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Patients With Severe Acute Pancreatitis Should Be More Often Treated In An Intensive Care Department

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Abstract

Background:Acute pancreatitis (AP) is a serious disease with a frustrating mortality rate, but with a very good quality of life reported among survivors, that justifies an optimised allocation of 'therapy intensity'.
Purpose: To audit monitoring and treatment of severe AP in our Intensive Care Department based upon Atlanta severity classification and following recommendations.
Methods:Retrospective study of all AP admitted to our ICU between 1st January, 1993 and 31st December, 1999 in a tertiary Universitary Hospital in Northern Portugal.

Results: Our sample (n=44) represents <1% of all patients observed in our ICU and ~3% of all patients with AP admitted to our Hospital between 1993 and 1999. All cases fulfilled at least one Atlanta criteria of severe AP. Mean length of stay was 11,6 days. Diagnosis of AP was established in less than 48 hours in 86% of cases: amylasemia and lypasemia were determined in 84% and 7%, respectively and 64% of cases were submitted to ultrassonography. The median

time between diagnosis and ICU admission was 2 days. Biliary calculus was responsible for 38% of cases and ethanol for 14%; 36% were considered idiopathic (in none was ERCP performed). Concerning local complications, necrosis was diagnosed in 56% and pseudocysts or abcesses in 23%. Infection was diagnosed by US/CT guided punction or by the presence of gas in CT (performed in 83% during the first ten days of disease) in 18% of the cases. 68% were put on parenteral nutrition (beginning on the 2nd day after admission to ICU in 50% of patients); and 51% had enteric feeding (median day of start =8,5 days). Antibiotics were prescribed in 91%. 45% of patients were submitted to surgery (median day of surgery was 6 days). No statistically significant differences were found concerning local or systemic complications according to different therapies. Mortality rate in our ICU was 36%, mostly during first and second weeks. Patients admitted to ICU later than the second day after diagnosis seem to die earlier (p<0,005). Outcome (death) was statistically related with organ dysfunction criteria, namely Atlanta criteria (renal failure), SOFA and proportion of days with organ dysfunction.
Conclusions: In our Institution (a tertiary hospital) AP diagnosis is quickly made, local and systemic complications are clearly diagnosed and monitored, but at least 50% of patient waited for 2 days until ICU admission. They might represent those who dye earlier. Sequential organ dysfunction systemic assessment (egSOFA) and Atlanta score were related with outcome.

INTRODUCTION

Acute pancreatitis is a common problem with an increasing incidence (38/100000 persons/year at the United Kingdom), representing 3% of all patients with abdominal pain at an Emergency Department. It represents also a serious problem concerning human (with a steady mortality rate of 6-15% for the last twenty years) and economic costs (20.000 £/patient treated) but patients who recover can expect to have a very good quality of life.

Two phases are recognized in acute pancreatitis process corresponding to the two peaks of death. Firstly, an acute systemic inflammatory response syndrome, due mainly to inflammatory mediators and pancreatic enzymes, that is responsible for one third of deaths; and secondly, several infectious complications (necrosis infection and other), justified by local ischemic processes and intestinal bacteria migration, that lead to a second peak in the incidence of death.

Several attempts were made for the definition of severity assessment or prognostic scores in acute pancreatitis. In Atlanta, in 1992, somehow mimetizing the above mentioned pathogenic sequence, severe pancreatitis was classified as that inflammatory process affecting pancreas, and in a variable degree near or distant organs, with signs of organic dysfunction (systolic arterial pressure below 90mmHg, paO_2<60mmHg, serum creatinin > 20 mg/dL, and evidence of digestive haemorrhage at a rate above 500ml/day) and/or evidence of local complications (necrosis infection, presence of an abscess or a pseudocyst). Classic Ranson and APACHE II indexes were also included – those patients with three or more Ranson criteria or eight or more APACHE II criteria can and should also be classified as having severe pancreatitis.

The British Surgical Society and the American College of Gastrenterology published recommendations concerning a sequential approach to a patient with an acute pancreatitis[7].

We decided to audit our data at S. João Hospital Intensive Care Department (Oporto, Portugal) trying to determine what were our local main outcome predictive factors, with the ultimate purpose of developing a protocol of standardized approach and data collection to severe pancreatitis.

