ORIGINAL ARTICLE

Management of Suspected Acute Inflammatory Pancreatopathies in a "Real-World" Setting: A Single-Centre Observational Study

Daniele De Nuzzo, Alessia Miconi, Paola Pierantognetti

Department of Translational Medicine, School of Medicine and Psychology,
University of Rome "Sapienza". Rome, Italy

ABSTRACT

Context Acute pancreatitis is defined as an acute inflammatory process in the pancreas with variable involvement of other regional tissues or remote organ systems. In Italy, the incidence ranges from 20 to 40 x100,000 inhabitants/year and the mortality rate ranges from 5 to 10%. **Objective** To assess the management of patients with suspected acute inflammatory pancreatopathy and to evaluate the impact of this management on clinical outcomes, including morbidity and mortality. **Methods** A "real-world" observational study based on the analysis of consecutive (one year) records from the Hospital Data Processing Centre: 112 cases with final diagnosis of "acute pancreatitis". **Results and Conclusions** Sixty-nine men and 43 women were analyzed; 91 (81.3%) patients were older than 40 years and 53 (47.3%) were older than 60 years. Two patients died. One-hundred and five patients (93.8%) had abdominal pain on admission. White blood cell count was greater than 15.0 $x10^3$/dL in 26 patients (23.2%). Hematocrit levels were greater than 40% in 30 patients (26.8%). Triglycerides were elevated in 21 patients (18.8%). In 3 of them (14.3%) levels were higher than 1,000 mg/dL. Creatinine was altered in 22 (19.6%) patients. CRP values were increased in all patients. In the majority of cases (58 patients; 51.8%) pancreatitis was of biliary origin, while alcohol accounted for 16 (14.3%) cases. Four tumors were found (3.6%). Forty patients (35.7%) were discharged in the first week, 41 (36.6%) in the second week, 19 (17.0%) in the third week, and 12 (10.7%) after 21 days. After 72 hours, acute pancreatitis was classified as mild in 80 patients (71.4%) and as severe in 32 patients (28.6%).

INTRODUCTION

Guidelines for clinical practice are tools developed to help all health-care providers and caregivers. They are intended to be flexible and suggestive of preferable (though not exclusive) approaches. They need to be verified, validated and implemented. Observational studies are considered a valuable approach to test these instruments in the "real-world" setting.

Acute pancreatitis is generally defined as an acute inflammatory process in the pancreas with variable involvement of other regional tissues or remote organ systems [1, 2]. Acute pancreatitis ranks second among the most common inpatient gastrointestinal diagnoses in the U.S.A. after cholelithiasis and acute cholecystitis and before acute appendicitis [3]. Acute pancreatitis seems to have two distinct stages according to the Atlanta classification of severity [4, 5]. The first one is related to the pathophysiology of the inflammatory cascade and this phase usually lasts a week. During this phase, the severity of the disease is related to extrapancreatic organ involvement. The pancreatic inflammation evolves dynamically to either resolution or to irreversible sterile necrosis, liquefaction or development of fluid collection in and around the pancreas. Approximately 75 to 80% of patients with mild (interstitial) pancreatitis obtain resolution of the disease process and do not enter in the second phase. The second phase often develops as a consequence of the necrotizing process and the subsequent events: infection of necrosis, abscess, pseudocysts, multiple organ failure (MOF) or post-surgical complications [6]. This phase usually lasts for some weeks to a few months. The diagnosis of the disease should be established within 48 hours from admission [7]. Early identification of patients at risk of developing a severe attack of acute pancreatitis is of great importance because rapid therapeutic interventions improve the outcome [8].

