Original Paper

Utilizing Multiparameter Scores and Procalcitonin as Prognosis Markers for the Degree of Severity of Acute Pancreatitis

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ABSTRACT: Aim: Corroborating the Ranson, Marshall, computer tomography severity index (EPIC score) multiparameter tests with the biological marker procalcitonin in order to establish the degree of severity of acute pancreatitis for therapeutic management and rate of complications. Material and method: 20 patients were surveyed, diagnosed with acute pancreatitis in the surgery clinic of the Military Emergency Hospital Dr. Ștefan Odobleja, between 2016-2017, with the aim of determining the clinical, etiological and severity diagnosis by corroborating the multiparameter scores with the plasma level of procalcitonin. Results: Following the use of multiparameter scores to identify the degree of severity of acute pancreatitis, we established that the best prediction is achieved by the Ranson score and the computer tomography severity index (EPIC score), with an accuracy of 90%. As for the values of the correlation coefficient, this was highly significant when correlating Ranson score and procalcitonin (r = 0.918). Other correlations were also highly significant, with values of r = 0.797 when correlating EPIC score and procalcitonin, and r = 0.736 when correlating Marshall score with procalcitonin. Conclusion: Our study achieved an early identification of the severe form of acute pancreatitis, by using the multiparameter tests and the biologic marker procalcitonin, allowing for the appropriate therapy to be implemented and thus decreasing the complication rate of this pathological entity. Levels of serum procalcitonin exceeded the normal limit of 2 ng/ml for 37.5% of the intermediate - severe form patients, and for 100% of the severe form patients. The levels of procalcitonin were highly correlated with the Ranson score, with a slightly lower correlation for the Marshall and EPIC scores.

***KEYWORDS**: multiparameter scores, procalcitonin, acute pancreatitis, correlations*

Introduction

Pancreatic pathology has two major representatives – acute pancreatitis and pancreatic neoplasms.

Our study was aimed at ensuring an early, complex (clinical, paraclinical and imagistic) diagnosis for acute pancreatitis, an entity which requires the early adoption of the appropriate therapy for the specific type of pancreatic inflammation.

The degree of severity for each case is assessed considering the value of multiparameter scores, alongside other biological markers. In 1993, Assicot described significant increases of procalcitonin, a biochemical parameter closely linked to the organism's inflammation response to these aggressions, in bacterial and fungal infections and in sepsis [1].

In acute pancreatitis, procalcitonin demonstrated a predictive potential for the infection of necrosis [2], classification as the severe form and application of an appropriate therapeutic surgical conduct.

All of which has oriented us towards correlating multiparameter scores with the levels of procalcitonin.

Material and method

20 patients were included in our study, diagnosed with acute pancreatitis in the surgery clinic of the Military Emergency Hospital Dr. Ștefan Odobleja, between 2016-2017. Our patient group included 14 men (70%) and 6 women (30%), aged between 20 and 75 years.

Study inclusion as well as exclusion criteria were established, and patients were required to sign an informed consent form when admitted.

These inclusion criteria contained presence of symptomatology at no later than 96 hours of admission, the presence of systemic inflammation response syndrome (SIRS), and an age greater than 18 years.

The exclusion criteria were represented by: patient age under 18 years, the absence of SIRS, the presence of hepatitis B, C or even HIV in the patient's personal history. The personal data of patients, which might have revealed their identity, was not documented.

The steps preceding the acute pancreatitis diagnosis are represented by: positive diagnosis, etiological diagnosis, and not least severity diagnosis. As etiology, 60% of the study patients presented biliary injury, 25% alcoholic cause, and a lower percentage (15%) other etiologies. The severity diagnosis was established on the basis of the multiparameter scores (Ranson, Marshall, the computer tomography severity index - EPIC score) and the biological marker procalcitonin.

The clinical diagnosis was represented by the presence of characteristic epigastric pain with posterior radiation, amylase levels over 3 times the normal, and characteristic computer tomography changes [3].

