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INTRA-ABDOMINAL PRESSURE, A PROGNOSTIC MARKER IN THE EVOLUTION OF ACUTE PANCREATITIS

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Abstract: *In acute pancreatitis some prognostic scores have been suggested, based on clinical, laboratory and radiological criteria. The most popular are: Ranson score, APACHE II score and CT severity index (CTSI). The trend is to find a prognostic marker that is easy to use, cheap, and reproductible. Recently, the increase of the intra-abdominal pressure (IAP) has drawn attention. Material and Methods: From January 2012 to April 2014, a group of 64 patients, admitted to the Clinical Department of Anaesthesia and Intensive Care and the Surgical Departments of the SCJU Sibiu, with the diagnosis of acute pancreatitis, were included in this observational prospective study. The cut-off values, the specificity and sensitivity of the prognostic scores were calculated using the receiver operating characteristics (ROC) analysis curves. Results: At a cut-off value of 12 mm Hg IAP max has a sensitivity of 0,75, similar to Ranson score at 48 h (0.72 at a cut-off value 3) and CTSI (0,73 at a cut-off value 4). Better results are just for APACHE II score at 24 h (0,88 at a cut-off value 8). IAP max has a specificity of 0,88, simillary to CTSI (0,83) and APACHE II score (0,82). Conclusions: In our study maximum IAP could be correlated with prognostic markers for severe evolution in acute pancreatitis.*

INTRODUCTION

Severe acute pancreatitis (SAP) is one of the main causes of intra-abdominal hypertension which can lead to multiple organic dysfunction, increase in mortality and days of hospitalization in the Intensive Care Unit.(1,2,3)

Few prognostic scores have been suggested based on clinical, laboratory and radiological criteria, the most popular of which are: Ranson score, APACHE II score, Balthazar and CT severity index (CTSI).

Computerized tomography is an important method for the diagnosis and the assessment of the severity and the complications of acute pancreatitis (AP).(4) There are studies that consider the CTSI the best prognostic marker of the severity of acute pancreatitis.

The trend of the latest research is to find a prognostic marker that is easy to use, cheap, and reproductible. Recently, the increase of the intra-abdominal pressure (IAP) after the onset of acute pancreatitis has drawn more and more attention.

AIM

The aim of this study is to analyze the utility of IAP as a prognostic marker in the evolution of acute pancreatitis. The study is based on the comparison of intra-abdominal pressure with the already known markers of acute pancreatitis severity – CTSI, APACHE II and Ranson score.

MATERIALS AND METHODS

The study has been approved by the Ethical Board of the Sibiu County Clinical Emergency Hospital (SCJU Sibiu).

From January 2012 to April 2014, a group of 64 patients admitted to the Clinical Department of Anaesthesia and Intensive Care and the Surgical Departments of the SCJU Sibiu, with the diagnosis of acute pancreatitis, were included in this observational prospective study. The diagnosis of acute pancreatitis was established on the basis of both clinical criteria (abdominal pain, dynamic ileus, nausea, vomiting etc.) and laboratory criteria – the three times elevation of the level of serum amylases.

The identification of the severity index for all types of pancreatitis was performed by respecting the Atlanta criteria and namely one criterion or more of the following:

1. The Ranson score on admission higher or equal to 3 (recalculated within the first 48 hours)
2. APACHE II score higher or equal to 8 (anytime during the evolution of the disease)
3. The presence of SIRS or one or more organ dysfunctions/failures
4. The presence of one or more local complications (pancreatic necrosis, abscess, pancreatic pseudocyst).

The exclusion criteria were:

1. Impossibility to perform investigations or tests dynamically due to technical conditions or due to the death of the patient, in case of fulminant outcome.
2. Elderly patients, with associated comorbidities which could have influenced the evolution towards severity of the disease and mortality (the age groups between 70-79 years and 80-89 years), the late age representing by itself a disturbing, confusing factor and it could negatively influence the evolution toward severity of the disease.

The patients were divided into two groups: those with

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mild acute pancreatitis (MAP) and those with severe acute pancreatitis (SAP) according to the Atlanta classification criteria.

