JOP. J Pancreas (Online) 2009 May 18; 10(3):271-275.

ORIGINAL ARTICLE

Correlates of Organ Failure in Severe Acute Pancreatitis

Jai Dev Wig[1], Kishore Gurumoorthy Subramanya Bharathy[1], Rakesh Kochhar[2], Thakur Deen Yadav[1], Ashwini Kumar Kudari[1], Rudra Prasad Doley[1], Vikas Gupta[1], Yellakanti Raghavendra Babu[1]

Departments of [1]General Surgery and [2]Gastroenterology,
Postgraduate Institute of Medical Education and Research. Chandigarh, India

ABSTRACT

Context The clinical course of severe acute pancreatitis may be complicated by organ failure. **Objective** We studied the incidence of organ failure and the correlation of the extent of necrosis and infective necrosis with organ failure. **Methods** The medical records of 161 patients with severe acute pancreatitis and persistent organ failure over a 4-year period were studied. **Main outcome measures** Pancreatic necrosis on CT was graded as <30%, 30-50% and >50% necrosis. Infected necrosis was diagnosed on the basis of a positive culture of fine needle aspiration or of a surgical specimen. Organ failure was defined according to the Atlanta criteria. Patient demographics, extent of pancreatic necrosis and presence of infection were correlated with organ failure. **Intervention** All patients were managed by a predefined treatment protocol. **Results** Of the 161 patients (124 males, 37 females, mean age 41.5±15.0 years), 52.2% had organ failure. In patients with organ failure, 48.8% had one, 33.3% two and 17.8% had multiple organ failure. Pulmonary failure was the most common organ dysfunction (76.2%). A more advanced age of patients and a higher APACHE II score were significant risk factors for the development of organ failure. Pancreatic necrosis on CT scan in patients with one, two and three organ failures was 48.8%, 51.8% and 83.3%, respectively while, in patients without organ failure, only 28.6% had more than 50% necrosis (P<0.001). No correlation was found between infected necrosis and organ failure. Overall mortality was 47.8% and mortality increased with an increasing number of organ failures. **Conclusion** Persistent organ failure occurred in 52.2% of our patients with severe acute pancreatitis. The advanced age of the patients, a higher APACHE II score and the extent of necrosis, but not infected necrosis, emerged as significant correlates of organ failure.

INTRODUCTION

The factors responsible for high mortality in patients with severe acute pancreatitis are organ failure and pancreatic necrosis. The reported incidence of organ failure in severe acute pancreatitis varies from 28 to 76% [1, 2, 3] and the resulting mortality ranges from 28 to 69% [4, 5, 6, 7]. The occurrence of organ dysfunction and progressive organ failure have a major impact on outcome [2, 8]. Patients with persistent organ failure have a higher mortality rate as compared to the group where organ failure is resolved [3, 8, 9]. Buter *et al*. [8] showed that worsening organ dysfunction was associated with death in more than half of their patients. Mofidi *et al*. [5] also reported that the prognosis deteriorated with an increase in the number of organs involved. The presence of persistent organ failure is also associated with the presence of local complications [6]. However, controversy still exists regarding the extent of pancreatic necrosis and its impact on organ failure, and whether the presence of infected necrosis correlates with organ failure [9, 10, 11, 12, 13, 14, 15]. The objective of this retrospective study was to evaluate the correlates of persistent organ failure in patients with severe acute pancreatitis.

Received August 10th, 2008 - Accepted February 20th, 2008

Key words APACHE; Multiple Organ Failure; Pancreatitis, Acute Necrotizing; Tomography, X-Ray Computed

Abbreviations CT: computed tomography; APACHE: Acute Physiology And Chronic Health Evaluation score; CTSI: computed tomography severity index

Correspondence Jai Dev Wig
8H5 Sector 12, PGI Campus, Chandigarh 160012, India
Phone: +91-981.501.6644; Fax: +91-172.274.4401
E-mail: jdwsjni@hotmail.com

Document URL http://www.joplink.net/prev/200905/07.html

MATERIAL AND METHODS

The study population consisted of 161 patients with severe acute pancreatitis who were managed in the GI unit of the Department of General Surgery and the Department of Gastroenterology of the Postgraduate Institute of Medical Education and Research, a tertiary care referral centre at Chandigarh, India over a period of four years (2003-2006). The diagnosis of acute pancreatitis was based on clinical features including acute abdominal pain, an elevated serum amylase concentration more than 3 times the upper reference limit and typical appearance on contrast-enhanced computed tomography (CECT). The patients were admitted at various stages of acute pancreatitis, some

already having developed multiorgan failure prior to admission while others developed it after admission. Severe acute pancreatitis was diagnosed if the patient had organ failure according to the Atlanta criteria [16], necrosis on a CECT scan or an APACHE II score more than 7. Computed tomography was performed on 157 patients 72 h from onset when Balthazar grading and Computed Tomography Severity Index (CTSI) scoring were done [17]. APACHE II scoring was able to be carried out for 101 out of the 161 patients at admission. Patients with organ failure for more than 48 hours were studied. Patients were referred to our tertiary care centre after a mean delay of 5 days.