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Key words Abdominal Pain; Disease Management; Pancreatic Diseases; Pancreatitis, Acute Necrotizing

Abbreviations DEA: Department of Emergency and Admission

Correspondence Paola Pierantognetti
Department of Translational Medicine; School of Medicine and Psychology; University of Rome "Sapienza"; "St. Andrea" University Hospital; Via di Grottarossa 1035; 00189 Rome; Italy
Phone: +39-06.3377.6028; Fax: + 39-06.3377.5526
E-mail: paola.pierantognetti@uniroma1.it

The guidelines for the management of acute pancreatitis particularly concern specific tests, and the timeframes within which it is useful to perform diagnostic tests. In addition, a number of different systems has been in use in order to assess the severity of acute pancreatitis [9, 10].

The incidence of acute pancreatitis in European countries increased from 12.4 to 15.9 per 100,000 inhabitants/year between 1985 and 1995, and although mortality has remained stable in Italy, the incidence ranges from 20 to 40 x100,000 inhabitants/year [11]. The incidence of acute disease of the pancreas ranges between 5-10 until 70-80 x100.000 inhabitants/years [12]. The disease calls for the use of huge medical resources in the U.S.A. [13].

The purpose of this study was to assess the management of patients with inflammatory pancreatopathy in the "real world" based on the analysis of the records of a hospital data processing centre. A secondary endpoint was to evaluate the impact of this management on direct and indirect outcomes, including morbidity and mortality, as well as the relative adherence of this management with the Atlanta criteria.

METHODS

An observational, retrospective, single-centre study was carried out through the analysis of the medical records of consecutive patients discharged from the St. Andrea Hospital (an academic hospital at the School of Medicine of the "Sapienza" University in Rome, Italy) from January 1st to December 31st, 2007 with a diagnosis of "pancreatitis" on admission at Department of Emergency and Admission (DEA). The Hospital Data Processing Centre provided a *post-hoc* list of numbers of records related to the diagnosis of interest. One-hundred and forty-seven patients with "suspected" acute pancreatitis were identified. In this study, we analyzed and reported data regarding the 112 patients (76.2%) with a final diagnosis of "acute pancreatitis". The severity of acute pancreatitis was assessed based on abnormal laboratory test findings (white blood cell (WBC) count, hematocrit values, creatinine values, blood glucose levels, C-reactive protein (CRP) levels, respiratory failure, paralytic ileum) as well as by imaging techniques, including ultrasound and CT scan.

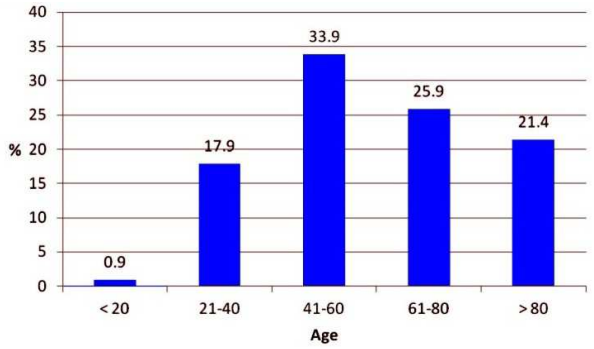

Figure 1. Distribution of patients according to age.

Table 1. The distribution of serum amylase and lipase values at admission.

ULR-fold	Amylase		Lipase	
	Range (U/L)	No. of cases	Range (U/L)	No. of cases
Up to 1	0-110	17 (15.2%)	0-300	12 (10.7%)
1-2	111-220	36 (32.1%)	301-600	10 (8.9%)
2-3	221-330	13 (11.6%)	601-900	11 (9.8%)
>3	>330	46 (41.1%)	>900	79 (70.5%)

ULR: upper limit of the reference range (amylase: 30-110 U/L; lipase: 20-300 U/L).

To characterize the impact of acute pancreatitis on the number of days of hospitalization, the analyses were made by stratifying the hospital stay into three categories according to the mean stay ±1 SD values as well as by weeks of stay: 1, 2, 3, and greater than 3.

ETHICS

Patients were treated, as well as written or oral informed consents for each procedure adopted were collected according to the usual clinical practice. The study protocol conforms to the ethical guidelines of the "World Medical Association (WMA) Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the 59th WMA General Assembly, Seoul, South Korea, October 2008. No approval by the institutional review committee was needed since this study retrospectively analyzed data recorded in the usual clinical practice.

