Can Serum and Peritoneal Amylase and Lipase Determinations Help in the Early Prognosis of Acute Pancreatitis?

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Serum and peritoneal amylase and lipase levels were determined at an early stage in 73 patients with acute pancreatitis confirmed by computed tomography (CT scan), surgery, and/or postmortem. Each patient was given an enzymatic score (ES), which reflects the predominance of the serum or peritoneal concentration of the two enzymes, as the case may be. This score can thus be either 0, 1, or 2; ES = 0 if neither enzyme is predominant in the peritoneal fluid, ES = 1 if amylase or lipase alone are predominant therein, and ES = 2 if both enzymes are predominant. This enzymatic score appears to be a good indicator of severity of disease, being as it is directly and significantly related to mortality rate, prognostic score as proposed by Ranson, and incidence of extrapancreatic spreads as demonstrated by CT scan. In 38 patients (including two fatalities) with an enzymatic score of 0 or 1, mortality was 5%, whereas in 35 patients (10 fatalities) with ES = 2, mortality was 29% ($p < 0.01$).

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THE POOR RELIABILITY of clinical findings in the prognosis of acute pancreatitis (AP)—according to McMahon,[1] only one out of three serious forms of AP is recognized as such at an early stage—explains the increasing use of standard prognostic tables,[2–4] the best known being that of Ranson[5]; however, none of the existing tables takes account of pancreatic enzymes such as amylase or lipase. This attitude toward pancreatic enzymes is due to the imprecise value of amylase and lipase as diagnostic factors in AP. Weaver[6] and Koehler[7] concluded from electrophoretic isoenzyme determinations of amylase in blood that approximately one-third of all cases of AP defined as "abdominal pain plus hyperamylasemia" are not, in fact, AP, even though this definition is the very basis of practically all studies on AP,[3–5] since surgical or postmortem confirmation is available in only a minority of cases. The purpose of this paper is, therefore, to make a critical prospective study of the value of amylase and lipase determined in blood and peritoneal fluid as prognostic factors in AP irrefutably confirmed by computed tomography (CT scan), surgery, and/or postmortem examination.

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Methods

The study covered 73 patients hospitalized at various times at the Clinic of Digestive Surgery of the Geneva University Hospital over the 5-year period between July 1980 and July 1985.

These patients all suffered from AP confirmed by surgery (35), computerized axial tomography (70) and/or postmortem (9), the three methods being sometimes used for the same patient. Of these, 46 were men (63%) and 27 women (37%), ranging in age from 21 to 84 years (average 51.7 years—men 47.3; women 59.1).

Four causes of AP were identified (Table 1): biliary lithiasis (25) confirmed by ultrasonography, CT scan, and/or surgery; alcoholism (26); a combination of both (7); and idiopathic factors (15). Table 2 documents the presence or absence of extrapancreatic spreads demonstrated by CT scan.

The incidence of mortality was approximately the same for both sexes: 17.4% (8 fatalities) for men and 14.8% (4) for women, with an overall incidence of 16.4%. The average age of the deceased patients was 67.4 years; it was substantially lower for men (60.9 years) than for women (80.5).

Peritoneal lavage was performed on all 73 AP patients within 24 hours of admission. Catheterization was always preceded by a CT scan to prevent instilled fluid from perturbing the image, *e.g.*, by producing phantom ascites. Upper anterior laparotomy or palpation of an abdominal mass contraindicated catheterization. No septic or traumatic accident was recorded, in spite of a few cases of

TABLE 1. *Etiology of 73 Cases of AP Distributed According to Sex*

		Alcoholic AP	Biliary AP	Alcoholic and biliary AP	Idiopathic AP
Male	N = 46	24 (2)*	8 (2)	5 (1)	9 (3)
Female	N = 27	2	17 (1)	2	6 (3)
Total	N = 73	26 (2)	25 (3)	7 (1)	15 (6)

* Figures in ( ) are the number of deceased patients and are included in the respective totals.

intraparietal, easily corrected misrouting. Isotonic saline serum (1000 cm^3) was instilled rapidly (in approximately 5 minutes) into the abdominal cavity and left for half an hour. The fluid was subsequently collected by placing the empty perfusion bag on the floor; a few cm^3 suffice for amylase and lipase determinations. This technique is the same as that which is widely used in the presence of abdominal trauma. The lavage itself offers the advantage of making enzyme determination more sensitive; it was performed even in the few cases of AP with pre-existent exsudate.

