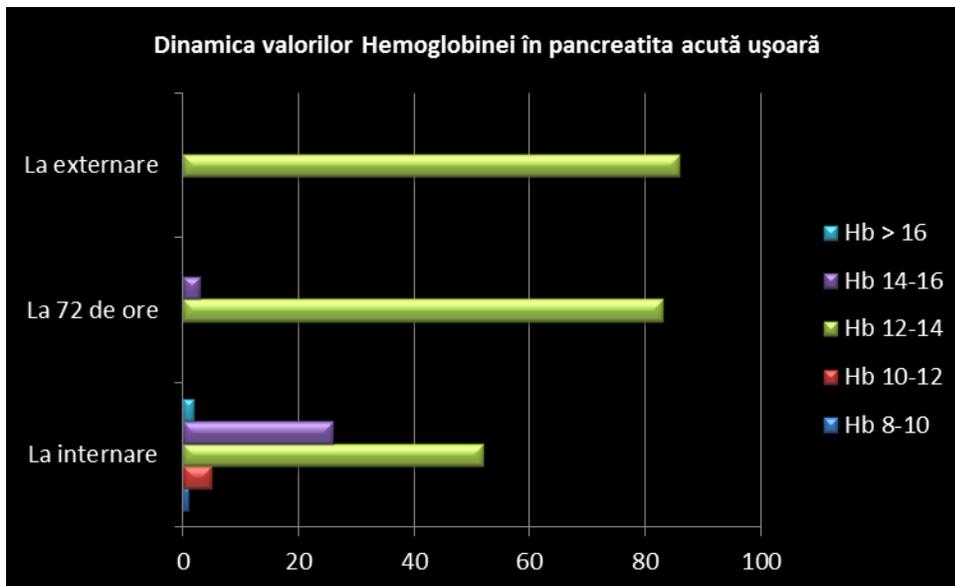
Studies on the prediction of severe pancreatitis were performed based on hemoconcentration, leukocyte counts, creatinine levels, amylase levels.

A study was conducted to see if hematocrit at admission and 24 hours after admission is associated with the severity of acute pancreatitis and pancreatic necrosis. The value of hematocrit was calculated in all patients at admission and in 104 (88%) patients 24 hours after admission, resulting 75 (87%) patients with mild pancreatitis and 29 (90%) patients with severe pancreatitis, obtaining the following results:

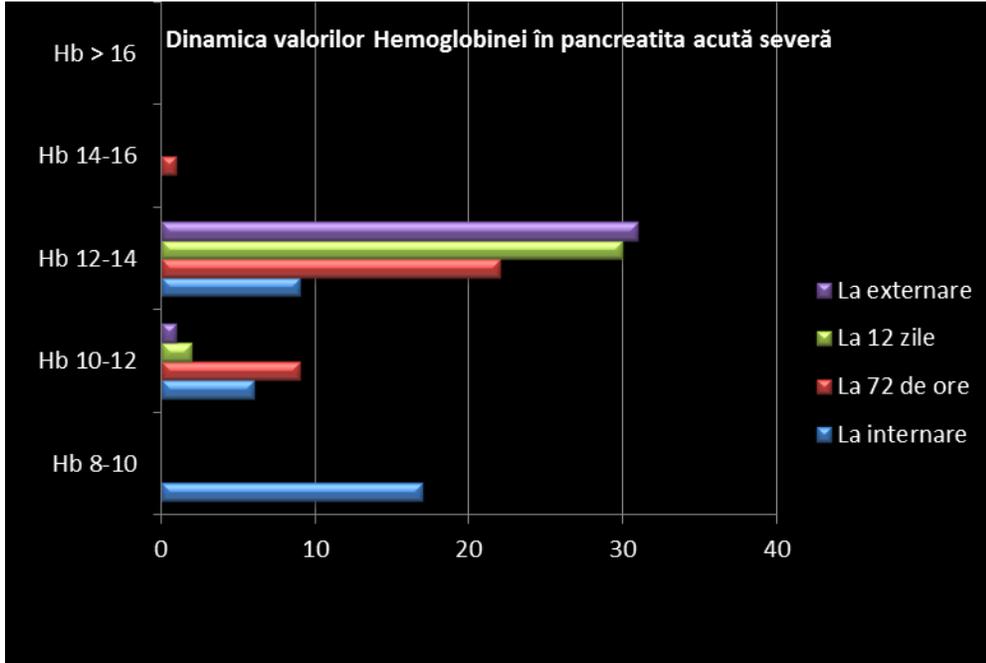
The study shows that the blood pressure analyzed in relation to sex, at admission and 24 hours after admission, has a good prognostic value for the severity of acute pancreatitis, patients without hemoconcentration have little chance of developing pancreatic necrosis or organic insufficiency.