METHODS

Using the Hospital S. João Data Base, we performed a retrospective study of all patients admitted to our Intensive Care Department in the last seven years (1st January, 1993 to 31st December, 1999) with a diagnosis of acute pancreatitis. Patients that were misclassified (eg, intestinal necrosis, diabetic cetoacidosis) and those that were in our Department after colecystectomy (for resolution of the cause and not because of their acute pancreatitis) were excluded.

Data on age, sex, time and timing of admission to ICU (in days), etiology, approach (prognosis criteria, medical and treatment performed) and outcome were collected. The diagnosis of acute pancreatitis was considered when reported in patient file and confirmed by reviewing file references to abdominal pain plus elevation of serum amylase or lipase. Severity was assessed considering several scores – Ranson, APACHE II, and Atlanta. Acute pancreatitis was classified as severe if at least 3 points in Ranson score were obtained; or 8 considering APACHE II; or if local or systemic complications were presented according to Atlanta criteria – necrosis, pseudocysts or abscesses or renal failure, digestive bleeding, shock or respiratory failure.

It is well known that patient's evolution is a better prognosis factor then the degree of dysfunction at admission. For this purpose we calculated Sequential Organ Failure Assessment (SOFA) at admission and delta SOFA (difference between SOFA at admission and the maximum value of SOFA). We also assessed the proportion (over the total number of days) of days with at least one dysfunction (considering SOFA).

Statistical Package for Social Sciences (SPSS®) was used to perform statistical analysis, including non-parametric tests (Chi-squared, Mann-Whitney) and Kaplan-Meier survival analysis.

RESULTS

Forty-four patients were analysed representing less than 3% of all acute pancreatitis in our Hospital during the same period of time (n= 1401), and less than 1% of all patients in our ICU.

GENERAL DATA

All patients were admitted to the ICU from the emergency department. 43% (n=19) came from other hospital. Fifty percent (n=22) were men, and fifty percent were women, with an overall median age of 59 years old (minimum- 20, maximum- 87).

ICU average length of stay was 11,6 days (median of 8 (minimum- 1, maximum-48) and the hospital one was 41,8 days (at least half of them staying 35 days (12-152).

No statistically significant differences were found on sex, origin, and duration of stay in ICU concerning the year of study.

DIAGNOSIS – CELERITY AND ETIOLOGY

In eighty-nine percent (n=38) of patients the diagnosis was reached in the first 48 hours after symptoms. In 11% (n=5) the diagnosis was made after those first 2 days. No differences were found among the several years considered in this study.

In 90% (n=36) of patients diagnosis was based on symptoms (all had abdominal pain, and 75% (n=21) emesis), hyperamylasemia [84%(n=37)] and/or rise in serum lipase [7%(n=3)], and ultrasonography [performed in 64% (n=37)]. In 10% (n=4) acute pancreatitis was diagnosed after laparotomy.

Concerning etiology (Table 1), the main cause was biliary calculus. Alcohol counted for 14%, and ERCP for 5% of all cases. In 36% (n=15) no cause was referred in clinical files.

Figure 1

Table 1: Prognostic assessment of severe acute pancreatitis using Atlanta criteria and its relation with outcome preditive factors (Ranson, APACHE II, SOFA), age, gender, and etiology and time consumed for diagnosis and access to ICU (n=44)

