

# Severe acute pancreatitis: results of treatment

## *Resultados do tratamento da pancreatite aguda grave*

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### A B S T R A C T

**Objective:** To evaluate the results of the Protocol for treatment of patients with severe acute pancreatitis. **Methods:** We consecutively analyzed age, gender, etiology, length of hospital stay, type of treatment and mortality of 37 patients with severe acute pancreatitis from January 2002. **Results:** The patients' ages ranged from 20 to 88 years (average 50 years), 27% were female and 73% male. Mean overall hospital stay was 47 days. Thirteen patients were treated surgically, the average operations per patient was two. There were six deaths among patients undergoing surgical treatment (46%) and two deaths in the group submitted to medical treatment alone (8.3%). The overall mortality was 21%. **Conclusion:** After modification in the form of management of patients with severe acute pancreatitis, there was a decrease in mortality and a trend for conservative management.

**Key words:** Pancreatitis. Pancreatitis, acute necrotizing. Therapeutics. General Surgery. Mortality.

### INTRODUCTION

Acute pancreatitis is a disease triggered by abnormal activation of pancreatic enzymes and release of several inflammatory mediators, whose etiology, in approximately 80% of cases, corresponds to biliary lithiasic disease or alcohol ingestion<sup>1,2</sup>. The diagnosis obeys clinical, laboratory and imaging parameters<sup>3</sup>. Most often, the disease is self-limiting to the pancreas, with minimal systemic repercussions; this mild form is characterized by good clinical outcome and low mortality rates<sup>2</sup>. However, in approximately 10% to 20% of the cases, the disease is more intense, with great systemic effects, leading to levels of up to 40% mortality.

After the Atlanta Symposium (1992)<sup>5</sup> two clinical well-defined acute pancreatitis became accepted: an interstitial form ("light" or "edematous") and a severe form, also known as necro-hemorrhagic or "necrotizing" pancreatitis, that usually implies some degree of pancreatic or peripancreatic necrosis, or both, with more complications, such as necrosis infection, peripancreatic fluid collections, abscesses, pseudocysts, and even multiple organs failure.

According to the Study Group for the Classification of Pancreatitis, severe acute pancreatitis (SAP)

is characterized by having three or more Ranson score criteria, eight or more points in the APACHE II classification, pancreatic complications or the presence of organ failure<sup>3</sup>. Although less frequent, this severe form of the disease continues to generate a lot of controversy<sup>6</sup>, especially with regard to the best treatment, becoming thus a challenge for surgeons, physicians, radiologists, endoscopists and intensivists<sup>7</sup>.

The goal of this series is to present the initial results obtained with the Severe Acute Pancreatitis Care Protocol in the Department of Surgical Gastroenterology and Surgical Emergency Surgery, São Paulo Hospital<sup>5</sup> UNIFESP/EPM.

### METHODS

We studied 37 patients consecutively admitted to the Emergency Department of General Surgery, São Paulo Hospital (HSP) and followed up at the Department of Surgical Gastroenterology, diagnosed with severe acute pancreatitis, respecting the criteria of the Atlanta classification<sup>3</sup>, between January 2002 and December 2010. We obtained information from each patient from medical

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records and analyzed the relationship of mortality with the variables: age, gender, etiology, length of stay and type of treatment.

For the analysis of treatment, patients were divided into two groups. The first group included 13 patients (group 1), 12 of which were submitted to surgical treatment and one to percutaneous drainage of infected pancreatic necrosis guided by imaging method. The indication of surgical and percutaneous drainage was performed after the diagnosis of sepsis in eight patients, and in five by gram staining and culture of secretions obtained by fine needle aspiration. In the second group, 24 patients clinically treated according to the protocol were enrolled (group 2).

Statistical analysis was performed using the chi-square, T-Student and Mann-Whitney tests. P-values <0.05 were considered statistically significant.

## RESULTS

The characteristics of variables analyzed are shown in table 1.

The age of patients included in the study ranged from 20 to 88 years (average 50). There was no statistically significant difference in mortality ( $p=0.154$ ). Ten patients were female (27%) and 27 (73%) were male. Likewise, there was no statistical significance for this variable with respect to mortality ( $p=0.312$  and  $p=0.359$ , respectively). The etiology of acute pancreatitis in the present sample was distributed as follows: in 22 (59.4%) patients, the cause was biliary disease lithiasic; in nine (24.3%), the cause was alcoholic; and in six (16.2%) patients the causal factor could not be determined. The etiology of pancreatitis was not associated with mortality ( $p=0.617$ ). The overall average length of stay was 47 days. For group 1 patients, the length of stay was 76 days (30-240 days), and for patients in group 2 it was 31.3 days (11-88 days). Statistical analysis revealed no significance correlating this variable to mortality

( $p=0.088$ ). Overall mortality was 21.6% (8/37). Of the total deaths, six occurred in group 1 (46%) and only two patients died in group 2 (8.3%).

The variable "type of treatment" reached the higher statistical significance when the mortality in group 1 was correlated with the mortality in group 2 ( $p = 0.028$ ).