All patients were managed according to a standard protocol in a high dependency unit which included intensive resuscitation, fluid and electrolyte monitoring, prophylactic antibiotics (ciprofloxacillin plus metronidazole or imipenem plus cilastin) and nutritional support (nasojejunal feeding or total parenteral nutrition and supportive care). The data of the patients who suffered severe acute pancreatitis and were managed in our unit during this time period were reviewed. Patients were informed about the disease, and its associated risks and complications. Surgery in the form of necrosectomy and closed lesser sac drainage was offered on evidence of infected necrosis or worsening organ failure despite medical management. Bacterial infection was diagnosed if image-guided fine needle aspiration or the operative specimen was culture-positive. The clinical course of these patients was followed until the completion of their hospital stay. The impact of organ failure on mortality was studied.

ETHICS

The study was approved by the ethical committee of our hospital which has a severe acute pancreatitis management protocol available and all patients are enrolled at admission and managed as per the treatment protocol.

Table 1. Patient characteristics.

Age; years (mean±SD; range)	41.5±15.0 (10-80)
Gender:	M:F ratio: 3.35:1
- Males	124 (77.0%)
- Females	37 (23.0%)
Etiology:	
- Alcohol	72 (44.7%)
- Gallstones	56 (34.8%)
- Idiopathic	27 (16.8%)
- Trauma	6 (3.7%)
APACHE score (mean±SD; range)	9.4±4.5 (2-26)
CECT necrosis (n=157)**:**	
- <30%	41 (26.1%)
- 30-50%	50 (31.8%)
- >50%	66 (42.0%)
CTSI (n=157)	
- <7	42 (26.8%)
- ≥7	115 (73.2%)

Table 2. Frequency of organ failure.

Organ systems failing	84 patients
One	**41 (48.8%)**
- Pulmonary	25
- Renal	13
- Cardiovascular	3
Two	**28 (33.3%)**
- Pulmonary + renal	18
- Pulmonary + cardiovascular	6
- Renal + cardiovascular	4
Three	**15 (17.9%)**
- Pulmonary + renal + cardiovascular	
Overall	**142**
- Pulmonary	64 (76.2%)
- Renal	50 (59.5%)
- Cardiovascular	28 (33.3%)

STATISTICS

Quantitative data were described as mean ± standard deviation with their 95% confidence intervals. The Pearson chi-square test, the chi square test for trend and the Fisher's exact test were applied to discrete variables. Continuous variables (age, APACHE II scores) were compared with the number of organs failing, using one-way ANOVA. The Statistical Package for Social Sciences (SPSS) was used for the statistical analysis. A P value (2-sided) of less than 0.05 was considered significant.

RESULTS

Table 1 gives patient characteristics. The mean age of the 161 patients (124 males, 37 females) was 41.5±15.0 years with alcohol being the most common etiology followed by gallstones and other causes. Of the 157 patients who had CECT at admission, 41 (26.1%) had less than 30% necrosis, 50 (31.8%) had 30-50% necrosis while 66 (42.0%) had more than 50% necrosis.

Organ Failure

Organ failure developed in 84 (52.2%) patients (Table 2). Of the patients with organ failure, 41 (48.8%) had single organ failure, 28 (33.3%) had two organ failures and 15 (17.9%) had failure of three organ systems. Pulmonary failure was the most common (n=64, 76.2%), followed by renal (n=50, 59.5%) and cardiovascular failure (n=28, 33.3%).

Age and Organ Failure

The mean age of patients without organ failure was 39.9±14.2 years. As shown in Table 3, an increase in mean age correlated with an increase in incidence of multiorgan failure (P=0.007).

Etiology and Organ Failure

Alcohol and gallstones were the main etiological factors. There was no significant association between the etiology of pancreatitis and the occurrence of organ failure (P=0.109; Table 3).

Table 3. Correlation between organ failure and baseline parameters.