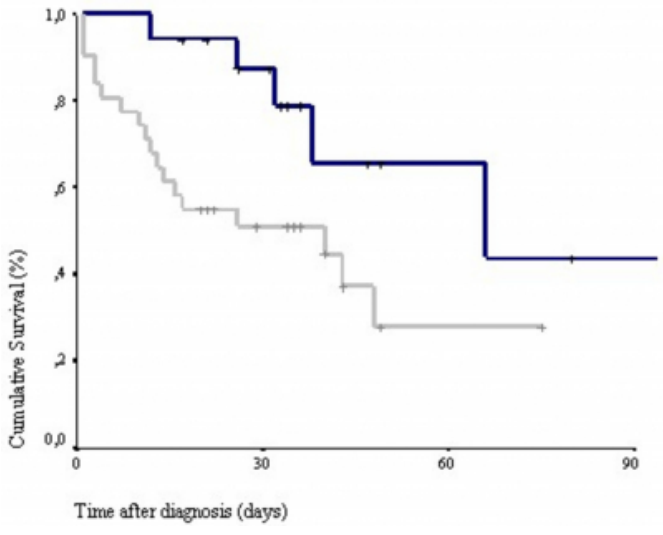
		Prognostic Assessment (Atlanta)			Mortality Rate	
		One criteria	Two criteria			
	TOTAL	n=16 (36%)	n=28 (64%)	p	(%)	p
General data						
Gender (%)				ns		ns
Male	50	50	50		50	
Female	50	50	50		54	
Age (median (m-M))	59 (20-87)	64 (29-77)	57,5 (20-87)	ns	68 (27-87)	0,001
Diagnosis						
Etiology (%)				ns		ns
Gallstones	38	31	69		69	
Idiopathic	36	47	53		60	
Ethanol	14	17	83		16	
PostERCP	7	50	50		50	
Trauma	5	33	67		33	
Timing (median (m-M))						
Diagnosis	1 (0-20)	1 (0-4)	1 (0-20)	ns	-	ns
Access to ICU	2 (0-41)	1 (0-33)	2 (0-41)	ns	-	0,035

* Differences on prognostic assessment between age and gender, and diagnosis
** Differences on the outcome of gender, diagnosis and prognosis assessment

Median time between admission to the hospital and admission to the ICU was 2 days; 25% of patients waited as long as 3 days. This group of patients who waited more time to be admitted to to the ICU (median of three days) seem to have the highest mortality rate – p=0,035 (See Figure 1).

Figure 2

Figure 1 : Global actuarial survival for patients with severe acute pancreatitis according to time of ICU admission Â– less or 2 days after acute pancreatitis diagnosis, and more than 2 days after acute pancreatitis diagnosis (Kaplan-Meier, log-rank test) (n=44)



PROGNOSIS/RISK ASSESSMENT

Considering Atlanta Criteria for severe acute pancreatitis, all our patients fulfilled at least one criteria namely either organ dysfunction and/or local complications or more than 3 Ranson criteria or an APACHE II score above 8.

Data on organ dysfunction were clearly insufficient. We could not determine digestive hemorrhage rate, based on clinical files data. Respiratory failure was present in 12% (n=2), shock in 22% (n=5), and renal failure in 100% (n=12) of patients whom we obtained related data.

At admission we found a median SOFA of 6 (minimum-2; maximum-13) and median delta SOFA was 4 (0-10).

Considering local complications, pancreatic necrosis was found in 56% (n=15) of the patients that performed a CT-scan (n=27). The presence of infection was confirmed in 18% of cases by aspirative punction (n=5) and/or the presence of gas in the CT scan (n=5). A pancreatic abscess was described in 6 patients and a pseudocyst in 4 (n=10=22,7%).

Eighty-five percent had at least 3 criteria of Ranson. APACHE II score was also calculated at admission and at 48 hours from the onset of symptoms. All patients had a score of 8 or higher. The APACHE II predicted mortality at admission was 41%.

MONITORING AND THERAPY

Eighty three percent (n=23) performed a CT scan. Only 11% (n=5) had serum reactive C-protein measured.

Sixty-eight percent were put on parenteral nutrition (beginning on the 2nd day after ICU admission in 50% of patients); and 51% had enteric feeding (median day of start =8,5 days). It seems that patients with systemic organ dysfunction had enteral feeding later than those without any sign of organ failure (p=0,034). No relation was found between the choice of parenteral or enteric nutrition and the presence of local complications.

Ninety-one percent (n=40) of patients received antibiotics: 25% (n=10) a carbapenem, 40% (n=16) a cephalosporin, 5% (n=2) quinolone plus metronidazole, and 25% (n=10) piperacilin/tazobactam. No relation was found between the presence of systemic or local complications and the use of antibiotics.

Surgery was performed in 45 % (n=20) and the median day of surgery was 6 days (after diagnosis). The presence of systemic or local complications did not seem to influence neither the decision nor the time for surgery.

ERCP was performed in 3 patients. None of those considered as idiopathic was submitted to ERCP.

OUTCOME

In 11% (n=5) of patients exocrine (n=1) or endocrine (n=4) failure was assumed as sequelae of acute pancreatitis.

The hospital global mortality was 52% (n=23) with a median day of death of 43 days. ICU mortality was 37% (n=16). During the first and second weeks 14 patients died (35%of overall mortality and 70% of that in the ICU).