STATISTICS

The Student's t test was used to compare length of hospital stay between males and females, while the Pearson and the linear-by-linear association chi-squared tests were applied to discrete variables. Multivariate regression was used in order to identify independent predictors of length of hospital stay. The data were analyzed by means of the MedCalc Software (Ostend, Belgium) and the SPSS Statistics 17.0 (IBM, Armonk, NY, USA). Two-tailed P values less than 0.05 were considered statistically significant.

RESULTS

Demographic Characteristics

Out of the 112 medical records analyzed from January 1st to December 31st, 2007, 69 (61.6%) patients were males and 43 (38.4%) were females.

Of all patients, 91 (81.3%) were aged more than 40 years and 53 (47.3%) were aged more than 60 years (Figure 1).

Clinical Manifestations

One-hundred and five (93.8%) patients with acute pancreatitis had abdominal pain on admission, whereas 7 (6.3%) did not, but all patients with abdominal pain showed a noteworthy (more than 3-fold the upper limit of reference) increase in amylase and/or lipase values; in particular 46 (43.8%) had increased amylase values and 79 (75.2%) had increased lipase values. Fifty-seven patients (50.9%) had nausea and vomiting and 50 patients (44.6%) had mild fever. Seven patients (6.3%) had a previous diagnosis of diabetes.

Laboratory Abnormalities

On admission, amylase and lipase values were measured in all patients. The distribution of serum amylase and lipase values is shown in Table 1. Amylase and lipase values were normal in 17 (15.2%) and 12 (10.7%) patients, respectively, while they were considerably abnormal (more than 3-fold the upper limit of reference) in 46 (41.1%) and 79 (70.5%) cases, respectively. After 72 hours, all patients had both amylase and lipase values increased by at least 3 times the upper limit of reference.

The WBC count was altered in the majority of patients (n=93, 83.0%; reference range: 4.3-10.8 $x10^3/\mu L$); in particular 26 patients (23.2%) had count values greater than 15.0 $x10^3/\mu L$ (70-80% neutrophils). The hematocrit value was greater than 40% in 30 patients (26.8%) and in 17 (15.2%) it was greater than 44%. Blood glucose values were slightly abnormal (between 1- and 2-folds the upper limit of reference that was 60-110 mg/dL in our laboratory) in the majority of the 105 non-diabetic patients (n=91, 86.7%) and the remaining 14 patients (13.3%) had blood glucose values within the reference range. Blood glucose was greater than 200 mg/dL in the 7 diabetic patients. Triglycerides were elevated (reference range: 0-150 mg/dL) in 21 patients (18.8%). In 3 of them (14.3%) levels were higher than 1,000 mg/dL. Creatinine values were altered (more than 2 mg/dL) in 22 patients (19.6%).

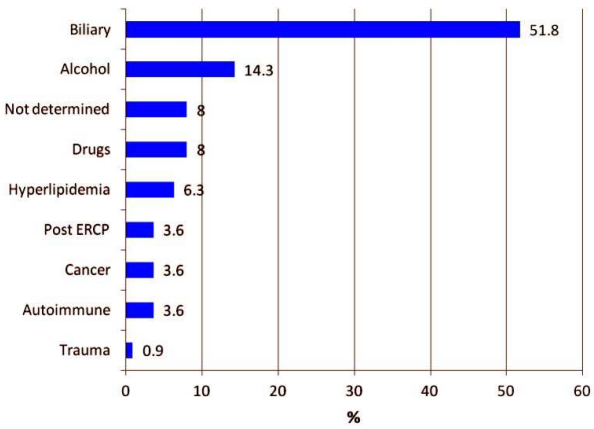

Figure 2. Distribution of patients according to the etiology of pancreatitis.