Hemoglobin values were calculated at admission, at 72 hours, at 12 days and at discharge for mild and severe acute pancreatitis, the results being shown in Figures 2 and 3:

**Figure 2. Dynamics of hemoglobin values in acute edematous pancreatitis**

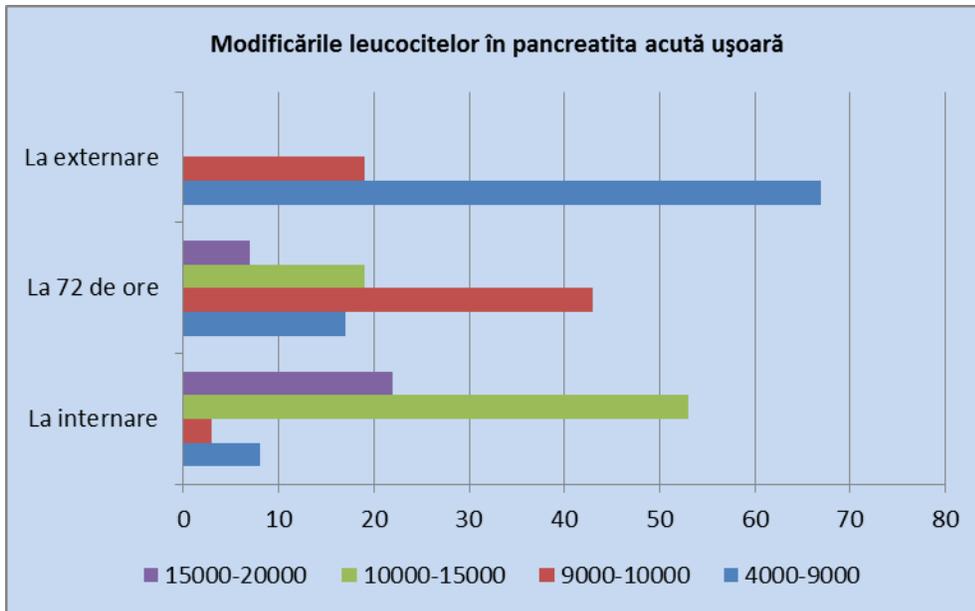


**Figure 3. Dynamics of hemoglobin values in severe acute pancreatitis**

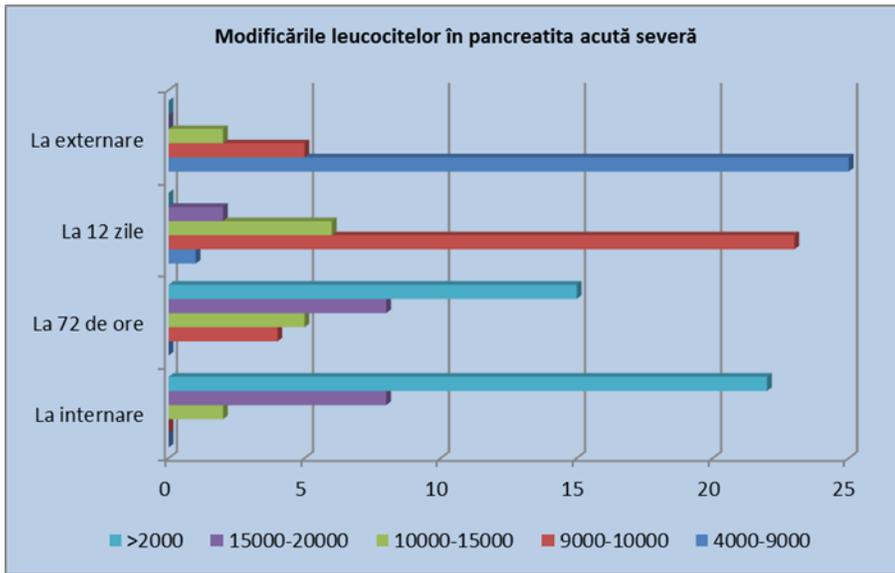


According to our study, there are increased values of leukocytes. This leukocytosis can be explained on the one hand by "enzymatic-humoral septicemia" and on the other hand by the presence in some patients of other associated infections. Leukocyte changes in acute pancreatitis are shown in Figures 4 and 5.