Plasma obtained by centrifugation of 0.6 ml of heparinized blood was used for amylase determination. The colorimetric method used is based on the reaction of iodine and starch.[8] Our reference values were 1.2–3.6 kU/L. The same colorimetric method was used to determine amylase in peritoneal fluid.

Serum and peritoneal lipase was determined by a turbidimetric method that assays trioleine degradation.[9] The reference values for lipasemia were 50–250 U/L.

Values for chi square and p were computed by using the program given in the *Statistical Package for the Social Sciences.*[10]

Results

General Observations

Ranson's prognostic score[5,11,12] was determined in each of the 73 patients with confirmed AP. This score is based on patient age and a total of 10 risk factors indicated in a test series performed on admission (leucocytosis > 16,000/mm^3, glycemia > 11.1 mol/L, LDH > 350 IU/L and SGOT > 120 IU/L) and during the subsequent 48-hour period (hematocrit fall > 10%, blood urea nitrogen increase > 5 mg%, serum calcium < 2.0 mmol/L, arterial pO_2 < 8.4 kPa, base deficit > 4.0 mmol/L, and fluid sequestration > 6 liters). Figure 1 indicates the distribution of the 73 patients, living or dead, according to their Ranson score. All the deceased except one had a score of 6 or over. The situation may be summarized as follows: Ranson score ≤ 5, 55 living and one dead; Ranson score > 5, six living and 11 dead, with $p < 0.0001$.

Nine of the 12 deceased patients underwent postmortem examination; eight had pancreatic necrosis and appear *a posteriori* to have died of their disease. Only one deceased patient, who also suffered from bacterial bronchopneumonia, was found to have pancreatic edema and can presumably be classified as "died of other cause," all the more so as he was also suffering from chronic bronchitis (Ranson score 3).

Amylase

In view of the variety of units of amylase measurement in the literature and the desirability of using a simple procedure that could be applied by the intern on duty, all AP patients were arbitrarily classified into two groups according to the predominance of their serum (*s*) or peritoneal (*p*) amylase levels (the same procedure was followed in the case of lipase). The results were as follows:

$s \geq p$: 34 cases (47% of all patients),

$s < p$: 39 cases (53%).

TABLE 2. *Distribution of 73 Cases of AP According to the Results Provided by CT Scan*

	Living AP Patients			Deceased AP Patients		
	No CT scan Performed	With EPS*	Without EPS	No CT scan Performed	With EPS	Without EPS
Number of patients	2	28	31	1	10	1
Subtotal	2	59		1	11	
	61			12		
Total	73					

* EPS = extrapancreatic spreads.

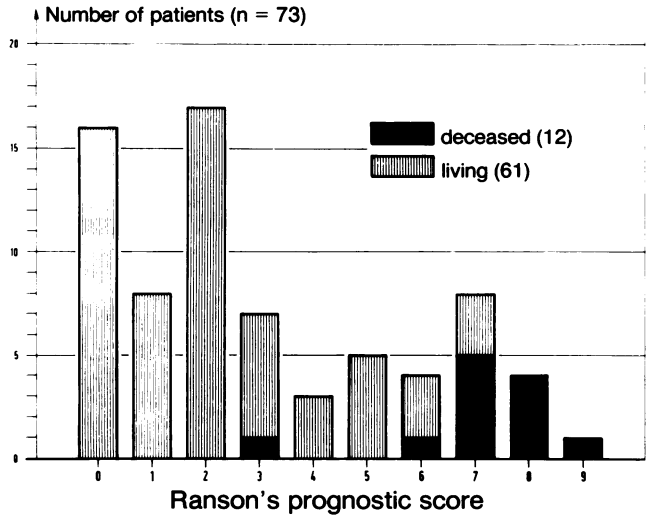

FIG. 1. Distribution of 73 cases of AP according to survival and Ranson score. All deceased but one had a Ranson score of 6 or over (mortality 65%, $p < 0.0001$).

The prognostic implications of the above classification were assessed in the light of favorable or fatal evolution of the condition of each patient and the possible presence of extrapancreatic speads (EPS) as evidenced by CT scan. The diagrammatic distribution of fatal cases and EPS as a function of the relevant serum and peritoneal amylase levels on admission is given in Figure 2. The overall results are as follows:

$s \geqslant p$: 34 cases in all, with two fatalities (mortality 6%), of which 32 CT with 11 EPS (incidence 34%),

$s < p$: 39 cases in all, with 10 fatalities (26%), of which 38 CT with 27 EPS (71%).