## DISCUSSION

In recent decades, several factors, such as the progress of intensive care, imaging methods, minimally invasive procedures, spectrum and pharmacokinetics of antibiotics and, crucially, a better understanding of some pathophysiological aspects of the disease, led to the increasing delay of surgical intervention, with the consequent reduction in mortality rates observed in SAP<sup>8</sup>.

Moreover, it has been repeatedly discussed how to best characterize and early detect SAP. Laboratory parameters and imaging scores such as APACHE II, Ranson criteria, Glasgow, Goris, among others, have been proposed<sup>6</sup>. However, there is still no consensus on the best method, with a trend for less sophisticated and more reproducible scores<sup>9</sup>, such as Marshall and modified sequential organ failure assessment (SOFA)<sup>9</sup>.

Despite the defects in the existing Atlanta classification<sup>6</sup>, this remains a reference in the attempt to standardize this characterization. For simplicity, we chose to obey its guidelines in order to characterize SAP.

The epidemiological characteristics of the disease appear to be well defined<sup>10</sup>, with variability only in the etiologic factor according to the topographical area where it is analyzed. The age and etiology in our sample did not differ from other publications resulting from observed samples<sup>11,12</sup> in Brazil. However, it is noteworthy the predominance of male patients, perhaps attributable to the small sample size.

**Table 1** - Variables analyzed with respect to mortality.

Variable	Group 1	Group 2	p
<b>Age</b>	32-74 (43)	20-88 (51)	0.154
<b>Gender</b>			0.295
Male	10	17	-
Female	3	7	-
<b>Etiology</b>			0.555
Biliary Tract	8	14	-
Alcohol	2	7	-
Indeterminate	3	3	-
<b>Length of stay</b>	(30-240) 76	(11-88) 31.3	0.088
<b>Type of treatment</b>	13	24	0.028

Age = (Median)

Length of stay (days) = average

Historically, the management of patients with SAP has prompted discussion and debate about what would be the best therapy<sup>13</sup>. Conservative measures, based on exclusively clinical supportive, differed immensely from those proposing early surgical approach and even more aggressive procedures, such as pancreatectomy<sup>14</sup>. High mortality rates led to abandon of the last two options mentioned above.

Works such as the one from Mier et al. confirmed that early operation in this patient carried a range of complications and high rates of mortality<sup>15</sup>. This was consolidated by better pathophysiological understanding of the disease, allowing the SAP to be split into two phases, the early, characterized by inflammatory dominance, the and late – from the tenth day of illness on – a phase in which patients can be affected by infectious complications<sup>16</sup>.

This is precisely one of the reasons why the papers published from the 90's clearly showed a tendency to delayed surgery in patients with this indication<sup>17-19</sup>. The main concern of this study was to analyze the approach of this type of patient and associate it to clinical outcome.

There are studies that advocate the postponement of surgery, at least until one has made all attempts to compensate clinical situations and there are no mandatory surgical or minimally invasive procedures indications<sup>20-22</sup>. Clearly, due to the peculiar characteristics

of these patients, length of stay is usually prolonged, thus reflecting increasing hospital costs. The length of stay of patients in this series was higher in group 1, undergoing surgical treatment ( $p < 0.01$ ), and although there have been no cost analysis, it is likely to have been significantly higher in this group.

In our study, the indication for surgical treatment followed the Care Protocol, already mentioned, based on the Atlanta criteria<sup>23</sup>. In this group, mortality rate, considerably higher than in group 2, could be related to severity, a fact demonstrated by longer hospital stays, although stratification was not performed according to severity.

Despite the small number of patients in our sample, we can infer that the standardization of the initial approach and the delayed surgical treatment of SAP constitute the best alternative in order to improve the results of this unique presentation of acute pancreatitis. Minimally invasive methods, such as percutaneous, endoscopic and laparoscopic, are gaining ground, with encouraging results when compared to traditional methods in selected patients<sup>24-26</sup>.

In conclusion, our study also confirms high rates of mortality in patients with infected SAP undergoing surgical treatment and shows a tendency towards conservative management in this situation.

## R E S U M O

**Objetivo:** Avaliar os resultados do Protocolo de Atendimento de pacientes com diagnóstico de pancreatite aguda grave. **Métodos:** Foram analisados, consecutivamente, a partir de janeiro de 2002, idade, sexo, etiologia, tempo de internação, tipo de tratamento e mortalidade de 37 pacientes portadores de pancreatite aguda grave. **Resultados:** A idade dos pacientes variou de 20 a 88 anos (média de 50 anos); 27% foram do sexo feminino e 73% do masculino. O tempo médio global de internação foi 47 dias. Treze pacientes foram tratados cirurgicamente; a média de operações realizadas foi duas por paciente. Ocorreram seis óbitos dentre os pacientes submetidos ao tratamento cirúrgico (46%) e dois óbitos no grupo submetido somente ao tratamento clínico (8,3%). A mortalidade global foi 21% **Conclusão:** Após a modificação na forma de abordagem dos pacientes com pancreatite aguda grave, houve diminuição da mortalidade e uma tendência para a conduta expectante.