Multiparameter scores were represented in our study by the Ranson score, determined both on admission and after 48 hours, based on the following parameters: age of above 55 years, number of leucocytes over 16.000/mm^3, aspartate aminotransferase (AST; SGOT) over 250 U/I, lactate dehydrogenase (LDH) over 350 U/I, glycemia over 200 mg/dl; later, after 48 hours: hematocrit decrease by more than 10% the admission value, oxygen partial pressure in arterial blood below 60 mmHg, a serum calcium level lower than 8mg/dl, an increase of blood ureic nitrogen of over 5mg/dl and fluid retention of over 6 l, with a bases deficit of over 4 mEq/l [4].

The modified Marshall score identifies the presence of organ dysfunction through the assessment of three systems: cardiovascular, respiratory and renal.

The diagnosis of persistent organ failure is established when a score of 2 or higher is reached, for one or even all the evaluated systems.

A transitory (below 48 hours), organ failure identifies the moderately severe form of acute pancreatitis [5].

As for pancreatic imagistic exploration, we utilized the extrapancreatic inflammation on computer tomography score (EPIC score), highlighting the characteristic changes to pancreatic and peripancreatic tissue, with the aim of establishing the appropriate therapeutic indications and prognosis correlations [5] with the Balthazar score.

Balthazar score

A-normal pancreas (0p);

B-enlargement of pancreas (1p);

C-densification of peripancreatic fat and edema (2p);

D-single peripancreatic fluid collection (3p);

E- ≥2 poorly defined peripancreatic fluid collections and/or the presence of gas bubbles (4p);

Pancreatic necrosis

None (0p);

≤ 30% necrosis (2p);

31-50% (4p);

> 50% (6p);

Mild pancreatitis 0-3p;

Intermediate/moderate pancreatitis 4-6p;

Severe pancreatitis 7-10p.

The level of procalcitonin was determined using the Elecsys 2010 MODULAR ANALYTICS System, by using an immunochemical test, electro-chemiluminescence immunoassay (ECLIA). This investigation uses certain organical compounds for marking, which generate light electrochemically. The principle used was the Sandwich type, with two incubation processes, and the results were presented in a calibration curve and a master curve [6].

Results

After processing the clinical observation, paraclinical and imagistic data, the degree of severity of acute pancreatitis could be established for the study patients, which is presented in table no.1. The group presented 8 cases of moderately severe acute pancreatitis (40%) and 12 cases of the severe form (60%) (Table 1, Fig.1).

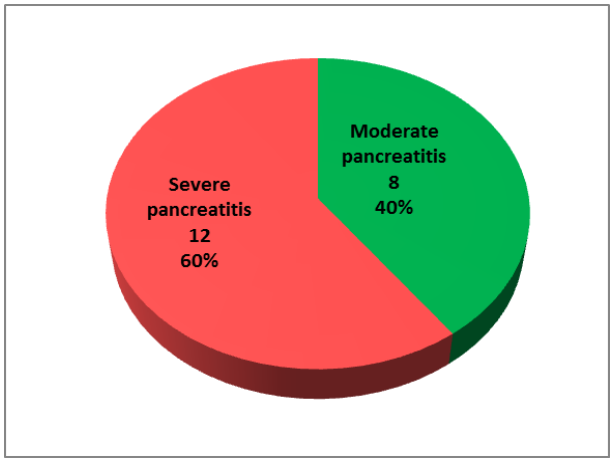

Fig.1. Distribution of the study group by pathology

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Table 1. Pathology of the study group

Acute pancreatitis	Cases	Percentage
Moderate pancreatitis	8	40.00%
Severe pancreatitis	12	60.00%
Total cases	20	100.00%