The laboratory and the physiological data were prospectively recorded, at admission and every 24 hours for APACHE II score and at admission and after 48 hours for Ranson score.

Intra-abdominal hypertension (IAH) is defined as the progressive increase of the intra-abdominal pressure over 12 mmHg (IAP >12 mmHg) while the abdominal compartment syndrome (ACS) is the combination between IAP >20 mmHg and the onset of organ dysfunction.(5,6,7,8,9) The abdominal pain may influence the measurement of IAP. This is the reason for measuring IAP only after the management of pain.

IAP was measured every 24 hours and the maximum value was used for the analysis and the correlation with imagistic prognostic factors (CT severity index). IAP was measured through the technique described by Kron *et al*. (10). We used a urine bladder catheter, connected to a pressure transducer. We introduced 50 ml of sodium chloride solution into the bladder and the pubic symphysis was considered the level 0. The maximum IAP was considered the highest value obtained at all measurements.

The tomographic computerized images found in our patients were interpretated with CTSI. The evaluation of the pancreatic necrosis levels (30%, 50% or over 50%) was achieved by performing contrast-enhanced CT.

The first CT-scan was performed at admission and the second after 48 - 96 hours, after the development of necrosis. CTSI is obtained by summing the inflammation and the necrosis scores.

CTSI = Balthazar score + Necrosis Score (11)

The statistical analysis was accomplished through the SPSS programme, 15.0 version (Statistical package for the social sciences). The quantitative variables were referred to as absolute numbers and percentages. The statistical analysis was performed with the student *t* tests, Mann –Whitney U test and Chi square test. The results of the statistical tests were presented, if applicable, with a confidence interval (CI) of 95%. P values less than 0.05 was statistically considered. The cut-off values, the specificity and sensitivity of the prognostic scores were calculated using the receiver operating characteristics (ROC) analysis curves.

RESULTS AND DISCUSSIONS

The demographic, clinical, biochemical variables are shown in table no. 1.

Table no. 1. The demographic, clinical, paraclinical variables of the group

Variables	
Age	24 – 66 years
Gender	40 men /24 women
Etiology	72% gallstones 25% alcoholic 3% dyslipidemia
APACHE II score on admission, mean (SD*)	7,6 (6,8)
APACHE II score at 24 h, mean (SD)	8,2 (6,3)
The Ranson score at admission, mean (SD)	1,6 (1,2)
The Ranson within 48 hours, mean (SD)	1,2 (0,6)
CT severity index, mean (SD)	3,8 (2,4)
The period of hospitalization (number of days)	3 – 97
Death (%)	9 (14%)

*Standard deviation

The clinical complications of the patients are shown in table no. 2.

Table no. 2. Clinical complications of the patients with AP

	MAP (n = 26)	SAP (n = 38)	Total	*p* Value
Local complications	2 (8%)	38 (100%)	40 (62,5%)	< 0.001
SIRS	11 (42%)	38 (100%)	49 (76,5%)	< 0.001
Organ failure on admission	0	21 (55%)	21 (33%)	< 0.001
Failure of one organ	10 (38%)	5 (13,15%)	15 (23,43%)	0.12
Multiple organ failure	0	33 (87%)	33 (51,5%)	< 0.001
Pancreatic necrosis	2 (8%)	38 (100%)	40(62,5%)	< 0.001
Extended pancreatic necrosis*	0	13 (34%)	13 (20%)	0.001
Infected pancreatic necrosis	0	18 (47%)	18 (28%)	< 0.01
Sepsis	0	18 (47%)	18 (28%)	0.02
Mortality	0	9 (24%)	9 (14%)	0.01

MAP- mild acute pancreatitis, SAP- severe acute pancreatitis
*Pancretic necrosis more than 50% of the pancreatic volume

Patients suffering from SAP presented at least one organ failure during admission. All patients with SAP presented pancreatic local complications. The mortality rate was 14% and was recorded at the SAP group. 21 out of 38 patients (55%) suffering from SAP presented one organ failure on admission and 6 (29%) of these patients died. Two patients died during the first week of admission as a result of MSOF. All patients suffering from one organ failure during hospitalization survived (table no. 2).