No relation was found between length of stay and mortality. Also sex or etiology did not significantly influence mortality. Neither medical nor surgical therapy, or their timing, significantly influenced mortality. Age (as defined in Ranson's and APACHE II's scores of severity) was significantly associated with mortality and organ dysfunction (as defined in Atlanta or SOFA scores) were significantly related to mortality.

Renal failure on ICU admission, with 20 mg/dL as the best cut-off (for 100% of specificity), was the organ dysfunction more consistently associated with mortality.

Delta SOFA (cut-off of 6) and the proportion of days with organ dysfunction (cut-off of 0,4) were associated with hospital mortality (p=0,001 and p=0,003 respectively).

No statistical significance was found comparing local complications or Ranson and APACHE II scores.

Figure 3

Table 2: Outcome assessment of severe acute pancreatitis using Atlanta, Ranson, APACHE II (using Atlanta criteria), and SOFA criteria (using cut-off values estimated in our sample using ROC curves) for severity (n=44)

	Outcome		
	Lived	Died	
		(median (m-M))	*p* *
Prognostic criteria			
Ranson (median (m-M))	3 (1-6)	4 (2-7)	0,04
<3 (%)	60	40	ns
>=3 (%)	41	59	
APACHEII at admission (median (m-M))	21 (12-34)	26 (14-44)	ns
< 8 (%)	0	0	ns
>=8 (%)	48	52	
SOFA at admission (median (m-M))	4 (2-9)	7 (3-12)	0,008
< 10 (%)	52	48	0,008
>= 10 (%)	0	100	
SOFA delta (median (m-M))	2 (0-5)	6 (0-10)	0,001
< 6 (%)	59	41	0,001
>= 6 (%)	0	100	
Percentage of days with organ dysfunction (median (m-M))	17 (8-40%)	29 (13-69%)	0,029
<40% (%)	50	50	0,038
>=40% (%)	11	89	
Atlanta			ns
One criteria (%)	56	44	
Two criteria (%)	42	58	

* comparison of values of prognostic criteria using Mann-Whitney and comparison of mortality rate among patients below and above defined *cut-offs* using Chi-Square.

DISCUSSION

Hospital S. João, in Porto, is an University Hospital, and the biggest hospital in Northern Portugal with around 1300 nursing beds. We analysed clinical data of all patients with acute pancreatitis treated in the Intensive Care Department between 1993 and 1999. They represent less than 3% of all acute pancreatitis treated in our institution in that period. If we consider that, in most series, severe acute pancreatitis (all our cases were could be considered severe according to Atlanta's criteria) represent around $15\%_2$ of all acute pancreatitis attacks (we could be missing at least 5-10% of our patients) we may conclude that some severe acute pancreatitis were never admitted to an ICU as they probably should.

Although diagnosis of acute pancreatitis was made a short time after symptoms, and relevant data for severity assessment was collected, no report on severity index was found in clinical files, and as previously mentioned only 3% of all acute pancreatitis were treated in ICU.

Could this be the reason for the high mortality rate (56%) – higher than the predicted one (41%)?

No relation was found between mortality and sex, origin (in

other hospital), symptoms, causes, length of stay in ICU, medical or surgical treatment. There was a high variability of medical therapies, and may be, according to evidence-based data, a precocious surgical intervention (median – 6 days); but, these facts were not mortality risk factors. Mortality was also not influenced by the etiology (alcoholic or post-ERCP pancreatitis), or by the presence of local complications (necrosis or abscesses).

All these patients had severe acute pancreatitis according to Atlanta criteria; no relation was found between these criteria and death rate. Only age (as defined in Ranson and APACHE II criteria, though in Atlanta), renal failure (as defined in Atlanta) and time until ICU admission were prognostic factors.

Most patients died after the second week, and beyond age and renal dysfunction, those who were admitted to the ICU more than 48 hours after diagnosis were those who died more ($p<0,05$).

Based on this study and our results, a clearly defined protocol of diagnosis, monitoring and treatment is under implementation in our hospital, with two main purposes: generalize prognostic information (based on Atlanta criteria), and simplify Intermediate or Intensive Care access and surveillance, so that patients with severe acute pancreatitis could be more quickly treated in an ICU.

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