The CRP values on admission (reference range: 0-0.5 mg/dL) were measured in 102 patients (91.1%), and 4.9% of them (n=5) had normal or slightly abnormal values (less than 2-fold the upper limit of reference) while 92 patients (90.2%) showed considerably elevated pathological values (more than 3-fold the upper limit of reference); thus 5 patients only (4.9%) had CRP values between 2- and 3-folds the upper limit of reference.

Imaging

Chest X-ray

Chest X-ray was performed in 106 patients (94.6% of cases) throughout the entire period of hospitalization. Three patients (2.8%) out of them had a pathological finding (pneumonia).

Plain Abdominal X-ray

Fifty-seven patients (50.9%) underwent the test and in 14 of them (24.6%) it was performed 72 hours after the onset of symptoms (for concomitant reasons, not necessarily related to the main pathology); 2 of them (3.5%) had a pathological finding (air-fluid levels).

Abdominal Ultrasound

Fifteen patients (13.4%) did not perform any ultrasound scan. In 7 (7.2%) of the 97 available cases (86.6%) it was performed within the first hours post-admission, and was repeated more than twice during the hospital stay; other 28 (28.9%) patients underwent an abdominal ultrasound scan within 72 hours and 62 (63.9%) after 72 hours. Sixteen cases (16.5%) had a pathological finding (abscess n=5; aneurism n=1; pseudocysts n=4; cholangitis n=2; cancer n=4).

CT Scan

Fifty-one patients (45.5%) did not perform any CT scan. Sixteen (14.3%) of the 112 patients had CT scan within 72 hours from admission; 25 (22.3%) after 72 hours; and 20 patients (17.9%) both before and after 72 hours. Seventeen (27.9%) of the 61 available patients had a pathological finding (abscess n=5; aneurism n=1; pseudocysts n=4; cholangitis n=1; cancer n=4; MOF n=1; bleeding n=1).

MR Cholangiography

Fifty patients (44.6% of the sample) underwent abdominal MR cholangiography after the abdominal ultrasound, when a biliary etiology was

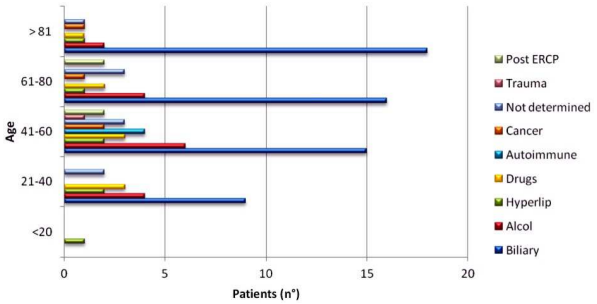

Figure 3. Distribution of patients according to etiology and age.

demonstrated. Eighteen patients (36.0%) had a pathological finding (abscess n=4; aneurism n=1; pseudocysts n=4; cholangitis n=1; cancer n=4; MOF n=3; bleeding n=1).

Etiology

As expected, in the majority of cases, pancreatitis were of biliary origin 58 (56.3%) and alcohol use accounted for 16 (15.5%). In 9 patients (8.0%) the etiology was not determined. It should be pointed out that 4 tumors (3.6%) were found. The distribution of patients according to the etiology of pancreatitis is shown in Figure 2.

Data from this study also shows that biliary etiology was present in all age groups, but the age group aged 20 years or less where one patient only was present (with etiology of hyperlipidemia). The frequency of biliary origin progressively increased with age (P=0.009, linear-by-linear association chi-square test; Figure 3) and accounted for 64.2% (34/53) in older patients (>60 years).

Length of Stay

The overall days of hospitalization were 1,259, the mean stay was 11.2±7.5 with a median of 8 days (range: 3-39 days). Forty patients (35.7%) were discharged in the first week, 41 between 8 and 14 days (36.6%), 19 between 15 and 21 days (17.0%) and 12 (10.7%) beyond 21 days.