Parameters	Number of organs failing				P value
	0 (no.=77)	1 (no.=41)	2 (no.=28)	3 (no.=15)	
Age; years (mean±SD)	39.9±14.2	41.2±15.0	41.0±15.9	51.7±14.2	0.007 [a]
Etiology:					0.109 [b]
- Alcohol	31 (40.3%)	21 (51.2%)	14 (50.0%)	6 (40.0%)	
- Gallstones	26 (33.9%)	11 (26.8%)	10 (35.7%)	9 (60.0%)	
- Idiopathic	14 (18.2%	9 (22.0%)	4 (14.3%)	0	
- Trauma	6 (7.8%)	0	0	0	
APACHE score (no.=101; mean±SD)	8.0±3.4	10.2±4.8	9.6±3.2	17.2±7.4	<0.001 [a]
CECT necrosis (no.=157)**:**					<0.001 [c]
- <30%	29 (37.7%)	6 (14.6%)	5 (18.5%)	1 (8.3%)	
- 30-50%	26 (33.8%)	15 (36.6%)	8 (29.6%)	1 (8.3%)	
- >50%	22 (28.6%)	20 (48.8%)	14 (51.9%)	10 (83.3%)	
CTSI (n=157)					0.009 [c]
- <7	29 (37.7%)	6 (14.6%)	6 (22.2%)	1 (8.3%)	
- ≥7	48 (62.3%)	35 (85.4%)	21 (77.8%)	11 (91.7%)	

[a] Linear term one-way ANOVA
[b] Pearson chi-square
[c] Chi-square for trend

APACHE II Score and Organ Failure

An APACHE II score was available for 101 patients. The mean APACHE II score of patients without organ failure was 8.0. Patients with single organ failure had a mean score of 10.2 whereas those with failure of three organ systems had a mean score of 17.2 and the higher the APACHE II score, the higher the incidence of multiorgan failure (P<0.001; Table 3).

CT Features and Organ Failure

Of the 157 patients who had CECT at admission (within 48-96 h), 66 had more than 50% necrosis (Table 3). There was a significant association between the extent of pancreatic necrosis and both the presence of organ failure and the number of organs failing (P<0.001; Table 3), with 48.8% of necrosis in zero organ failure, more than 50% in single organ failure, 51.9% in two organ failures and 83.3% in three organ failures. A significant difference was also found between the two groups divided on the basis of a CTSI less than 7 or equal to, or greater than, 7, with 91.7% of the patients with three organ failures having a CTSI equal to, or greater than, 7 (Table 3).

Infective Necrosis

A total of 66 (41.0%) patients had culture-proven infective necrosis. No relationship was found between the presence of infective necrosis and the occurrence of organ failure (29/77, 37.7% in patients without organ failure *vs*. 37/84, 44.0% in patients with organ failure; P=0.427), or the number of organs involved (Table 4).

Management and Outcome

Eighty-four (52.2%) patients were managed conservatively while 77 (47.8%) underwent surgical necrosectomy. A total of 77 (47.8%) patients died, 60 of the 84 with organ failure and 17 of the 77 without organ failure (71.4% *vs*. 22.1%; P<0.001). There was a significant correlation (P<0.001) between the number of organ failures and mortality, with a mortality rate of 58.5% (24/41) in those with one organ failure, 75.0% (21/28) in those with two organ failures and 100% (15/15) in those with three organ failures.

DISCUSSION

In the present study, we looked at the demographic and disease characteristics of patients with severe acute pancreatitis in relation to persistent organ failure. Among the possible correlates of organ failure, we did not find etiology to be linked to organ failure. However age of the patients was a risk factor for multiple organ failure. In a recent study, the age of the patients and co-morbidity were shown to be strong predictors of multiorgan failure and early death [4]. We also found a significant correlation between a mean APACHE II score at admission and the occurrence of organ failure. All the reported studies concur [8, 9] on this issue. In our study, the APACHE II score was superior to the CTSI as well in predicting organ failure. Another recent study by Mofidi *et al*. [18] also reported higher APACHE II scores in patients with persistent organ failure and consequent mortality. It has been suggested that the proven value of APACHE II as a predictor of severe acute pancreatitis, probably relates to the ability of this system to identify patients likely to develop organ failure [19].

Two of the factors linked to the development of organ failure are the extent of the pancreatic necrosis and

Table 4. Relationship between organ failure and infective necrosis.