**Figure 4. Variation in leukocyte values in mild acute pancreatitis**



**Figure 5. Leukocyte changes in severe acute pancreatitis**

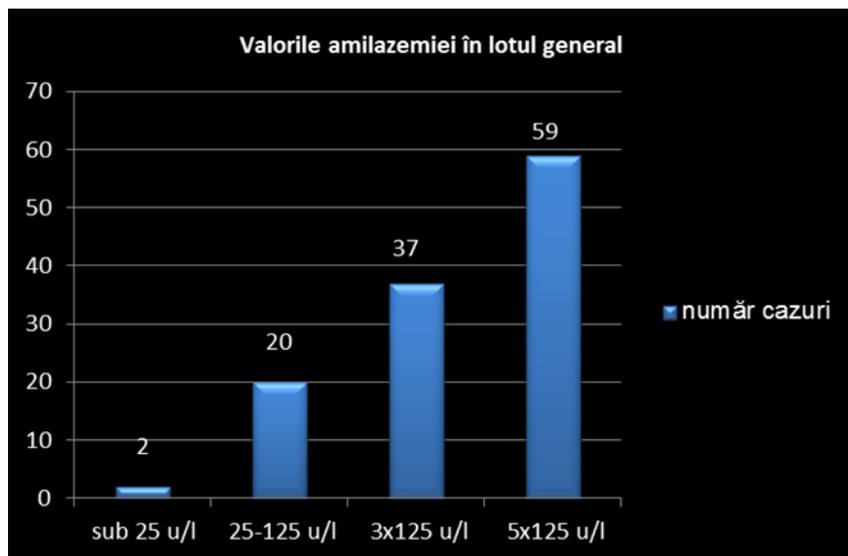


A prospective study composed of 118 patients was performed, creatinine was determined at admission in 85 patients and 48 hours after admission in 118 patients, and the severity of pancreatitis was assessed based on these results. The p-value was calculated on the relationship between creatinine and the severity of acute pancreatitis with a p-value at admission and at 48 hours  $<0.001$ , which shows a statistically significant high value on the relationship between creatinine values above 1.8 mg/dl and the severity of acute pancreatitis. Our study reveals that at creatinine values greater than 1.8 mg/dl 48 hours after admission there is a strong association with the development of pancreatic necrosis, with a positive predictive value of 89%, with similar values presented by other studies, Muddana presents a VPP of 93%. [147] In association with pulmonary pleurisy, it is a useful prognostic factor for severity in the first 24 hours.

As a clinical recommendation, we consider that patients with creatinine values  $> 1.8$  mg/dl 24 hours after admission should be closely monitored, as there is an increased risk of developing severe pancreatitis despite favorable initial clinical outcome.

The value of amylasemia was studied in the 118 patients in the general group. Amylases were determined by photometric method, the reference range being between 25-125 u/l and 5 times above the upper value, the results are shown in Figure 6. This diagram shows that at a number of 96 (81.3%) cases, amylasemia has proven to be a useful test in the diagnosis of acute pancreatitis.

**Figure 6. Amylase values in the general group**



Imaging investigations have an important role in evaluating patients with acute pancreatitis, in establishing the diagnosis, staging the severity of the inflammatory process and monitoring the occurrence of complications.

Imaging techniques include assessment of the pancreas by abdominal ultrasound, computed tomography, nuclear magnetic resonance, retrograde endoscopic cholangiopancreatography and angiography.

Imaging scans provide valuable information on the etiology and local complications of acute pancreatitis.

Thoracic radiography and empty abdominal radiography remain an important paraclinical indicator in emergencies for the exclusion of acute surgical abdomen.

Abdominal ultrasound performed in all patients showed a change in the volume of the pancreatic gland in 56 patients 47.5%, but with very little information about pancreatic morphology.

The benefit of abdominal ultrasound was more in the detection of gallstones, the appearance of changes in the main bile duct, the follow-up of the evolution of pancreatic and peripancreatic pathological collections.

Tomography has two major roles in the assessment of patients with pancreatitis, namely:

- initial staging of the severity of the inflammatory process - early detection of complications, identification of pancreatic, peripancreatic and parenchymal necrosis.

- as a method of monitoring in case of deterioration of the general condition or in case of lack of therapeutic response in patients confirmed as having acute pancreatitis.

Computer tomography remains a method that provides maximum information through dynamic comparisons of morphological changes. A major indication is CT in assessing the extent of necrosis and peripancreatic abscesses, as well as in highlighting the recurrence of abscesses after surgery.

The computed tomography severity index was designed for the existence of a gradual numerical system given by changes in computed tomography, which would reflect the severity scale of pancreatitis. [151] Thus, this system numbered from 0 to 10 is correlated with the morbidity and mortality rate: a severity score of 7-10 corresponds to a 92% complication rate and a 17% mortality rate, while a score of 0-1 corresponds to a morbidity and mortality rate of 0%. [151] The presence or absence of pancreatic necrosis is an important element in this scale.