The mortality rate and the incidence of EPS show significant differences for the two groups $s \geqslant p$ and $s < p$, with $p < 0.05$ for the mortality rate and $p < 0.01$ for the incidence of EPS. It should be noted that the latter was determined in a total of 70 patients only; the three remaining cases (two living and one dead) had not had a CT scan at admission (Table 2). On the other hand, the deceased patient with a Ranson score of 3 at admission belongs to the group $s \geqslant p$.

Lipase

All patients were similarly classified according to the predominance of their serum (s) or peritoneal (p) lipase levels. In this case, all dead patients but one belonged to the group $s < p$. Contrary to the situation for amylase, nearly two-thirds of the patients had, on admission, a lipasemia lower than their peritoneal lipase. The overall picture is summarized in Figure 2 and in the following data:

$s \geqslant p$: 26 cases in all, with one fatality (mortality 4%), of which 24 CT with 8 EPS (incidence 33%),

$s < p$: 47 cases in all, with 11 fatalities (23%), of which 46 CT with 30 EPS (65%).

Contrary to the situation found with amylase, mortality did not differ substantially for the two groups, as $p < 0.1$ only.

Amylase and Lipase Levels and the Enzymatic Score (ES)

If the amylase and lipase levels in blood and peritoneal fluid in each patient are considered together, three possible alternatives can be seen, each of which can be defined by what we termed the "enzymatic score (ES)":

ES = 0: the two enzymes are predominant in blood ($s \geqslant p$),

ES = 1: one enzyme is predominant in blood and the other in the peritoneal fluid,

ES = 2: the two enzymes are predominant in the peritoneal fluid ($s < p$).

Figure 3 illustrates the distribution of our 73 patients according to their ES, their Ranson score, and their clinical course (favorable or fatal). Mortality remains practically unchanged for ES values of 0 or 1, the respective rates being 5 and 6%; but there is a marked and significant difference in the mortality rate if one considers the two groups 0 and 1 taken together, on the one hand, and the group 2, on the other, since the mortality rate jumps from

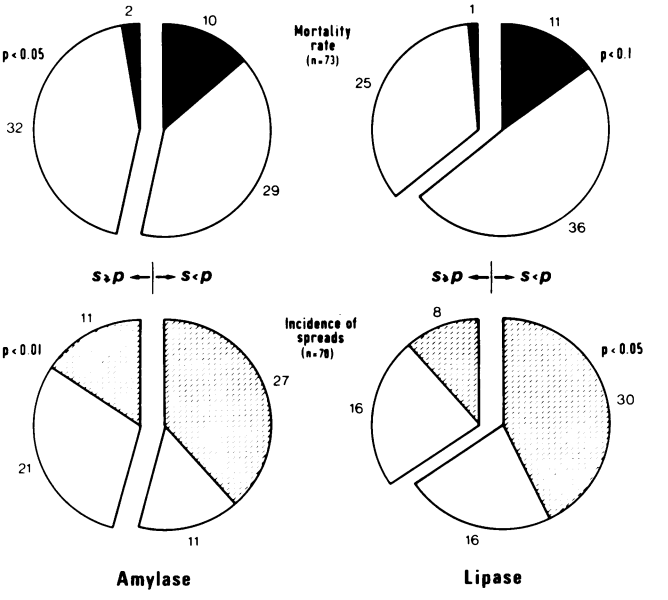

FIG. 2. Distribution of 73 cases of AP according to the predominance of serum ($s \geqslant p$) or peritoneal ($s < p$) amylase and lipase levels, respectively. Hatched areas represent deceased patients, whereas dotted ones refer to patients with extrapancreatic spreads evidenced by CT scan.