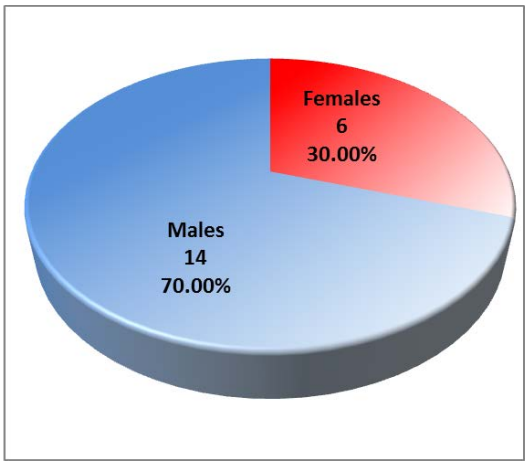

Fig.2. Gender distribution of the study group

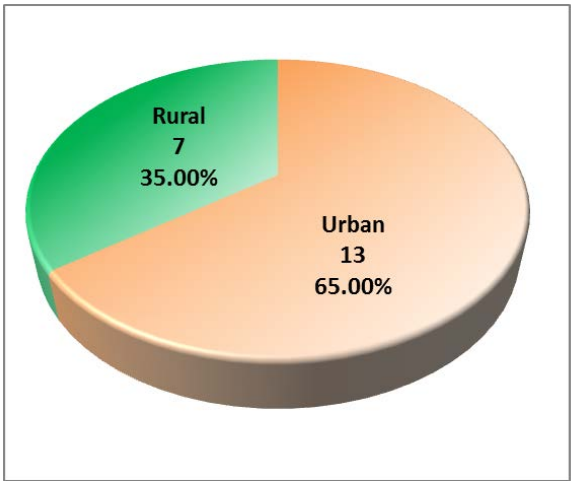

Fig.3. Area of residence distribution of the study group

The patients included in the study were represented, according to the Balthazar score, by 70% Balthazar D score patients, followed by 20% Balthazar C score and 10% Balthazar B score.

Out of the total 20 patients, 14 were men (70%) and 6 women (30%), with an mean age of 43.5 years (ages between 18-75 years) (Table 2, Fig. 2), of which 65% were from urban areas and 35% from rural areas (Table 2, Fig.3)

Table 2. Gender and area of residence distribution of the study group

Gender	No. of cases	Percentage
Females	6	30.0%
Males	14	70.0%
Total	20	100.00%
Residence	No. of cases	Percentage
Urban	13	65.00%
Rural	7	35.00%
Total	20	100.00%

The procalcitonin serum values were increased for 37.5% of cases (5 patients) of intermediate severe acute pancreatitis, and for 100% of cases (12 patients) of severe acute pancreatitis (Table 3, Fig. 4). Transient organ failure (under 48 hours) was present in 8 patients, presenting changes to the renal apparatus in a proportion of 50% and changes to the cardiovascular apparatus also in a proportion of 50%.

Table 3. Serum values of procalcitonin in AP forms

AP	Procalcitonin	No. of cases	Percentage
Intermediate severe	>2 ng/mL	3	37.50%
	<2 ng/mL	5	62.50%
Severe	>2 ng/mL	12	100%
	<2 ng/mL	0	0%

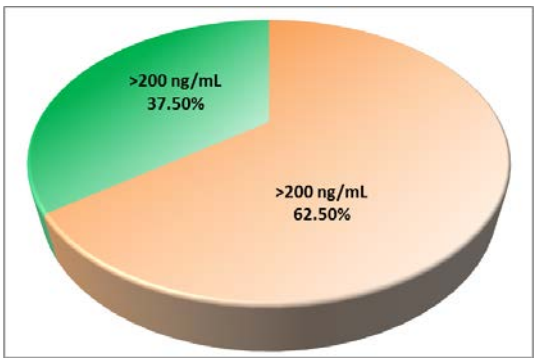

Fig.4. Graphical representation of procalcitonin levels in acute pancreatitis forms

As for persistent organ failure (over 48 hours), of the 12 patients classified as suffering from severe acute pancreatitis, changes to the renal apparatus were present in a proportion of 30% and changes to the cardiovascular apparatus in a proportion of 70%.