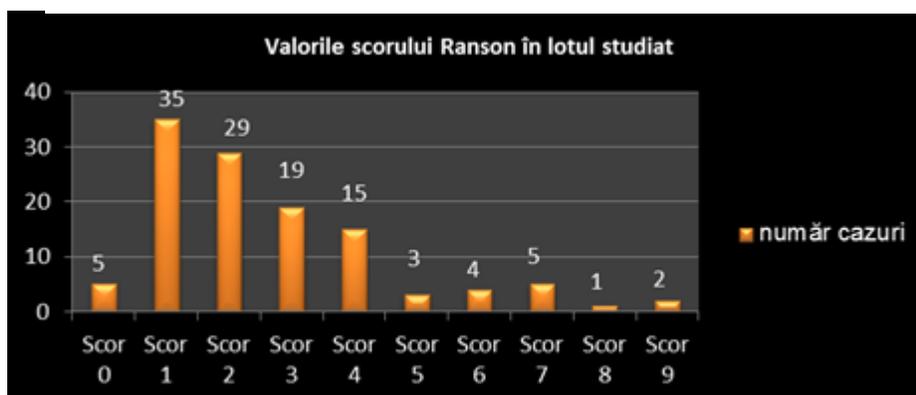
The CT scan was performed at admission in all patients studied. Only 32 of these were able to perform CT with contrast at admission for objective reasons.

**Figure 7. Staging by Balthazar score**



The assessment of severity in acute pancreatitis was made according to the Ranson and Apache II scoring systems.

**Figure 8. Ranson score in patients in the general group**



The table above shows that most cases were included in the Ranson score 1 and 2 corresponding to the mild form of pancreatitis.

For the 118 patients diagnosed with acute pancreatitis included in the prospective study, the severity of acute pancreatitis was determined within the first 24 hours by the Apache II criteria and 48 hours after admission by the Ranson criteria. Laboratory data and physiological parameters were taken at 24 hours for the Apache II score and at 48 hours for the Ranson score.

**Table 1. Mean Ranson and Apache II scores with mild acute pancreatitis and severe acute pancreatitis<sup>a</sup>**

	PAU (n=70)	PAS (n=48)	Valoare p
Ranson	1.70±1.23	3.73±1.80	<0.0001
Apache II 24ore	7.62±3.49	9.47±4.25	<0.004

<sup>a</sup> Data are presented as means ±standard deviations (SD). The calculation was performed with the Mann-Whitney U test

Mean values of Ranson and Apache II scores have been shown to be reliable in predicting the severity of acute pancreatitis.

The study shows that the Apache II test does not differ much from the Ranson Score in predicting the severity of acute pancreatitis. The results obtained in our study are similar to those published in the literature with values between 67% and 93%. [154]

The main goal of the research is the application of the surgical therapeutic window protocol in acute pancreatitis and the evaluation of early biliopancreatic decompression performed minimally invasive in this disease. The aim of this study is to present an original approach for minimally invasive treatment in acute pancreatitis and to show its benefits by presenting the results obtained on a group of patients.

Acute pancreatitis occurs most frequently due to increased pressure in the main intracanalicular bile duct, resulting in the reflux of enzymes from the Wirsung's canal. This hyperpressure occurs through the following production mechanisms:

- by papillary obstruction caused by the inclusion of a stone or papillary edema caused by lesions caused by the passage of a stone by the papilla, a pathogenic mechanism that occurs in biliary pancreatitis

- by the reflux of the duodenal contents given by the relaxation of the Oddi sphincter or the bile reflux by the spasm of the Oddi sphincter in the pancreatic canalicular system, a mechanism found in alcoholic pancreatitis.

The evolution towards a severe acute pancreatitis is the result of maintaining a hypertension in the main and intracanalicular bile duct, being influenced by the duration of its persistence as well. Early decompression of the biliary-pancreatic tree is necessary to prevent progression to severe acute pancreatitis. Decompression is performed minimally invasive medically and surgically.

The minimally invasive pathogenic therapeutic approach in acute pancreatitis consists of laparoscopic decompression of the bile duct by

- cholecystostoma
- transcistic drainage
- Kehr drain - adapted to the case

*Objectives:*

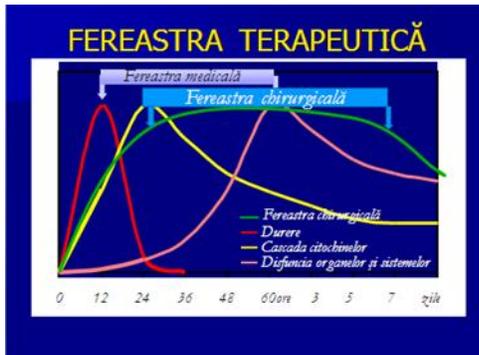
1. cutting the links of the pathogenic chain in acute pancreatitis by early biliopancreatic decompression by laparoscopic approach, aiming to improve the evolution of acute pancreatitis
2. cutting pain, dyspeptic syndrome, vomiting, dynamic ileus
3. prevention of local and systemic complications.

Norman (Am. J. Surg. 1998) [30, 155] introduced the term therapeutic window in the treatment of acute pancreatitis.

His study focused on cytokines and their role in the pathogenesis of acute pancreatitis, knowing that they are responsible for systemic complications of acute pancreatitis, up to MSOF, as evidenced by experimental animal studies. [30, 155] Knowledge of how they occur and their systemic action may allow the development of new therapies in acute pancreatitis.