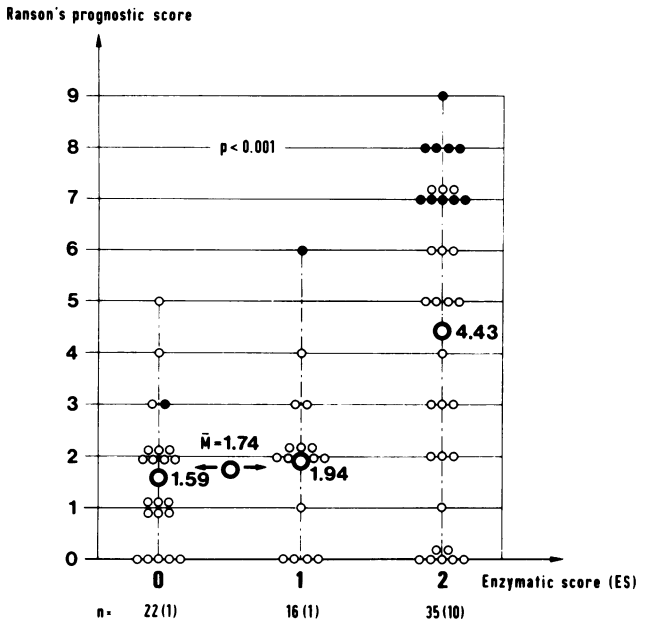

FIG. 3. Scattergram of 73 cases of AP, living (O) or dead (●), according to their enzymatic score (ES = 0, 1, or 2) and Ranson's prognostic score (from 0 to 9). Mean values, superimposed as large circles, correspond to the average Ranson score achieved by all patients having the same ES. The number of patients is given in the lower line, the number of deceased being given in brackets.

5.5 to 29% ($p < 0.01$). Figure 4 documents the presence or absence of EPS (detected by CT scan) for the 70 patients who underwent this examination. Finally, Figure 5 represents the variation, in relation to ES, of the incidence of EPS and the mortality rate.

In our patient population, slightly more than one AP out of two showed definite peritoneal enzyme contamination; this predominance ($s < p$) was somewhat more marked for lipase (64% of the population) than for amylase (53%). The correlation between a possible peritoneal hyperconcentration and the clinical course of the disease appears to be significant insofar as 10 out of 12 fatalities in our population belong to the group of 35 patients (48% of total population) for whom both amylase and lipase levels were found to be higher in peritoneal fluid than in blood; this group has an ES of 2 and its mortality rate is 29%, with $p < 0.01$. The second group comprises the 22 patients (30% of the total) who had higher amylase and lipase levels in serum than in peritoneal fluid (ES = 0) and the 16 patients (22%) who had a peritoneal hyperconcentration of one enzyme only (amylase or lipase, ES = 1); the mortality of the two categories ES 0 and 1 taken together was 5.5%; it would have been lower still if we had not included a patient who had an ES = 0 and a Ranson score of 3 (this patient died of bacterial bronchopneumonia and his necropsy did not reveal, in the abdominal region, anything else but an edematous pancreas). The remaining 11 patients who died all had a necrotic pancreas confirmed by surgery or postmortem examination.

Discussion

The purpose of our prospective study was to assess the contribution of serum and peritoneal amylase and lipase determinations to the prediction of the evolution of an attack of AP within the first hours following hospitalization.

In addition to its value in the diagnosis of abdominal contusions[13] and the treatment of AP patients,[14,15] peritoneal dialysis can provide useful prognostic information; broadly speaking, there exists a series of macroscopic and chemical criteria in this respect. The color of the ascitic fluid is a first sign of severity: the most serious forms of AP display the darkest fluids.[15] McMahon[1] uses three se-

