SUMMARY

ACUTE PANCREATITIS ETIOPATHOGENIC, PROGNOSTIC AND THERAPEUTIC FACTORS

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CONTENTS

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1. INTRODUCTION

During the doctoral thesis entitled " **Acute pancreatitis etiopathogenic factors, prognostic and therapeutic** " conducted by graduate Gabriel-Sebastian Petrescu at the Clinic I General Surgery, a retrospective analysis of all patients admitted for acute pancreatitis was performed between January 1, 2013 and December 31 2018 in the First Surgery Clinic of the University Emergency Hospital from Craiova to identify patients who developed specific complications during hospitalization. The cases were structured in two subgroups: uncomplicated cases (group 1) and complicated cases (group 2).

The bachelor's thesis is structured in two main parts: the stage of knowledge and personal contributions.

2. THE STAGE OF KNOWLEDGE

The chapter contains current data on etiopathogenic factors, prognostic and therapeutic factors in acute pancreatitis and reviews articles in the literature on acute pancreatitis and etiopathogenic factors, prognostic and therapeutic.

Acute pancreatitis is a pathological entity that presents many problems of diagnosis and treatment. Acute pancreatitis is an inflammation, ranked among the most common reasons of gastrointestinal etiology for hospitalization in a surgery clinic, without a specific therapy so far. The severe form is a real challenge for a doctor, because it has multiple obscure causes, as well as a complex pathophysiology. Thus, the diagnosis is difficult, and the choice of the right time for surgical treatment is controversial, the treatment being more often non-specific, supportive for the various systems and organs affected.

In a group of 337 patients, laboratory and imaging investigations were performed to diagnose and determine the severity score of acute pancreatitis and the level of correlation between the values of the neutrophil-lymphocytes ratio and the Balthazar score, as a valid evaluation method for the local and systemic inflammation changes. The study of the distribution of acute pancreatitis by sex, according to etiology, confirms the predominance of acute ethanolic pancreatitis in men, but also the higher proportion (54%) of male pancreatitis (181 men compared to 156 women) with the male / female sex ratio 1 16 / 1. Average neutrophil-lymphocytes ratio value varied depending on severity score Balthazar, which became larger as acute pancreatitis has become more advanced and beyond a certain limit may be considered a simple indicator to determines the severity of acute pancreatitis.

In a group of 314 patients, laboratory and imaging investigations were performed to diagnose acute pancreatitis and lymphocyte-monocyte ratio. Results: CT scanning was performed in three quarters of patients, and 25% of patients were in favourable evolutionary stages. It is important for patients to be aware of the evolutionary stage and to accept and follow the treatment. The lymphocyte-monocyte ratio means lower values displayed in cases of severe form of acute pancreatitis compared to mild to severe acute pancreatitis and mild acute pancreatitis (2.49 vs 2.69 compared to 3.77). The value of the ratio between lymphocytes and monocytes varies proportionally depending on the extent of the local inflammation process. In the first 72 hours after the presentation of the lymphocyte-monocyte ratio in patients with organ failure was lower than in patients without organ failure. The lymphocyte-monocyte ratio can be used as a simple method to identify the severe evolution of acute pancreatitis, along with other already agreed clinical-imaging scores.

Lymphocytes-monocytes ratio, platelet-lymphocytes ratio and neutrophil-lymphocytes ratio parameters are simple and can easily get to assess the inflammatory condition of a patient who is suspected of acute pancreatitis. Laboratory investigations and imaging have been performed to diagnose and determine the severity score of acute pancreatitis lymphocytes-

monocytes ratio, platelet-lymphocytes ratio and neutrophil-lymphocytes ratio. Results: Average neutrophil-lymphocytes ratio and platelet-lymphocytes ratio in patients with complications was lower than in patients with complications. It is important for patients to be aware of the evolutionary stage and to follow the treatment and programming and to do an abdominal or pancreatic tomography, in contrast to the control and prevention of complications with late onset. The determination of lymphocytes-monocytes ratio, platelet-lymphocytes ratio and neutrophil-lymphocytes ratio is a simple investigation and can help to control and prevent the onset of late complications.