Number of organ systems failing	Infective necrosis
0	29/77 (37.7%)
1	17/41 (41.5%)
2	15/28 (53.6%)
3	5/15 (33.3%)
Total	66/161 (41.0%)

P=0.547; chi-square for trend

infected necrosis. We found a good correlation between the extent of the necrosis as well as the CTSI and the occurrence of organ failure; the number of organ failures also increased with an increase in the extent of necrosis. A number of studies have reported no correlation between the extent of the necrosis and organ failure [11, 12, 13, 20]. Other workers, however have found a correlation between the extent of necrosis and organ failure [10, 14, 21, 22]. Isenmann *et al*. [14] reported that the incidence of organ failure was determined by the degree of necrosis in patients with sterile necrosis while, in infected necrosis, there was no correlation with the extent of the necrosis. McKay *et al*. [23] observed that, while pancreatic necrosis is associated with organ failure, nearly half of the patients with multiorgan failure have no significant necrosis. They suggested that the aim, therefore, should be to identify and treat organ failure rather than to look for pancreatic necrosis. However, the extent of pancreatic necrosis has been included in the criteria which define the severity of pancreatitis [16]. Both experimental and clinical observations confirm that the development of pancreatic necrosis is accompanied by an increase of local and systemic organ complications, increasing the risk of morbidity and mortality [24].

The question of the relationship between infected necrosis and organ failure remains unsettled. We did not find any association between infected necrosis and organ failure, 66 (41.0%) of our patients had infected necrosis. Of these, 37.7% did not have organ failure while, 48 of the 95 patients without infection (50.5%) did not have organ failure. While our results are in agreement with those of some researchers [13, 25], they are contradictory to the observations of others [3, 9, 10, 14], and some studies have not addressed this issue [22, 26]. However, the results of different studies are not strictly comparable as the total number of patients and the number of patients in different groups varies in different studies, and the timing of the onset of organ failure in relation to the documentation is not available in most studies. Since our study was retrospective, it also suffers from the latter drawback. It has been suggested that the heterogeneity of the criteria for the selection of patients with pancreatic necrosis at inclusion coupled with the different methods of defining organ failure, is responsible for the variability in results in the different studies [9]. In the last decade, a distinction between early and late, and transient and persistent organ failure was pointed out by some researchers [6, 27]. There is only one report which addresses the relationship between the reversibility of organ failure and infected necrosis [9]. Mee *et al*. [9] observed that the rate of organ failure reversibility was comparable whether the necrosis was infected or not. Thus, infection alone cannot necessarily induce the inflammatory process involved in the pathogenesis of multiorgan failure [28].

Organ failure is a major cause of mortality in patients with severe acute pancreatitis. We found a strong correlation between the number of organs involved and mortality. Other researchers have also made similar observations [9]. Overall mortality was 47.8% in our study which seems to be high. However, other researchers have also reported mortality rates as high as 35-55% in patients with persistent organ failure [8, 22, 26, 27]. Similar to the study from Serbia [26], our data are from a tertiary care centre where the majority of patients are admitted as referrals from other centers. Lack of optimum intensive care treatment in peripheral hospitals could be a factor responsible for the high mortality rate in these two studies. Our high (47.8%) rate of necrosectomy was necessitated by the clinical conditions of the patients. It is not possible to say whether this contributed to high mortality. Sharma *et al*. [27] have agreed conversely that the high mortality in their study could be due to non-operative treatment. They suggest that it is not the type of treatment but the nature and severity of the illness which determines the poor outcome in severe acute pancreatitis [27].

Our study suffers from all the limitations of a single centre and a retrospective study. The exact timing of the onset of organ failure was not available, and only data available on persistent organ failure were recorded, and data on comorbidities were also not available.

To conclude, in this study from a tertiary care centre in India, organ failure occurred in 52.17% of patients with severe acute pancreatitis. The occurrence of organ failure correlated with an increase in age, a higher APACHE II score and the extent of pancreatic necrosis and not with infected necrosis. Overall mortality was 47.8% and this correlated with the number of organs failing.

Conflict of interest The authors have no potential conflicts of interest

References

1. Shaheen MA, Akhtar AJ. Organ failure associated with acute pancreatitis in African-American and Hispanic patients. J Nat Med Assoc 2007; 99:1402-6. [PMID 18229777]

2. Halonen KI, Pettila V, Leppaniemi AK, Kemppainen EA, Puolakkainen PA, Haapianen RK. Multiple organ dysfunction associated with severe acute pancreatitis. Crit Care Med 2002, 30:1274-9. [PMID 12072681]

3. Lytras D, Manes K, Triantopoulou C, Paraskeva C, Delis S, Avgerinos C, Dervenis C. Persistent early organ failure: defining the high-risk group of patients with severe acute pancreatitis? Pancreas 2008; 36-249-54. [PMID 18362837]

4. Frey C, Zhou H, Harvey D, White RH. Co-morbidity is a strong predictor of early death and multi-organ system failure among patients with acute pancreatitis. J Gastrointest Surg 2007; 11:733-42. [PMID 17417710]

5. Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg 2006; 93:738-44. [PMID 16671062]