The connections between the levels of procalcitonin and the multiparameter scores determined in acute pancreatitis to investigate organ dysfunction (Marshall, EPIC) or the evolution type (Ranson), were analyzed using the Pearson r correlation coefficient. All the values of the correlation coefficients were highly significant ($p<0.001$), the most important correlation being between the Ranson score and procalcitonin (r=0.918). The correlation with the EPIC score had an r value of 0.797, and the correlation with the Marshall score an r value of 0.736 (Table 4, Fig. 5, Fig. 6, Fig. 7).

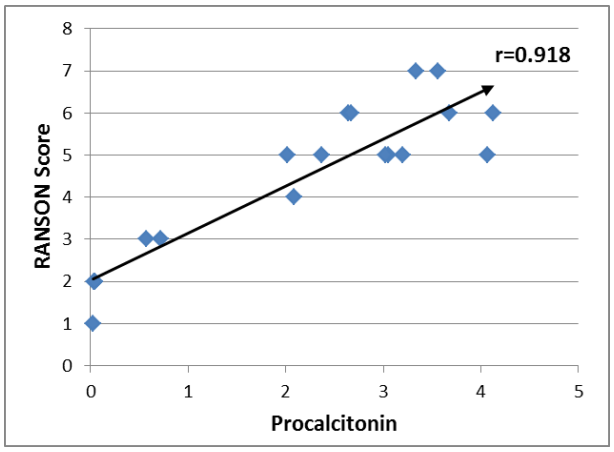

Fig.5. Correlation between procalcitonin levels and RANSON score

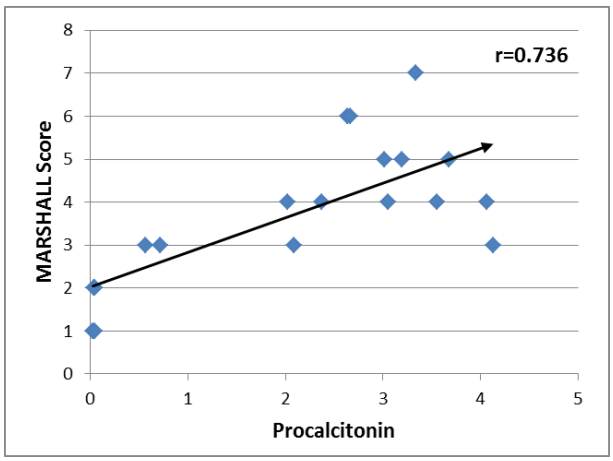

Fig.6. Correlation between procalcitonin levels and MARSHALL score

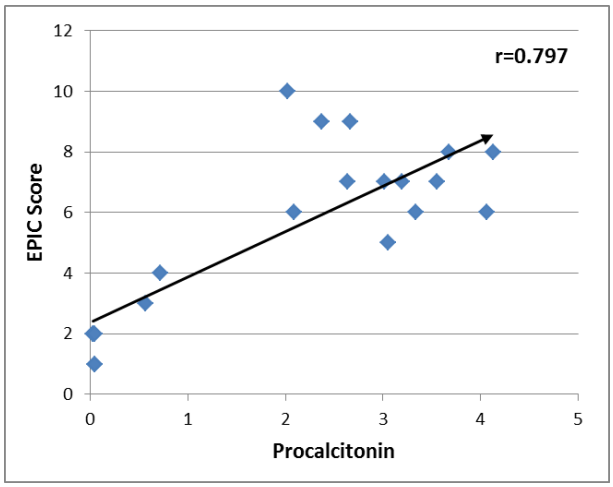

Fig.7. Correlation between procalcitonin levels and EPIC score

Table 4. Correlation coefficients among the study variables

Pearson's r	Procalcitonina	Ranson	Marshall
Ranson	0.918		
Marshall	0.736	0.863	
EPIC	0.797	0.840	0.727

In a moderate-severe acute pancreatitis case, a procalcitonin level of below 2ng/ml was recorded, and computer tomography showed changes typical for an acute cholecystopancreatitis, grade C, inflammation score and necrosis 0 (Fig.8).