The ROC curves for APACHE II score at 24 h, Ranson score at 48 hours, maximum IAP and CTSI are illustrated in Fig. 1, 2, 3, 4, 5. For a cut-off value of 12 mmHg, maximum IAP had a sensitivity (Se) of 75% and a specificity (Sp) of 88% the positive predictive value (PPV) is 78%, then negative predictive value (NPV) is 83% with a 81% accuracy for the prediction of the severe evolution of acute pancreatitis [AUC: 0,876 (95% CI: 0,766 – 0,986), p<0,001] (figure no. 3).

Figure no. 1. ROC curve for APACHE II at 24 h

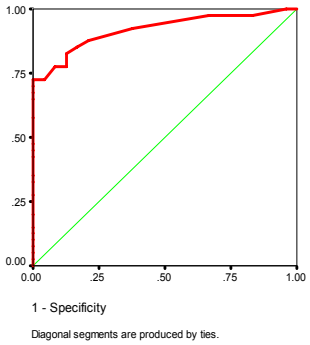


Figure no. 2. ROC curve for Ranson score at 48 h

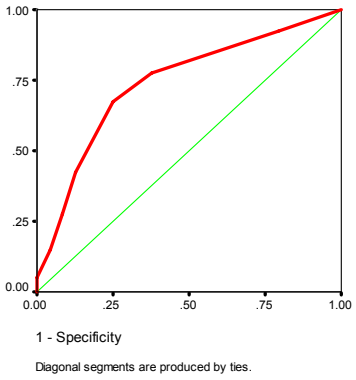
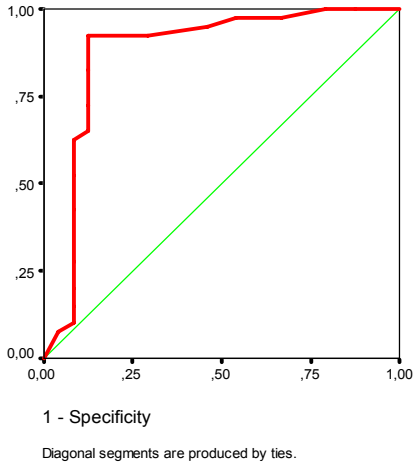


Figure no. 3. ROC curve for maximum IAP values



For a cut-off value of 4, CTSI has a sensitivity (Se) of 73% and a specificity (Sp) of 83% then positive predicitve value (PPV) of 76% negative predictive value (NPV) of 79% and a 78% accuracy for the prediction of the severe evolution of acute pancreatitis [AUC: 0,817 (95% CI: 0,704 – 0,929), p<0,001] (figure no. 4).

Figure no. 4. ROC curve for CTSI

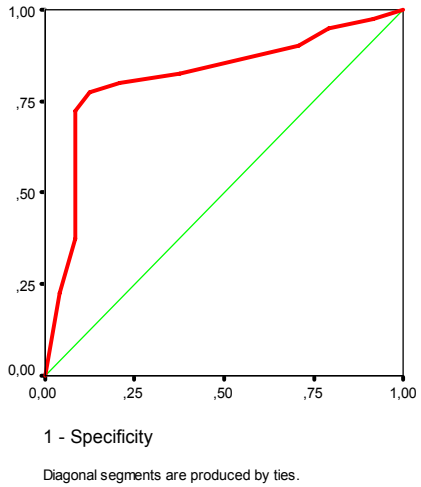
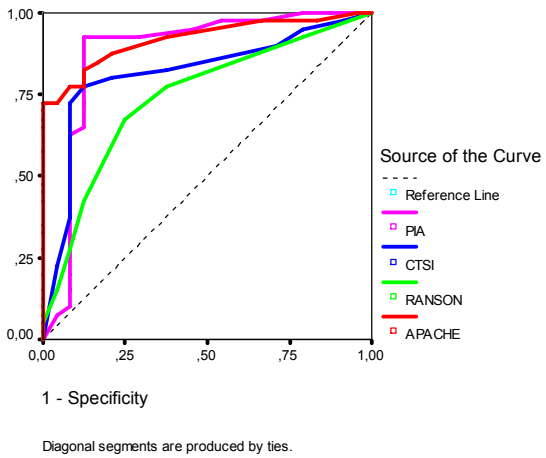