Most patients with pancreatitis see a doctor on average 24 hours after the onset of pain. The next step is the production of cytokines that lasts several days. Although manifestations of SIRS may be from admission, most show severe systemic manifestations of pancreatitis after 2-4 days. This type of presentation allows, in the therapeutic window, the administration of cytokine antagonists that can attenuate or block the development of MODS.

**Figure 9. Therapeutic window in acute pancreatitis after Normann [30], modified Sabău**



Based on these arguments, we consider performing early biliopancreatic decompression combined with minimally invasive medical and surgical procedure, as a basic pawn in stopping the mechanism of triggering SIRS and local and general complications of severe acute pancreatitis. Complementary paraclinical examinations such as biochemical monitoring and repeated CT scans lead to avoidance of early exploratory laparotomy, with results in increased mortality.

Medical therapy included the following protocol:

1. Rapid canal decompression performed by
  - oddian spasmolysis by papillary contact anesthesia (Xylin1%) and lysis of oddian spasm in general (coronary dilator)
  - blocking the secretion performed by digestive emptiness (gastric tube) and pharmacologically by specific antisecretory agents-Sandostatin, general antisecretory agents-Atropine and gastric antisecretory agents
2. Analgesics (sometimes epidural analgesia in patients with severe pancreatitis)
3. Antibiotic therapy, by principle administration of Meronem. It was administered to all patients with severe pancreatitis (100%) at doses of 3 grams/day for at least 10 days.
4. Installation of central venous catheter for hydroelectrolytic rebalancing by administration of crystalloid and colloidal solutions and administration of parenteral feeding
5. External local refrigeration.

Early surgical-laparoscopic treatment performed in the surgical therapeutic window has the following objectives:

- exploratory - staging of pancreatitis, sampling of pancreatic ascites, evaluation of cystosteatonecrosis and pancreatic necrosis;
- pathogenic - biliopancreatic decompression (cholecystostomy), contact vagolysis by laparoscopic introduction of a periesophageal catheter, continuous capsular analgesia, by administration of contact anesthetics (Xylin, Lidocaine);
- radical indications - by draining the peripancreatic collections with lavage-drainage, necrectomies performed in laparoscopically selected cases, if not performed by open surgery and pathogenic treatment.

The technical procedure consisted of:

- the celioscopic approach of the upper abdominal stage by inserting the trocars after performing the pneumoperitoneum - the first trocar, the optical one is introduced supraumbilically, the following ones being introduced under optical control
- exploration of the peritoneal cavity, with confirmation of the diagnosis of acute pancreatitis and with the establishment of the intra-abdominal lesion balance
- decompression - biliary drainage performed by cholecystostomy, transcystic drainage or Kehr
- continuous capsular analgesia: by administration of contact anesthetics (Xylin, Lidocaine)
- drainage of the omental bursa through the section of the gastrocolic ligament
- necrectomy in advanced stages
- drainage and continuous postoperative washing in severe forms is performed with large caliber tubes to allow the evacuation of purulent secretions and beetles, with their postoperative washing with saline, lactic acid.

**Figure 10. Alternative introduction of the telescope for the best possible visualization of the lesions**



Alternative introduction of the telescope into all three 12 mm trocars

- ☞ alternative introduction of the telescope in all three 12 mm trocars (supraumbilical, epigastric and in the right flank);
- ☞ the telescope inserted through the right flank allows the approach of the pancreas to the level of the tail;
- ☞ the telescope with working channel facilitates the access to the necrotic corporeocaudal areas

**Figure 11. Telescope with working channel**

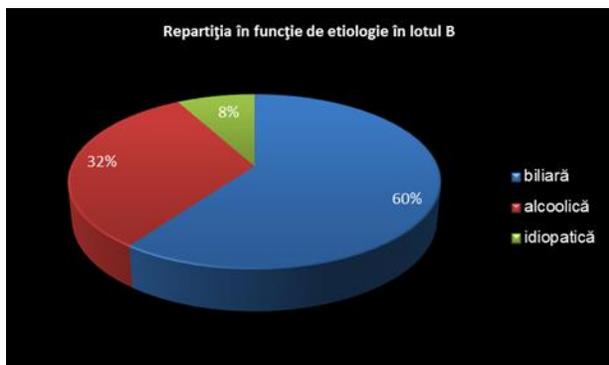


The study was performed on a group of 60 patients with acute pancreatitis, hospitalized and treated between January 2016 and December 2020. 36 were men and 24 women, with a mean age of 51.6 years  $\pm 11$  ( $p=0.57$ ). The distribution by age shows an average age of 55 years for women and 51 years for men, value  $p=0.087$ .

From the etiology point of view, lithiasis predominates with 36 cases (60%). An alcoholic etiology is observed in the 25-45 age group, with a number of 19 cases.