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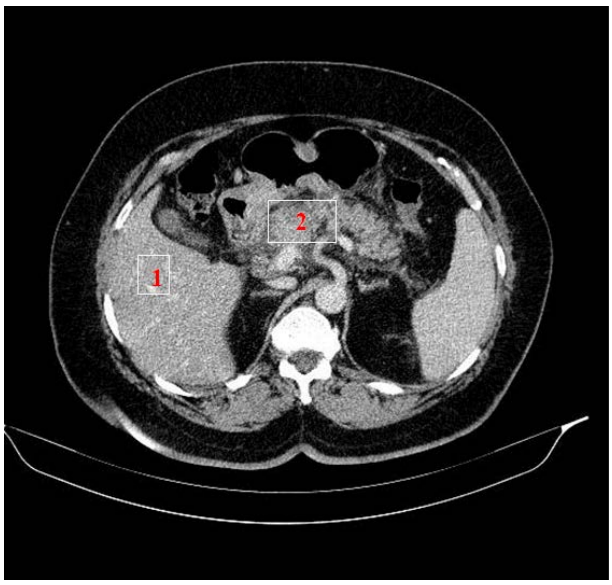

Fig.8. Acute cholecystopancreatitis grade C 1. Homogenous liver, no localized processes. Cholecyst presents multiple lithiasis, up to 1.7 cm with thickened walls, diffuse contour. 2. Lipomatous pancreas, diffuse contours, cephalic anteroposterior diameter 3.37 cm, infiltration of pre and retropancreatic adipose tissue, diffuse inflammatory infiltration, thickening of the anterior pararenal fascia, no abscess or pseudocyst formations – which suggests an inflammation score of 2, grade C, necrosis 0, computer tomography severity index of 2 (image from the archive of the Military Clinical Emergency Hospital Dr. Stefan Odobleja)

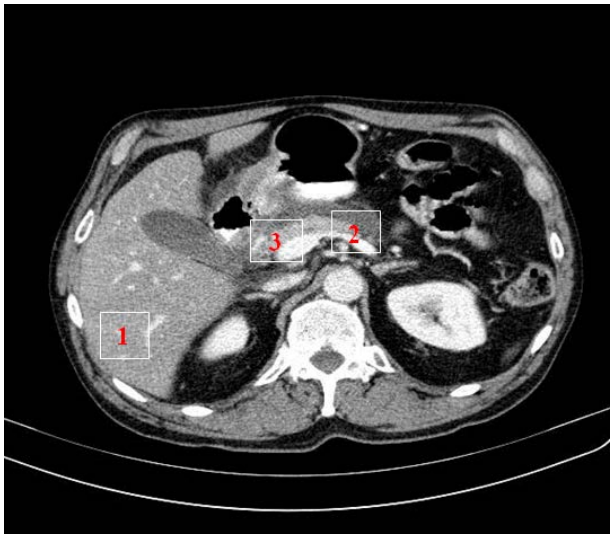

Fig.9. Acute cholecystopancreatitis grade D. 1. Homogenous liver, steatosis. Infundibular septate cholecyst, no radiopaque calculi. 2, 3. Pancreas - cephalic anteroposterior diameter 5.5 cm, corpocaudal anteroposterior diameter 2.6 cm, diffuse cephalic contour, with the presence of peripancreatic fluid collection. (image from the archive of the Military Clinical Emergency Hospital Dr. Stefan Odobleja)

Also in the group of those suffering from intermediate severe acute pancreatitis, a patient presenting a procalcitonin level of over 2ng/ml, with computer tomography highlighting a Balthazar grade D acute pancreatitis (Fig.9).