Figure no. 5. ROC curves for APACHE II score, Ranson score, maximum IAP and CTSI



At a cut-off value of 12 mm Hg IAP max has a sensitivity of 0,75, similar to Ranson score at 48 h (0.72 at a cut-off value 3) and CTSI (0,73 at a cut-off value 4). IAP max has a specificity of 0,88, simillary to CTSI (0,83) and APACHE II score (0,82) (table no. 3).

Table no. 3 Characteristics of prognostic markers in acute pancreatitis

	AUC (95% CI)	*P Value*	Cut – off value	Sensitivity	Specificity
APACHE II score at 24 h	0,904 (0,853-0,985)	< 0,001	8	0,88	0,82
Ranson score at 48 h	0,742 (0,616-0,868)	0,002	3	0,72	0,63
IAP max	0,876 (0,766-0,986)	< 0,001	12 mm Hg	0,75	0,88
CTSI	0,817 (0,704-0,929)	< 0,001	4	0,73	0,83

AUC – area under the curve, IAP max – maximum intra-abdominal pressure, CTSI – CT severity index

IAH is one of the most important causes of morbidity and mortality in SAP. The early diagnosis and the rapid treatment through abdominal decompression may be essential in the prevention of the subsequent development of organ dysfunctions caused by the increase of intra- abdominal pressure.

In our study we have investigated the correlation between the APACHE II score, Ranson score, CTSI and the maximum IAP obtained at all measurements. It is a study which supports the use of IAP as a prognostic marker in the evolution of AP. IAP is a cheap, reproducible, easy to obtain prognostic marker.

IAH and ACS affect the blood circulation at the level of all organs and play a significant role for the patient's outcome. The early detection of the increase in IAP is an essential factor in the management of acute pancreatitis and it can lower the morbidity and mortality associated with the disease.(12)

One of the main problems in the management of AP is anticipating complications which may arise during the evolution of the disease. There have been created and used both scoring systems with multiple variables (Ranson, Glasgow, APACHE, Imrie), some of them difficult to use, as well as independent prognosis markers (ex. C-reactive protein). The ideal marker should be easy to obtain, reproductible, cheap and should anticipate the worsening of the disease and the need to implement more diagnostic and therapeutical procedures. IAP is a prognostic marker which meets these demands.

Hong Cheng *et al.* define abdominal hypertension as the presence of IAP $\geq$ 12 mmHg and abdominal compartment syndrome as the presence of IAP $\geq$ 20 mmHg and the presence of at least a dysfunction or an organ failure that was not present before the onset of the disease. They also describe HIA and ACS to appear frequently at patients with AP (59,46%, 27,03 % respectively).(8)

In our study IAH and ACS appeared with a frequency of over 50%, 12,5% respectively.

Although the diagnosis of ACS is based on clinical data and on measuring IAP, Pickhardt *et al.* describe CT signs at four patients with a confirmed diagnosis of ACS.(13) They observe that the ratio between the abdominal antero-posterior diameter and the transverse one is higher ("round belly sign") in patients with ACS (0,85 as compared to 0,7 at the patients in the control group). Al-Bahrani *et al.* conclude in their

prospective study that the presence of "the round belly sign" and the thickening of the intestinal wall on CT imaging must alarm the clinician about the possibility of the IAH's or ACS's presence.(14)

In our study, at a cut-off value of 12 mmHg the maximum IAP had a 75% sensitivity and a 88% specificity for the prediction of severe evolution of AP, better than the CTSI sensitivity and specificity (73%, 83% respectively) for a 4 points cut- off value.