From a biochemical point of view, there were increased values of amylase at least 3 times the normal value, leukocytosis  $>16,000 \text{ mm}^3$  is statistically ( $p < 0.001$ ) and percentagely significant for patients with severe pancreatitis ( $n = 15$ ; 25%).

**Figure 12. Distribution according to etiology in group B**



The etiology in patients in group B was similar to that in the general group. The severity of acute pancreatitis was established by:

- Atlanta criteria - the presence of visceral dysfunctions, the presence of local evolutionary complications;
- Ranson score  $> 3$
- amylase value  $> 3$  times the normal value

According to these criteria, we encountered 45 mild pancreatitis and 15 severe pancreatitis.

The patients were included in the complex medical-surgical therapeutic protocol applied in acute pancreatitis as from January 2016 in the Surgery Clinic II of Sibiu County Emergency Clinical Hospital.

Patients were admitted urgently in 95% of cases and 5% by transfer from other non-surgical wards.

The following paraclinical investigations were used at admission: simple abdominal radiography, thoraco-pleuro-pulmonary radiography, electrocardiogram, biochemistry, hemoleukogram, ionogram, inflammatory samples, coagulation tests.

Ultrasound was used in all hospitalized cases, as a routine investigation, but especially for the detection of gallstones.

CT scan was performed in all cases, the severity of pancreatitis assessed by CT according to the Balthazar score according to table 2.

**Table 2. Balthazar score**

<i>Stadiu</i>	<i>Număr cazuri</i>	<i>%</i>
<b>A</b>	<b>17</b>	<b>24</b>
<b>B</b>	<b>29</b>	<b>42</b>
<b>C</b>	<b>4</b>	<b>15</b>
<b>D</b>	<b>6</b>	<b>12</b>
<b>E</b>	<b>4</b>	<b>7</b>
<b>Total</b>	<b>60</b>	<b>100</b>

Laparoscopic surgical interventions were performed according to the therapeutic protocol presented, most performed in the first 7 days (n=60), being practiced in all cases of acute edematous pancreatitis, thus achieving the decompression of the bile tree and the cutting of the pathogenic chain, with the reduction of SIRS and local and systemic complications.

**Table 3. Laparoscopic surgery**

<b>Interventia chirurgicală laparoscopică</b>	<b>Cazuri</b>
Colecistostomie+lavaj/drenaj bursă omentală + plex celiac și pericolecistic	36
Colecistectomie+drenajtrancistic/Kehr+lavaj/drenaj bursă omentală și plex celiac	15
Colecistectomie +drenaj	12
Necrectomie pancreatică+colecistostomie +drenaj/lavaj bursa omentala și plex celiac	8
Laparoscopie exploratorie+drenaj	6

77 interventions were performed in the 60 patients in group B, which shows that several interventions were performed in some patients during the same hospitalization.

Local postoperative complications were present in n=9 cases and general complications occurred in 7 patients.

**Table 4. Average hospital days to patients in group B**

<i>Spitalizare</i>	<i>Timp mediu de spitalizare</i>	<i>Limite</i>
Total	13.2 zile	7-34 zile
ATI	7.6 zile	5-22 zile

Mortality for group B was 5% (n = 2). The two cases died by MSOF, patients with severe pancreatitis since admission.

The study presented give us the possibility to draw some conclusions suggesting that laparoscopic treatment of acute pancreatitis has many advantages. We can explore, irrigate, perform biliopancreatic tree decompression and drain pancreatic lodge, also we can perform postoperative lavage through drainage tubes. The advantages of decompression of the extrahepatic bile ducts performed regardless of the etiological form and severity (we applied it to all cases of edematous pancreatitis) allows the removal of bile stasis, it can avoid the development of acute enzymatic cholecystitis or ascending angiolitis, it causes the reduction of pancreatic edema especially cerebrospinal edema, it prevents the progression to acute pancreatitis.

The extension of the condition can be determined and so we can apply the right treatment. The laparoscopic technique creates less trauma in the early stages of acute pancreatitis. Postoperative lavage and drainage also remove the harmful, irritating autodigestive effect of pancreatic ascites and prevent toxic products from entering the systemic circulation. Drainage tubes also serve to introduce lavage fluid, which allows the elimination of necrotic strips and detritus or the introduction of lactic acid to cut the harmful effect of intraperitoneal extravasated pancreatic juice. Pancreatic abscess can be drained by transcutant approach under ultrasound or CT control, performed by us in two cases, with subsequent favorable evolution.

Laparoscopic surgery is one of the treatment aspects of acute pancreatitis. Medical therapy is equally important in the patient's recovery and consists of hydroelectrolytic rebalancing to compensate for losses in the third space, gastric decompression, enzyme therapy, treatment of organ failure in severe acute pancreatitis, antibiotic therapy, parenteral nutrition, respecting as much as possible the proposed medical protocol.