In order to characterize the impact of acute pancreatitis on the number of days of hospital stay, we stratified the sample in three sub-groups on the basis of the mean stay ±1 SD (i.e.: cut-off values of 3.8 and 18.8 days, respectively): the group at lower hospital stay included 6 patients (all of them had 3 days of stay; 2 males, 4 females); the main group included 88 patients (56 males, 32 females) with 8.9±3.9 days, and the third group included 18 patients (11 males, 7 females) with 25.2±5.9 days (Figure 4). Moreover, the gender did not affect the length of stay (males *vs*. females: 10.9±6.8 days *vs*. 11.8±8.6 days; P=0.540, Student's t test).

In order to evaluate the role of the different etiologies on the length of hospitalization, we compared their respective frequencies with the different lengths of time in hospital stay identified from the above stratification criteria (Figure 5). A significant relationship was found between the length of hospitalization and different etiologies (P=0.005, Pearson chi-squared test); in particular a lower frequency of patients with biliary pancreatitis was found in the high class (4/18, 22.2%) than in the middle (51/88, 58.0%) and lower (3/6, 50.0%) classes of hospital stay (P=0.029, linear-by-linear association chi-squared test) as well as trauma accounted for 5.6% (1/18) in the high class of hospital stay *vs*. no cases both in the middle and lower classes (P=0.047, linear-by-linear association chi-squared test).

After 72 hours, acute pancreatitis was classified as mild in 80 patients (71.4%) and as severe in 32 patient (28.6%). Out of all patients, 16 patients (14.3%) were hospitalized for variable periods of time in the intensive care unit (ICU), all belonging to the severe pancreatitis group. Two of these patients died (one due to MOF and the other to cholangitis; 12.5% of the patients hospitalized in ICU and 1.8% of the overall population); more than one concomitant comorbidity was involved in these

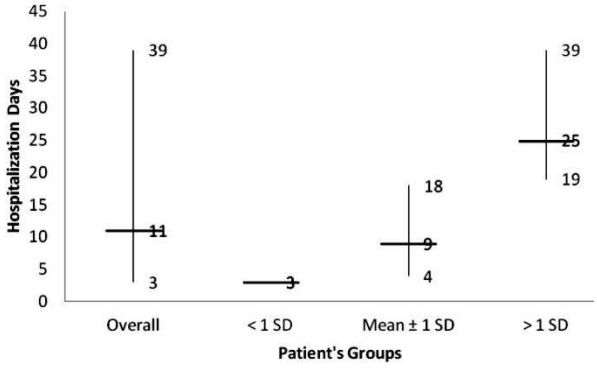

Figure 4. Description of hospitalization stay. Median and range values of days of hospitalization are shown in the three groups of patients at short, medium, and large hospitalization length.

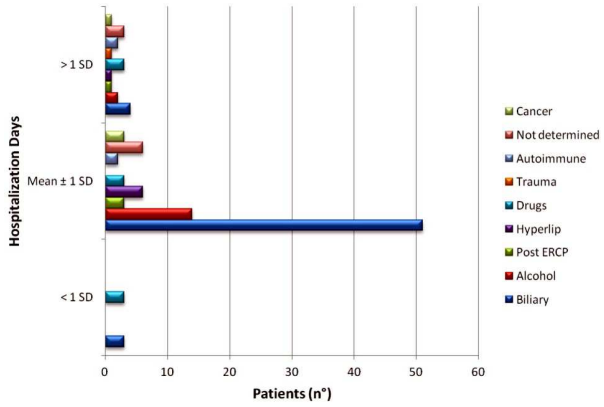

Figure 5. Distribution of etiology according to time of hospitalization. The times of hospital stay of the 3 groups are the following: 3 days (less than mean-1SD); 4-18 days (mean±1SD); and 19-39 days (more than mean+1SD).

Table 2. Comorbidities and complications in 12 patients with hospital stay exceeding 3 weeks (mean stay: 27.9 days).