3. OWN CONTRIBUTIONS

The personal contributions chapter is divided into 3 subchapters: the working hypothesis and general objectives, the research methodology and results. In the 1st subchapter of this thesis the hypotheses underlying the research topic are mentioned, choosing and justifying the methods used to test these hypotheses (there are analyzed and interpreted the data obtained, the statistical methods used are mentioned), as well as the limits of the chosen research methods. Also, to butter referred ate sources et and how to collect it data.

In subchapter "research methodology" the topic of the doctoral thesis is approached through the approach assumed by the doctoral student of the investigation process, in which is describe to guide and justify the theoretical basis of research is. At the same time there is described the material and method used by listing the raw materials used (chemicals, reagents etc.) and biological materials used in the study, the peculiarities and the way of research are described (the collection , analysis and processing data), which provides information on the chosen research methods / techniques and tools, the type and design of the study, justifying the choice of methods. Also, in this section there are mentioned the statistical methods used. The materials and methods are set out in detail to ensure the

reproducibility of the research. In this subchapter there are mentioned the statistical processing methods and research ethics commission agreement UMF Craiova for the conducted studies.

In the *management of acute pancreatitis,* the Atlanta Consensus Conference played a key role in directing clinical practice. Then a classification system based on objective anatomoclinical assessment criteria of the disease was developed, which caught the creation of the premises for optimizing the treatment. Thus, the surgical treatment largely gave way to conservative therapy, but continued to have many controversies regarding the indication, the operative moment and the technique used.

The information was collected from the hospital's electronic database, as well as from patients' medical records and medical records. Data collected included: year of hospitalization, sex, age, Balthazar score, symptoms, leukocytes, neutrophils, platelets, monocytes, urea, creatinine, amylase, transaminases, diet, analgesics, antispasmodics, complications, type of surgery (if performed), length of hospital stay, comorbidities.

Using the data from the literature and the experience from 1st Surgery Clinic, we performed a complex study on acute pancreatitis establishing study objectives. Following the setting of the objectives, the inclusion and exclusion criteria have been established, as well as the complications that will be taken into account.

RESULTS

In the 1st Surgery Clinic of the Craiova County Emergency Clinical Hospital, 337 patients were hospitalized between January 1, 2013 - December 31, 2017 with the diagnosis of Acute Pancreatitis out of a total of 10,402 hospitalized patients, representing approximately 16.20% of the total hospitalized patients, being distributed by years, as follows: 4.7% were cases of acute pancreatitis for 2013, 3.5% were cases of acute pancreatitis for 2014, 3.1% were cases of acute pancreatitis for

2013 2015, 2016 3% were cases of acute pancreatitis for 2016, 1.9% were cases of acute pancreatitis for 2017. Thus, we can see a decrease in cases of acute pancreatitis from one year to another.

The distribution of cases per month is different each year, not being able to predict a month in which there should be more or fewer cases of acute pancreatitis: 16% of cases were in January 2013, 13% of cases were in March 2014, 17% of cases were in January 2015, 14% of cases were in February and 14% the following month for 2016, 15% of cases were in January and 15% in November for 2017.

The evolution of acute pancreatitis in 65% of cases was self-limited, with a favourable response to conservative treatment, and in 35% of cases acute pancreatitis had a severe evolution.

The disease has no age limits, but according to the literature the maximum incidence is found in decades 6 and 7, which is also confirmed by our study, which shows the average age of onset of acute pancreatitis of 61.88 years, with limits between 19 and 98 years. The lower limit for females was 19 years, and the upper limit was 93 years. The lower limit for males was 22 years, and the upper limit was 98 years. A maximum number of patients was observed in the age range 70-79 years (74 patients), followed by the range 60-69 years (68 patients). The mean age of male patients was 60.03 years, and the mean age of female patients was 64.01 years. It is observed that in male patients the disease started 1 year and a half earlier than the average age of the study group and a difference of 4 years compared to females.

The study by the sex distribution of acute pancreatitis according to etiology confirms the predominance of acute ethanolic pancreatitis in males, but also the higher proportion of pancreatitis in males (181 men compared to 156 women), with a male / female sex ratio of 1.16 / 1. In the study group, males predominated, having a percentage of 54%.