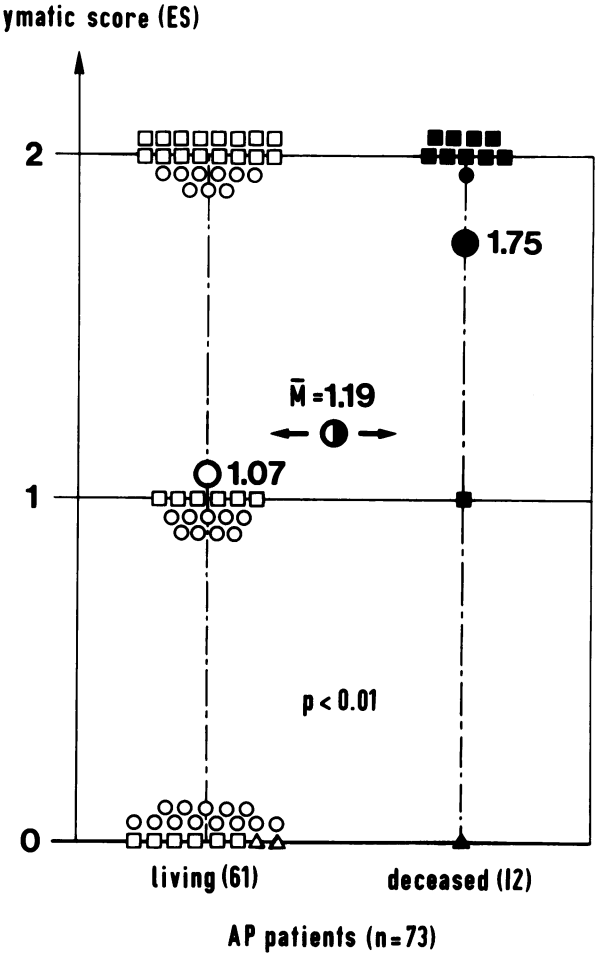

FIG. 4. Scattergram of 73 cases of AP, living or dead, according to their enzymatic score ES (0, 1, or 2) and the results of their CT scan. The light symbols refer to surviving patients, as follows: □ for the 28 patients with EPS detected by CT, O for the 31 patients without EPS, and △ for the two patients without CT scan. The dark symbols represent deceased patients: ■ for the 10 patients with EPS detected by CT scan, ● for the patient without EPS, and ▲ for the patient without CT scan. The bold figures and circles give the mean ES values for the living and dead patients.

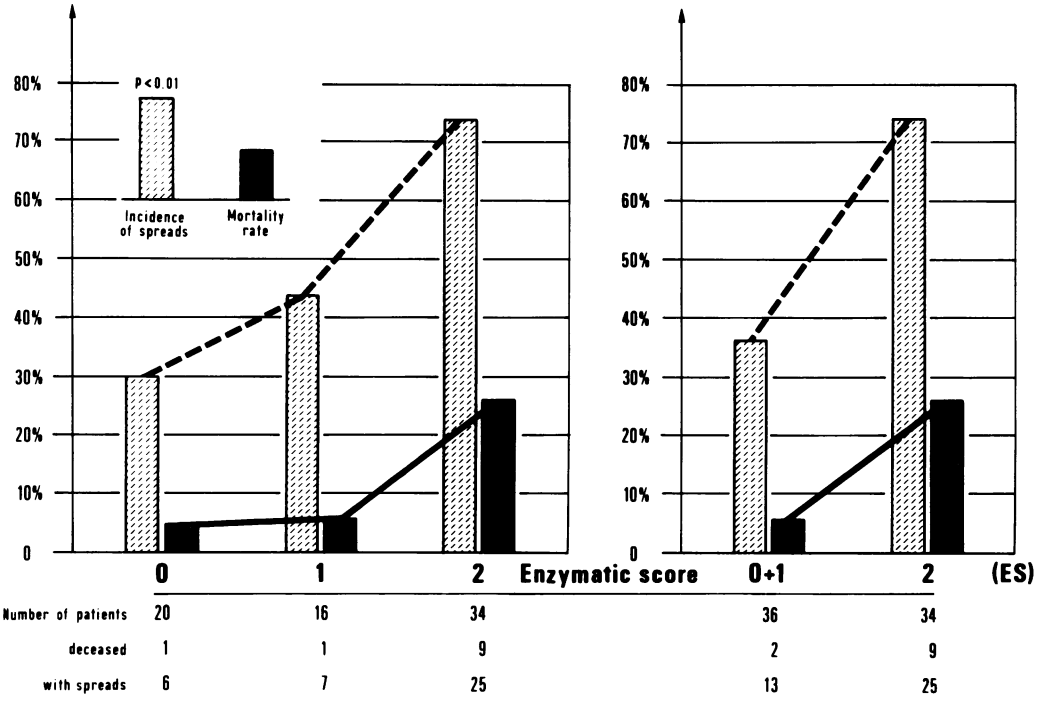

FIG. 5. Incidence of extrapancreatic spreads (EPS) and mortality rate in relation to the enzymatic score (0, 1, or 2). The diagram on the right amalgamates the two groups ES = 0 and ES = 1. The dark columns represent the deceased patients, whereas the dotted ones refer to patients with EPS (living and dead taken together). The population of each ES group is given below. As regards EPS, $p < 0.01$. Chi square and p values were not computed for the mortality rate (for statistical reasons). The mortality for the group ES = 2 is 26% only, as this group does not include one patient without CT scan.

verity criteria based on the color and volume of pancreatic ascites, which enable him to predict more than one out of two serious attacks of AP (in a group of 120 dialyzed patients). The chemical and enzymatic composition of the dialysate is also of prognostic value. It is common knowledge that the presence of amylase in a pleural or peritoneal effusion indicates a pancreatic origin.[16] Doutre[17] even claimed that the presence of lipase in ascitic fluid was a clear sign of necrotizing AP.