Comorbidities and complications	No. of cases
Diabetes	4 (33.3%)
Pseudocysts	4 (33.3%)
MOF	3 (25.0%)
Obesity	3 (25.0%)
Abscess	2 (16.7%)
Cholangitis	2 (16.7%)
Dead	2 (16.7%)
Aneurism	1 (8.3%)
Bile common duct	1 (8.3%)
Cancer	1 (8.3%)
Cirrhosis	1 (8.3%)
Fistula	1 (8.3%)
Elevated triglycerides	1 (8.3%)
Bleeding (stomach)	1 (8.3%)
Stones	1 (8.3%)

patients. After 3 to 4 days of hospital stay in the emergency department, the patients were moved either to the gastroenterology (n=46; 41.1%), internal medicine (n=44; 39.3%) or surgery (n=22; 19.6%) departments. Out of the 96 patients not hospitalized in ICU, 82 (73.2%) were treated with medical therapy and best supportive care, while 14 (12.5%) underwent a surgical procedure: cholecystectomy (n=11) and pancreatic resection (n=3).

When we evaluated the hospitalization on a weekly basis, we observed that, in the first week, 40 patients (35.7%) had a mean stay of 5.0 days (minimum 3 days) and 7 (17.5%) of them had peripancreatic fluid only as complication. During the second week, 41 patients (36.6%) had a mean stay of 9.6 days and 16 (39.0%) of them had various complications, including necrosis (n=3), peripancreatic and perihepatic ascites (n=5), pleural effusions (n=1), jaundice (n=3), reversible renal failure (n=1), cholecystitis or cholangitis (n=3). During the third week, 19 patients (17.0%) had a mean of 17.2 days of stay, mostly following surgical (n=14) and/or ERCP procedures (n=3), and finally, all the last 12 patients (10.7%) had multiple comorbidities or associated complications during a mean hospital stay of 27.9 days (maximum 39 days) (Table 2).

Multivariate regression showed that sex, as well as, amylase and lipase levels were not significant independent predictors of length of hospital stay (P=0.552, P=0.727, and P=0.162, respectively), while CRP value was an independent predictor of the hospital stay (P=0.008). The relationship between mean values of hospital stay and mean CRP values in the four groups of patients stratified according to week of hospitalization is shown in Figure 6.

DISCUSSION

This study reports data on the management of patients with suspected acute pancreatitis admitted at the DEA of St. Andrea Hospital. One-hundred and 12 patients were diagnosed having pancreatitis during the examination at the DEA and were discharged after hospitalization with a diagnosis of "acute pancreatitis". Sixteen patients (14.3%) required to be moved to ICU, 14 (12.5%) underwent a surgical procedure (11 cholecystectomies and 3 pancreatic resections), and 82 (73.2%) were given a medical treatment.

On admission, 105 patients (93.7%) with acute pancreatitis had pain; 7 patients (6.3%) who had no pain were considered as having "acute pancreatitis" on the basis of pathologically increased enzymes. All laboratory parameters having predictive value were measured within the first 72 hours [14].

The center where this study was carried out resulted to be non-adherent to guidelines in the clinical management of suspected acute pancreatitis. In fact, imaging procedures were carried out without adherence to the guidelines based on the Atlanta criteria [15].

Chest X-rays were performed in 106 of patients (94.6%). Abdominal ultrasound was performed in 97 patients (86.6%). 7 (7.2%) underwent this examination within the first 72 hours [16], the other patients did the procedures in the following days at least once. CT scan was performed in 54.5% of the study population (61 patients) [17]. Thirty-six patients (32.1%) only did the procedures within three days from admission, while the remaining 25 patients (22.3%) did it in the following days at least once. MR cholangiography was carried out in 50 patients (44.6%), when the biliary origin was suggested by ultrasound and laboratory data [18]. The timing of imaging procedures is than different from the recommendations of Atlanta criteria. In fact, these criteria focus on the first 72 hours as the critical time window that allows to determine the potential severity of the disease, as well as to distinguish mild from severe cases [19].