The presented cases demonstrate a significant extension of the limits of laparoscopy, with the increase of the indication and "aggressiveness" of the surgical act, with the appeal to the laparoscopic procedure and reintervention, none of the cases being solved with the help of open surgery.

The favorable evolution of laparoscopically treated cases, as well as the hospitalization period with variations between 7 and 34 days, require the evaluation of laparoscopy in the surgical treatment of acute pancreatitis, as the first and sometimes the only surgical form of treatment of some acute pancreatitis cases, selected in dynamics.

The patients included in the first group, Group A with conservative therapy, were 28. There were 11 women and 17 men. The mean age was  $55.75 \pm 0.7$  years. The severity diagnosis was established according to known clinical and paraclinical criteria. Thus, 17 cases were classified as severe acute pancreatitis and 11 as mild acute pancreatitis.

The objectives of the conservative treatment in the intensive care unit aimed at treating the systemic inflammatory response syndrome and organic dysfunctions, preventing and treating complications.

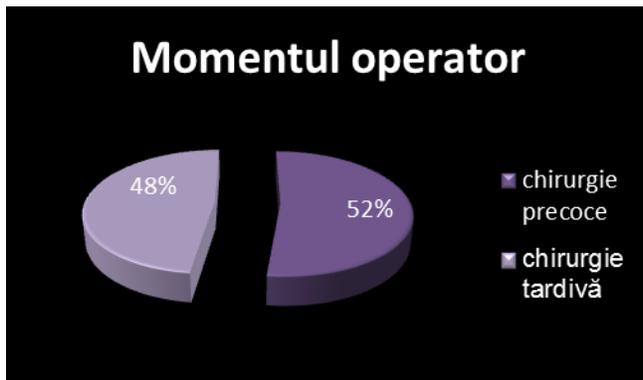
Conservative treatment of acute pancreatitis included: pain treatment, pathogenic treatment, supportive treatment of homeostatic functions and balances, hydro-electrolytic support, antibioprohylaxis, anti-enzymatic therapy, nutritional support.

The average number of hospitalization days for patients in group A was 21.2 days, with limits between 16 and 55 days.

90 patients (76%) from the general group were operated, the type of surgical interventions being different depending on the operative moment (early surgery or late surgery).

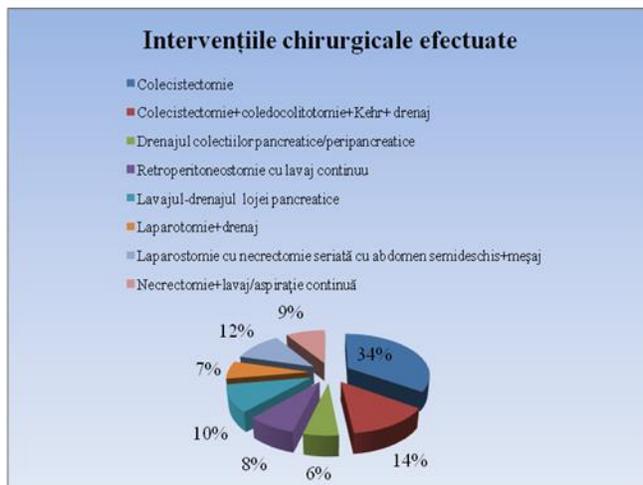
The indications and the type of surgery were different depending on the etiology of pancreatitis, the operative time, the age, strongly associated, the CT appearance, suspicion of pancreatic infection, septic shock, emergency interventions, persistent MODS.

**Figure 13. Distribution of interventions by operative moment**



The most common surgical technique applied is cholecystectomy, of which 22 laparoscopic cholecystectomies, followed by cholecystectomy and drainage of the main bile duct, this is due to the biliary etiology of acute pancreatitis which is 45% in the group of 118 patients

**Figure 14. Type of surgery**



Early surgery (first 14 days) was performed in 47 patients (52%), under the conditions presented in table 9:

Late surgery (over 14 days) was performed in 43 (48%) cases with the indications presented in table 5:

**Table 5. Late surgery**

Intervenții chirurgicale tardive (peste 14 zile)	
Tipul operației	Număr cazuri
Laparotomie+necrectomie seriată+meșaj	18
Evacuarea colecțiilor pancreatice și peripancreatice	9
Retroperitoneostomie+necrectomie cu lavaj continuu	9
Necrectomie și lavaj/aspirație continuă	7

Mortality according to the operative moment is represented in table 6.

**Table 6. Mortality by operative time**

Moment operator	Cazuri (n = 90)	Mortalitate (n=26)
Operații precoce	47	16
Operații tardive	43	10

The average hospital stay was 35.5 days, with limits of 15 days to 56 days. In Intensive Care Unit, the average hospital stay was 26 days, with limits from 12 days to 40 days.