From the group of patients suffering from severe acute pancreatitis we showcase a case presenting procalcitonin level below 2ng/ml, with computer tomography changes characteristic of a Balthazar grade E acute pancreatitis (Fig.10).

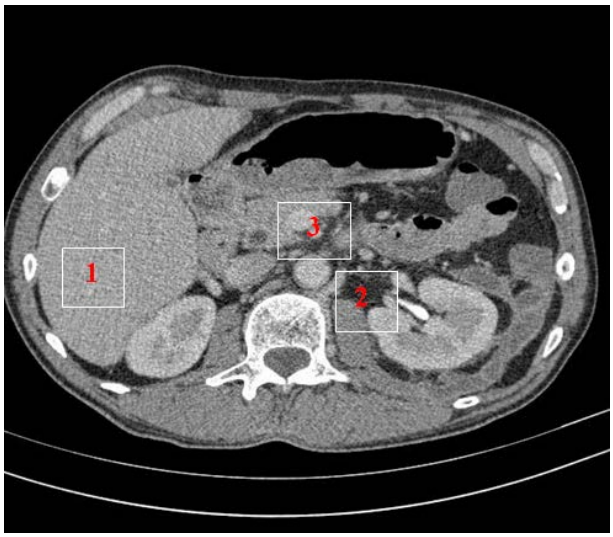

Fig.10. Acute cholecystopancreatitis grade E. 1. Homogenous liver, no localized processes. Infundibular septate cholecyst, multiple radiopaque calculi. 2,3. Pancreatic corpocaudal hypertrophy, diffuse contour, diminished corpocaudal compared to cephalic region, and peripancreatic fluid collection; collection is extended into the omental bursa, to the perisplenic, pararenal anterior and posterior areas, and respects the perirenal space and the left parieto-colic space. (image from the archive of the Military Clinical Emergency Hospital Dr. Stefan Odobleja)

We computed the ROC (receiver operating characteristic) curves, as well as the usual parameters for clinical tests: sensibility, specificity, positive and negative predictive values, accuracy, to compare the prediction value for severe pancreatitis of the 4 tests.

The results led to the conclusion that the best prediction is achieved by the Ranson and EPIC scores, with an accuracy of 90% (Fig. 11, Table 5).