Patients with AP are prone to develop IAH or ACS due to large intra-abdominal and peripancreatic inflammatory fluid collections, capillary leak, intestinal and splanchnic oedema, aggressive fluid resuscitation etc. Gastro-intestinal ileus and distention in AP contribute to IAH. Both the air and the fluids from the cavity organs may elevate IAP and lead to IAH. On the other hand, IAH leads to intestinal and visceral edema, thus creating a vicious circle (8). IAH determines the disturbance of organ perfusion and leads to organ dysfunction. ACS manifestations include disturbances in the cardiovascular, respiratory, renal, splenic and neurological areas. The hypoperfusion of the gastrointestinal tract has been reported at IAP values of 12 mmHg (15). Oliguria and a noticeable decrease of the cardiac output are secondary to a IAP elevation of more than 20 mmHg.(16,17)

The relationship between the increase of IAP and the severity of pancreatitis expressed through the well-known criteria and the CT severity index have been the focus of our study. There are some studies that conclude that CTSI is the best method for the prediction of the severity of acute pancreatitis. The disadvantages of the method resided in the fact that it is an expensive, irradiating method and it cannot evaluate in dynamics all the patients (it must not be performed for mild types). The determination of IAP is a simple, easily applicable, non-invasive and reproducible method. A significant correlation between the increase of IAP and CTSI has been illustrated in our study. Maximum IAP seems to be a highly accurate marker, as results from the study made by Jose Manuel Hidalgo Rosas et al. Its predictive value is better after 48 hours of admission. However, the IAP measurement should not be performed only after the management of pain.(18)

The average mortality rate in our study was 14% and was recorded only in the SAP patient group. The mortality of SAP patients was 24%, comparable to the data in literature. Regarding the group of patients who developed ACS, the mortality was 87,5%.

Although it is acknowledged that the conservative medical treatment plays a major role for the prevention and treatment of organ dysfunction due to IAP's increase in AP, surgical decompression is frequently considered the sole treatment for severe ACS.

Patients prone to develop ACS must be carefully monitored in order to choose the moment for surgical decompression. A few studies have shown that the persistence of splanchnic hypoperfusion can lead to irreversible damage and to organs disfunction and death.(19,20,21) Significant evidence of organ dysfunction has been highlighted at values over 10 mmHg.(22) In 1990, following some animal research, some authors noticed the existence of a positive correlation between bacterial translocation and IAP, even though IAP remained high for less than an hour. This result was caused by the increase of intestinal permeability secondary to splanchnic ischemia, with or without reperfusion.(23,24)

IAH may be associated with the increase of bacterial translocation, especially when the increase in IAP is followed by splanchnic ischemia or after ACS decompression. ACS decompression may cause and increased release of proinflammatory cytokines that are responsible for another mechanism of MSOF and fulminant reperfusion syndrome.(8)

It is very important to establish the time interval between the ACS diagnosis and invasive surgical decompression, this vulnerable window, to prevent reperfusion lesions, bacterial translocation and the infection of pancreatic necrosis.

The key of the management of IAH and ACS is their early diagnosis and the prevention of their devastating effects. It is preferable to prevent than to cure the entire clinical manifestations of the compartment syndrome. Nevertheless, regarding the timing and the indications of surgical decompression there are controversies in very many articles. Decompression must be firmly taken into consideration when IAP continues to increase or clinical deterioration occurs.

The ACS patients' prognosis is highly reserved in our study. In order to achieve a good ACS prevention, it is essential to identify some independent risk factors for ACS in AP, of some predictive patterns for this syndrome, so that the treatment of high risk patients should be modified or done, before the organ dysfunctions and sequels occur.

CONCLUSIONS

In our study maximum IAP could be correlated with CTSI and traditional prognostic markers for severe evolution in acute pancreatitis. At a cut-off value of 12 mm Hg IAP max has a sensitivity similar to Ranson score at 48 h (cut-off 3) and CTSI (cut-off 4). Better sensitivity has APACHE II score at 24 h (cut-off 8). IAP max has a specificity simillar to CTSI and APACHE II score but better than Ranson score.

Maximum IAP values are closely correlated with severe complications and mortality rate. The mortality rate was extremely high at patients with ACS. Repeated measurement of IAP is a simple, noninvasive, reproductible and cheap determination. The optimal timing of surgical decompression as well as its effect on the clinical evolution in acute pancreatitis should be further studied.

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