The incidence of patients from rural areas was slightly higher, 171 from rural areas compared to 166 from urban areas, without finding a satisfactory explanation. The percentage of the source environment was only 51% for the rural

area compared to the urban area of 49%. This incidence has a rural / urban ratio of only 1.03 patients in rural areas to 1 patient in urban areas.

Imaging scans (empty abdominal radiography, abdominal ultrasound, computed tomography) are part of the algorithm for diagnosing acute pancreatitis, as well as the algorithm for monitoring the evolution of acute pancreatitis. Chest radiography, empty abdominal radiography, abdominal ultrasound, CT (computed tomography) with or without contrast material are essential elements for establishing a correct positive diagnosis, etiological diagnosis and severity diagnosis, as well as monitoring the evolution of acute pancreatitis.

Amylasemia was present in 76% of patients. Amylases had normal values in 81 of the patients, in 256 they were above normal values, the highest value being 6555 U / l.

The most representative visceral dysfunction was represented by cardiovascular diseases (37%).

Balthazar A, B and C scores reflect clinically significant acute pancreatitis mild represented 19%, 24% and 22% of cases, and grades D and E, which indicate severe acute pancreatitis have a share of 15% and 20 %. The highest share was Balthazar B acute pancreatitis with 24% with enlarged pancreas, with an intraglandular fluid collection and changes in the pancreatic parenchyma. 72% of cases had a favourable evolution with the remission of clinical and biological phenomena and imaging changes under conservative treatment. Of the patients with an unfavourable prognosis, 50% had a Balthazar E score.

4. Discussions

The surgical treatment has precise indications, being important the choice of the optimal moment of the institution of the surgical treatment.

It is important for patients to be aware of their developmental status and to follow the treatment and to accept the performance and scheduling of contrast-

enhanced abdominal or pancreatic computed tomography in order to control and prevent late-onset complications. The patient should be hospitalized, monitored clinically, paraclinical and radiologically. Establishing treatment for the correction of hypovolemia and hemodynamic optimization are crucial for initial survival. Proper infection prevention and control are essential for subsequent survival. Supportive therapy of systems and organs is essential in the prevention and treatment of dysfunction syndrome and/or plurivisceral insufficiency. The combination of the biological markers procalcitonin and C-reactive protein, which have the best sensitivity, for the detection of severe forms of acute pancreatitis. The timing of cholecystectomy in acute pancreatitis due to gallstones remains controversial. In patients with mild to moderate pancreatitis (three or fewer Ranson criteria), performing early cholecystectomy before the resolution of laboratory abnormalities or physical examination would result in a shorter hospitalization without adversely affecting the results.

In patients with mild to moderate biliary pancreatitis, an early cholecystectomy policy could result in a significant reduction in hospitalization without increasing complications or mortality.

The study group included patients with acute pancreatitis who were entered into the most complete database possible, followed by a statistical analysis of the results using an analysis program to calculate risk factors, determining the limit value above which complications can occur, as well as the chance of their occurrence.

The neutrophil to lymphocytes ratio, the platelet to lymphocytes ratio and the lymphocyte to monocytes ratio are simple parameters that can be used to easily assess the inflammatory condition of a patient suspected of acute pancreatitis.

The results for the mean neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in uncomplicated patients was lower compared to patients with complications. In contrast, for the lymphocyte-monocyte ratio, the mean was lower for patients with complications.

5. CONCLUSIONS

At the level of conclusions, since the counting of the elements shown in the blood is usually performed at the hospitalization of the patient, the determination of these reports is simple, fast and cheap and can help control and prevent complications with late onset. The role of NLR, PLR and MRL as predictive factors in the evolution of acute pancreatitis has not been thoroughly studied and can provide a simple and effective tool for assessing the severity of the disease.

In conclusion, I want to emphasize that my study of the etiopathogenic, prognostic and therapeutic factors in acute pancreatitis cannot claim to be complete and perfect and I would like to remind you that in a study it is impossible to exhaust a certain subject given that anytime I can add and discover and other issues that have not been described enough or that you failed even to treat.