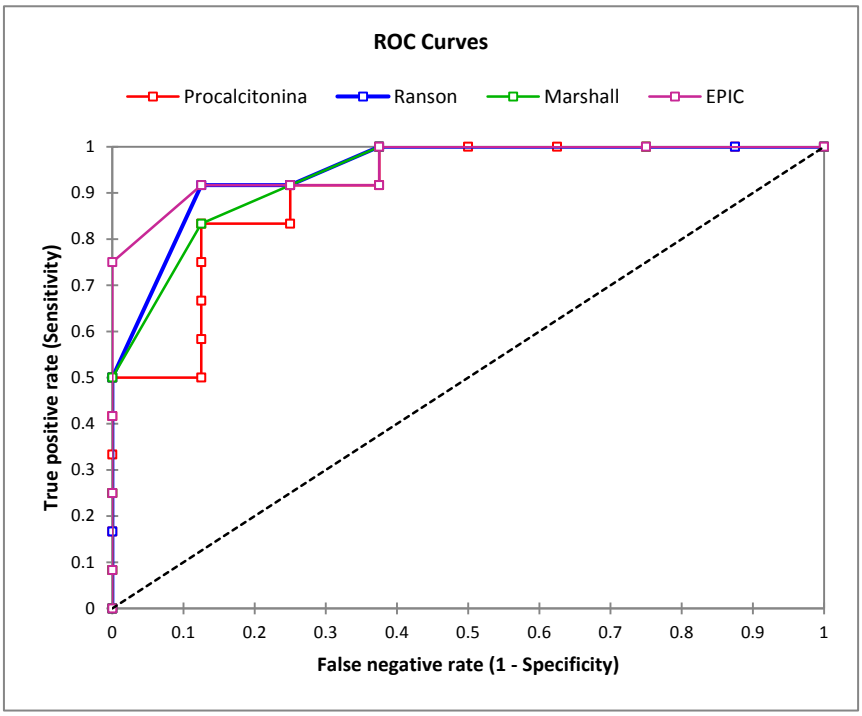

Fig.11. Comparison of the ROC curves for the study variables

Table 5. ROC curves area under the curve (AUC) values and measures of accuracy of the predictor variables for severe pancreatitis (sensitivity, specificity, positive predictive value – PPV, negative predictive value NPV, positive and negative likelihood ratios – LR, accuracy)

Variable	AUC	Threshold	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Sn+Sp	Accuracy
Procalcitonin	0.906	2.090	83.33%	87.50%	90.91%	77.78%	6.667	0.190	170.83%	85.00%
RANSON	0.948	4.000	91.67%	87.50%	91.67%	87.50%	7.333	0.095	179.17%	90.00%
MARSHALL	0.938	3.000	83.33%	87.50%	90.91%	77.78%	6.667	0.190	170.83%	85.00%
EPIC	0.958	5.000	91.67%	87.50%	91.67%	87.50%	7.333	0.095	179.17%	90.00%

Discussions

A large number of studies show the role of plasma procalcitonin, in comparison with other inflammation markers, in the prediction of the severity degree of acute pancreatitis and infection of necrosis [7,8]. This is an important marker used for evaluating the degree of severity, the emergence of multiple organ dysfunction syndrome (MODS) as well as hemorrhagic pancreatic necrosis [9].

In the Bettina study, procalcitonin as well as C reactive protein were analyzed, to the conclusion that monitoring these parameters allows a better assessment of patients at risk of major complications and an adequate clinical assistance to infections [10]. Some studies exist which maintain that procalcitonin is not a safe marker for evaluating the severity of acute pancreatitis without infectious complications [11], even if in some studies procalcitonin is useful in establishing the therapeutic conduit for surgical treatment, being associated with biliary etiology in the Brunkhorst et all paper [12].

A prospective study by Byung Geun Kim demonstrated the role of procalcitonin in the prediction of the severity of pancreatic inflammation damage and showed that a level of procalcitonin of 0.5 ng/mL has a sensibility and specificity of 87% and 24% respectively, compared to the Ranson score, which on values higher than 3 has a sensibility and specificity of 92% and 97% respectively [13].

In our study we used the correlations between the values of procalcitonin and the multiparameter scores used in evaluating organ dysfunction (Marshall, EPIC) and the type of evolution (Ranson), and obtained the best correlation between the Ranson score and procalcitonin, r=0.918.

Numerous correlations between the plasma levels of procalcitonin and the degree of severity

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of acute pancreatitis scores were noted in literature, however the most faithful and useful correlation remains the one with the Ranson score, also highlighted in our study.

As for the prediction of the severe form of acute pancreatitis, in our research the Ranson and EPIC scores have an accuracy of 90%, similarly to the data in literature [5].

The computer tomography severity index (EPIC score) was noted in literature as presenting a positive correlation between complications and the mortality rate of acute pancreatitis patients [14,15].

In the case of a pilot study, an EPIC score between 7-10 was used in predicting a 92% morbidity and 17% mortality rate in patients diagnosed with acute pancreatitis, in comparison with an severity index value between 0-1, which presented a 2% morbidity and 0% mortality [16].

Conclusion

Our study achieved an early identification of the severe form of acute pancreatitis, by using the multiparameter tests and the biologic marker procalcitonin, allowing for the appropriate therapy to be implemented and thus decreasing the complication rate of this pathological entity.

Levels of serum procalcitonin exceeded the normal limit of 2ng/mL for 37.5% of the intermediate - severe form patients, and for 100% of the severe form patients.

The levels of procalcitonin were highly correlated with the Ranson score, with a slightly lower correlation for the Marshall and EPIC scores.

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