Numerous studies,[18-22] most of them experimental, have determined enzyme concentrations in peritoneal effusion in cases of AP; variation of these concentrations in time has also been determined, although no correlation with the severity of the disease has been established. Reynaert, Otte, and Kestens[23] are among the few authors who have attempted to correlate the serum and peritoneal concentrations (*s* and *p*, respectively) of amylase, lipase, and LDH; in the follow-up of 21 cases of severe AP, where pancreatic necrosis was certified in 13 instances by laparotomy, the *p/s* ratio was invariably greater than 1. In this series, however, all peritoneal enzyme determinations were carried out on free, spontaneously flowing ascites without previous instillation of a dialysate. These rough determinations can be expected to be quite elevated.

Identical prognostic observations apply to methemalbumin, with the difference that methemalbuminemia in itself is an indication of severity.[24,25]

In our study, the following criteria were used for prognostic purposes: (1) the clinical evolution of the patient; (2) Ranson's prognostic score[5]; and (3) the presence or absence of EPS evidenced by CT. When present, EPS involvement corresponded iconographically to an infiltration of the retroperitoneal connective tissue and affected the renal regions, the root of the mesentery or mesocolons, or the posterior cavity of the omenta. The unfavorable prognosis of this extrapancreatic extension was stressed by Dammann[26] and Rohner and Hauser.[27,28] Of 68 cases of AP confirmed by CT, 36 (53%) showed involvement; all eight fatalities belonged to this subgroup. The mortality rate dropped from 22% to 0 in cases of AP with or without spreads, respectively. The severity of this involvement was further enhanced when correlated with calcemia.[28]

As previously indicated, peritoneal enzyme levels were determined in the lavage fluid from peritoneal dialysis. This simple, rapid, inexpensive, and almost invariably safe procedure has few contraindications; nevertheless, it entails a few simple precautions (gastric and vesical decompression[29]).

For a number of reasons, peritoneal determinations are by no means always comparable: (a) *period of incubation:* the 30-minute period required for peritoneal lavage is usually approximate, and the enzyme concentration will probably increase proportionally with the length of the lavage period; (b) *localization of the catheter:* tubes do not always follow the same route, and it may be assumed that those which are closer to the pancreas will collect a fluid with a higher enzyme content. In one of our patients, peritoneal concentrations determined for control purposes and on the first postoperative day on two adjacent drains placed during laparotomy showed variations ranging from 100 to 150%, depending on the enzyme concerned; (c) to minimize discomfort, *patient position* was not changed

as often as would have been advisable for ensuring better serum mix and more uniform concentrations—this is an additional source of potential error.

For these reasons, moderate peritoneal enzyme levels may well be lower than actual values and should, therefore, be interpreted with some caution, particularly in the case of attacks of AP that appear rather severe in the light of the relevant CT results. However, the existence of high peritoneal enzyme concentrations cannot be questioned, inasmuch as it cannot be explained by a technical artifact. Consequently, ES values of 2 appear more reliable than 0 or 1 values.

The decision to use two enzymes instead of only one in the determination of a patient's ES was based on the poor results obtained using either amylase alone (mortality 26% if $s < p$, with $p < 0.05$) or lipase alone (mortality 23% with $p < 0.1$) (Fig. 2).

The prognostic value of the enzymatic score ES can further be underlined as follows. There exists, on the one hand, an excellent correlation with Ranson's score; the latter has a mean value of 1.74 for the ES 0 and 1 groups together, and a mean value of 4.43 for the ES 2 group, with $p < 0.001$ (Fig. 3). On the other hand, EPS demonstrated by CT scan were predominant among patients showing a peritoneal hyperconcentration: 74% of the patients with an ES of 2 had one or more EPS, in contrast to 36% of the patients having an ES of 0 or 1 (with $p < 0.01$) (Fig. 5).

In conclusion, comparative serum and peritoneal amylase and lipase levels appear to be reliable and simple indicators in the early prognosis of AP. As a practical consequence, AP patients with the highest ES should, in our opinion, benefit from more aggressive forms of treatment, including more abundant and prolonged peritoneal lavage than is usually recommended, before resorting, if necessary, to additional, purely surgical techniques. On the other hand, therapeutic dialysis, which remains a costly and exacting measure,[30] does not appear suitable for patients who have a peritoneal enzyme hypoconcentration, *i.e.*, an ES of 0 or 1.

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