**Descritores:** Pancreatite. Pancreatite necrosante aguda. Terapêutica. Cirurgia Geral. Mortalidade.

## REFERENCES

- Steinberg W, Tenner S. Acute pancreatitis. *N Engl J Med.* 1994;330(17):1198-210.
- Cappell MS. Acute pancreatitis: etiology, clinical presentation, diagnosis, and therapy. *Med Clin North Am.* 2008;92(4):889-923, ix-x.
- Acute Pancreatitis Working Group. Revision of the Atlanta classification of acute pancreatitis. 2008. Acessado em: 2012 Fev 10. Disponível em: <http://pancreasclub.com/wp-content/uploads/2011/11/AtlantaClassification.pdf>
- Heinrich S, Schäfer M, Rousson V, Clavien PA. Evidence-based treatment of acute pancreatitis: a look at established paradigms. *Ann Surg.* 2006;243(2):154-68.
- Bradley EL 3rd. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. *Arch Surg.* 1993;128(5):586-90.
- Bollen TL, van Santvoort HC, Besselink MG, van Leeuwen MS, Horvath KD, Freeny PC, et al. The Atlanta Classification of acute pancreatitis revisited. *Br J Surg.* 2008;95(1):6-21.
- Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. *Am J Gastroenterol.* 2006;101(10):2379-400.
- Rau BM. Outcome determinants in acute pancreatitis. *Am J Surg.* 2007;194(4 Suppl):S39-44.
- De Campos T, Cerqueira C, Kuryura L, Parreira JG, Soldá S, Perlingeiro JA, et al. Morbimortality indicators in severe acute pancreatitis. *JOP.* 2008;9(6):690-7.
- Frossard JL, Steer ML, Pastor CM. Acute pancreatitis. *Lancet.* 2008;371(9607):143-52.

11. De Campos T, Braga CF, Kuryura L, Hebara D, Assef JC, Rasslan S. Changes in the management of patients with severe acute pancreatitis. *Arq Gastroenterol.* 2008;45(3):181-5.
12. Carneiro MC, Manso JEF, Eulálio JMR, Renteria JM, Costa MD. O papel da avaliação inicial simplificada no prognóstico da pancreatite aguda. *Rev Col Bras Cir.* 2006;33(3):161-8.
13. Werner J, Feuerbach S, Uhl W, Büchler MW. Management of acute pancreatitis: from surgery to interventional intensive care. *Gut.* 2005;54(3):426-36.
14. Bradley EL 3rd, Dexter ND. Management of severe acute pancreatitis: a surgical odyssey. *Ann Surg.* 2010;251(1):6-17.
15. Mier J, León EL, Castillo A, Robledo F, Blanco R. Early versus late necrosectomy in severe necrotizing pancreatitis. *Am J Surg.* 1997;173(2):71-5.
16. Beger HG, Bittner R, Block S, Büchler M. Bacterial contamination of pancreatic necrosis. A prospective clinical study. *Gastroenterology.* 1986;91(2):433-8.
17. Uhl W, Warshaw A, Imrie C, Bassi C, McKay CJ, Lankisch PG, et al. IAP Guidelines for the Surgical Management of Acute Pancreatitis. *Pancreatol.* 2002;2(6):565-73.
18. Nieuwenhuijs VB, Besselink MG, van Minnen LP, Gooszen HG. Surgical management of acute necrotizing pancreatitis: a 13-year experience and a systematic review. *Scand J Gastroenterol Suppl.* 2003;(239):111-6.
19. Besselink MG, Verwer TJ, Schoenmaeckers EJ, Busken E, Ridwan BU, Visser MR, et al. Timing of surgical intervention in necrotizing pancreatitis. *Arch Surg.* 2007;142(12):1194-201.
20. Farkas G, Marton J, Mandi Y, Leindler L. Surgical management and complex treatment of infected pancreatic necrosis: 18-year experience at a single center. *J Gastrointest Surg.* 2006;10(2):278-85.
21. Bradley EL 3rd. Surgery of acute pancreatitis. *Am J Surg.* 2007;194(4 Suppl):S20-3.
22. Bradley EL 3rd, Howard TJ, van Sonnenberg E, Fotoohi M. Intervention in necrotizing pancreatitis: an evidence-based review of surgical and percutaneous alternatives. *J Gastrointest Surg.* 2008;12(4):634-9.
23. Apodaca-Torrez FR, Goldenberg A, Lobo EJ, Triviño T. Pancreatite aguda. In: Lobo EJ, Lopes Filho GJ, Del Grande JC, Triviño T. *Guia de Gastrocirurgia – Guias de medicina ambulatorial e hospitalar.* São Paulo: Manole; 2008. p. 403-15.
24. Zyromski NJ. Necrotizing pancreatitis 2010: an unfinished odyssey. *Ann Surg.* 2010;251(5):794-5.
25. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A Step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med.* 2010;362(16):1491-502.
26. Wysocki AP, McKay CJ, Carter CR. Infected pancreatic necrosis: minimizing the cut. *ANZ J Surg.* 2010;80(1-2):58-70.

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