**Table 7. Hospitalization period**

<i>Spitalizare</i>	<i>Timp mediu de spitalizare</i>	<i>Limite</i>
<b>Total</b>	35,5 zile	15-56 zile
<b>ATI</b>	26 zile	12-40 zile

## CONCLUSIONS

1. The correct diagnosis of acute pancreatitis must be completed within 24 hours after admission. Otherwise, postponing emergency treatment in favor of a full investigation can lead to intra-abdominal "catastrophes".
2. The prospective study of 118 patients shows that the incidence of acute pancreatitis is 1.5 times higher in men than in women.
3. The incidence of acute pancreatitis is 2.5 times higher in urban patients compared to rural patients.
4. Depending on the age at which this condition appeared, the average age of onset was 53.2 years, with a peak between 40-49 years, with a maximum between 60-69 years for women and 50-59 years for men.
5. The most incriminated etiology is the biliary one (45%), followed by the ethanolic etiology (30%), other causes being the unknown ones, post-traumatic, respectively metabolic (25%).
6. Early and accurate staging of the severity of acute pancreatitis should be performed by careful clinical evaluation, and in severe clinical forms using Ranson score, APACHE II score, as well as computed tomography with non-ionic contrast agent.
7. Clinical data alone are not predictive and may lead to errors in classifying disease forms in 50% of cases. The presence of clinically detected organ failure (pulmonary, circulatory or renal) is an indication of the severity of the episode of acute pancreatitis.
8. Clinical evaluation is very important and should not be underestimated in medical practice.
9. The etiology of acute pancreatitis should be determined in at least 75-80% of cases and no more than 20-25% should be classified as idiopathic.
10. After the onset of acute pancreatitis, the evolution of the disease is no longer influenced by the etiological factors that underlie its onset.
11. The mortality rate is influenced by the age of the patients than by the various etiologies of the disease, being directly proportional to the severity of the complications.
12. Despite the low specificity, ultrasound is recommended as an initial examination in all patients suspected of acute pancreatitis and may be repeated whenever clinical conditions

require it. Its value is often limited by the dynamic ileus accompanying acute pancreatitis, through the gases accumulated in the intestine (sentinel loop).

13. Computed tomography is the most important imaging exploration for the diagnosis of acute pancreatitis. Maximum information about pancreatic and peripancreatic morphological rearrangements is obtained within 3-4 days after onset. Computed tomography should be performed in all cases between the 3<sup>rd</sup> and 10<sup>th</sup> day after admission with non-ionic contrast agents.
14. Chest radiographs performed within the first 24 hours after admission in combination with creatinine values > 1.8 mg/dl may be useful markers for predicting the severity of acute pancreatitis.
15. Chest radiography and empty abdominal radiography remain indicated in urgency and for the exclusion of acute surgical abdomen.
16. Acute pancreatitis remains a condition with unpredictable and very serious evolution sometimes fatal, with a sudden evolution, regardless of the age of the patients.
17. The introduction of the surgical therapeutic protocol of severe pancreatitis stops the evolution of pancreatitis towards the necroto-hemorrhagic form, with a full success related to the healing of patients, with a minimum percentage of complications and deaths.
18. Laparoscopic treatment in acute pancreatitis has multiple advantages, it allows exploration of the abdominal cavity, biliopancreatic decompression, drainage of toxic substances from the abdominal cavity and postoperative lavage that eliminates the enzymatic toxic effect of the abdominal cavity and prevents the occurrence of SIRS and MODS.
19. The optimal treatment is the one adapted to each case, with the mention of the accreditation of the ideas of "therapeutic window", pathogenic treatment and minimum invasiveness. The laparoscopic approach is a choice, due to the minimal aggression on an unbalanced organism.
20. We systematically recommend laparoscopy of surgical cases, in the interval of the surgical therapeutic window (first week), for the stage diagnosis of acute pancreatitis, early treatment in the edematous phases, cutting the evolution to aggravation by biliary decompression and neurolysis.

21. Currently, along with the improvement of the treatment of critical patients, many patients with severe acute pancreatitis survive in the initial phase of the systemic inflammatory response and enter the second phase, dominated by septic complications and the consequences of multiple organ dysfunction.
22. The introduction of the protocol of the surgical therapeutic window of acute pancreatitis with a pathogenic, minimally invasive therapeutic approach consisting in laparoscopic decompression of the biliary tree (cholecystostomy, transpapillary drainage, Kehr drainage-adapted to the case), showed a favorable evolution of cases, with a minimum mortality (2 patients), with reduced hospitalization period, reduced postoperative complications, reduced hospitalization costs compared to patients who have reached the stage of acute pancreatitis complications.
23. The treatment of acute pancreatitis requires a complex, multidisciplinary approach, involving the surgeon, the gastroenterologist, the Anesthesia and Intensive Care specialist and the Imaging specialist.
24. All cases of severe acute pancreatitis will be treated and monitored in intensive care units, where they will benefit from the entire therapeutic arsenal.