6. Johnson CD. Organ failure in acute pancreatitis. J Organ Dysfunction 2006; 2:171-5.

7. Eşrefoğlu M, Gül M, Turan F. Comparative effects of several therapatic agents on hepatic damage induced by acute experimental pancreatitis. Dig Dis Sci 2008; 53:1303-10. [PMID 17934852]

8. Buter A, Imrie CW, Carter CR, Evans S, McKay CJ. Dynamic nature of early organ dysfunction determines outcome in acute pancreatitis. Br J Surg 2002; 89:298-302. [PMID 11872053]

9. Le Mée J, Paye F, Sauvanet A, O'Toole D, Hammel P, Marty J, et al. Incidence and reversibility of organ failure in the course of sterile or infected necrotizing pancreatitis. Arch Surg 2001; 136:1386-90. [PMID 11735865]

10. Garg PK, Madan K, Pande GK, Khanna S, Sathyanarayan G, Bohidar NP, Tandon RK. Association of extent and infection of pancreatic necrosis with organ failure and death in acute necrotizing pancreatitis. Clin Gastroenterol Hepatol 2005; 3:159-66. [PMID 15704050]

11. Remes-Troche JM, Uscanga LF, Peláez-Luna M, Duarte-Rojo A, González-Balboa P, Teliz MA, et al. When should we be concerned about pancreatic necrosis? Analysis from a single institution in Mexico City. World J Surg 2006; 30:2227-33. [PMID 17103098]

12. Perez A, Whang EE, Brooks DC, Moore FD Jr, Hughes MD, Sica GT, et al. Is severity of necrotizing pancreatitis increased in extended necrosis and infected necrosis? Pancreas 2002; 25:229-33. [PMID 12370532]

13. Tenner S, Sica G, Hughes M, Noordhoek E, Feng S, Zinner M, Banks PA. Relationship of necrosis to organ failure in severe acute pancreatitis. Gastroenterology 1997; 113:899-903. [PMID 9287982]

14. Isenmann R, Rau B, Beger HG. Bacterial infection and extent of necrosis are determinants of organ failure in patients with acute necrotizing pancreatitis. Br J Surg 1999; 86:1020-4. [PMID 10460637]

15. Franco-Pons N, Marsillach J, Joven J, Camps J, Closa D. Serum paraoxonase undergoes inhibition and proteolysis during experimental acute pancreatitis. J Gastrointest Surg 2008; 12:891-9. [PMID 18330656]

16. 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; 128:586-90. [PMID 8489394]

17. Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology 1990; 174:331-6. [PMID 2296641]

18. Mofidi R, Lee AC, Madhavan KK, Garden OJ, Parks RW. Prognostic factors in patients undergoing surgery for severe necrotizing pancreatitis. World J Surg 2007; 31:2002-7. [PMID 17687599]

19. Larvin M, McMahon MJ. APACHE-II score for assessment and monitoring of acute pancreatitis. Lancet 1989; 2:201-5. [PMID 2568529]

20. Lankisch PG, Pflichthofer D, Lehnick D. No strict correlation between necrosis and organ failure in acute pancreatitis. Pancreas 2000; 20:319-22. [PMID 10766460]

21. Rodenkovic DV, Bajec D, Popovic N, Masulovic D, Karamarkovic A, Greogoric P, Milicevic M. Correlation between pancreatic necrosis and organ failure in patients with necrotizing pancreatitis. HPB 2005; 7 (suppl1): 25.

22. Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 2004; 53:1340-4. [PMID 15306596]

23. McKay CJ. When should we be concerned for pancreatic necrosis? Discussion. World J Surg 2006; 30:2234-35.

24. Beger HG, Rau BM. Severe acute pancreatitis: Clinical course and management. World J Gastroenterol 2007; 13:5043-51. [PMID 17876868]

25. Zhu AJ, Shi JS, Sun XJ. Organ failure associated with severe acute pancreatitis. World J Gastroenterol 2003; 9:2570-3. [PMID 14606099]

26. Bumbasirevic V, Radenkovic D, Jankovic Z, Karamarkovic A, Jovanovic B, Milic N, et al. Severe acute pancreatitis: overall and early versus late mortality in intensive care units. Pancreas 2009; 38:122-5. [PMID 18797421]

27. Sharma N, Banerjee D, Garg PK. Characterization of newer subgroups of fulminant and subfulminant pancreatitis associated with a high early mortality. Am J Gastroenterol 2007; 102:1-8. [PMID 17662103]

28. Norman J. The role of cytokines in the pathogenesis of acute pancreatitis. Am J Surg 1998; 175:76-83. [PMID 9445247]