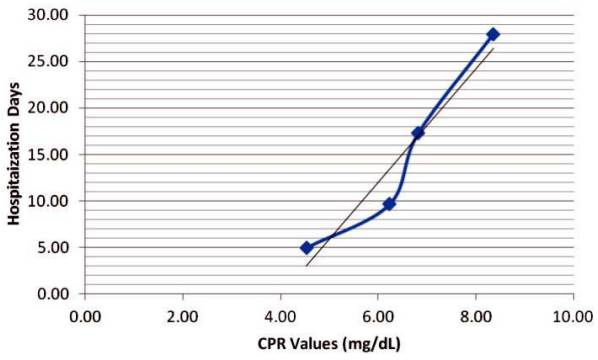

Figure 6. Correlation between the days of hospitalization and CRP values. Data are stratified in four groups according to the week of stay (first, second, and third weeks, and more than 21 days). Mean values of days of hospital stay are drawn according to mean CRP values in the four groups.

Eleven patients (9.8%) did not performed any organ imaging procedures and they were just discharged when the enzymes were normalized. Thirty-five patients (31.3%) have done an organ imaging procedure until 72 hours. The remaining 66 patients (58.6%), have done the imaging procedures after 72 hours, because the persistent complications and persistent altered biochemical parameters or for increased level of severity of the disease: so not for a predictive order but for a confirmatory one.

The etiology was not identified in 8% of the population (9 cases), while in the remaining patients, as expected, the cause was biliary origin in 58 patients (51.8%) and alcoholic in 16 patients (14.3%) [20, 21]; in patients older than 80 years, the biliary etiology (64.2%) was significantly higher than younger patients (40.7%) [22].

The total hospital stay were 1,259 days (range: 3-39 days); 6 patients (5.4%) were discharged after 3 days, 18 patients (16.1%) after 19 days, while the majority (88 patients, 78.6%) were discharged between 4 and 18 days. When data are expressed by weeks, 40 patients (35.7%) were discharged in the first week, 41 (36.6%) during the second week, 19 (17.0%) in the third week, and 12 (10.7%) beyond 3 weeks. These results are consistent with the data of other report [23]. The patients discharged within 7 days did not show any imaging organ abnormalities even if 20 of them (50.0%) showed a peripancreatic fluid collection.

The biochemical parameters have been a predictive value; in particular CRP resulted from our data as an independent predictor of length of hospital stay.

Thirty-nine percent of patients hospitalized from 8 to 14 days had complications, including peripancreatic fluid collection, necrosis, cholecystitis and cholangitis, WBC, CRP, hematocrit and creatinine abnormalities. These patients were discharged after successful medical or endoscopic treatment or were sent to surgery [24, 25]. In the group of 12 patients (10.7%) with longer stay (more than 3 weeks) 28 complications and comorbidities were found; thus, complicated diabetes, obesity, severe infections of the biliary system, MOF, pseudocysts and abscess can be considered as important factors in prolonging the length of hospital stay [26].

Only 2 patients died (overall mortality: 1.8%); more than one concomitant comorbidity was involved in these patients.

Etiology, age, sex, and severity of the disease did not interfere with the length of hospitalization and these results are in agreement with the data reported in literature [23]. Our data shows that the value of CRP at the admission is an independent predictor of length of hospital stay. In fact, CRP values were significantly and independently correlated with this outcome (Figure 6).

The non-adherence to standards (i.e., delayed imaging procedures) slightly influenced the length of hospital stay in some way, leading to an increase in direct costs especially due to the need of repeated procedures, rather than to morbidity.

CONCLUSION

In conclusion, the disease severity partially accounts for the length of hospital stay and, therefore, the difference between mild and severe acute pancreatitis seems reasonable [27]. From these data it appears that there is a group that does not reflect all the characteristics of severity of the disease and within the same group these characteristics do not appear to be homogeneous.

This study demonstrates that the approach is not homogeneous and that the treatment of acute pancreatopaties is related to the clinical condition of the individual patient rather than to the use of predictive values. This study cannot certainly state that lack of adherence to guidelines may justify an increased number of days of hospital stay. Further investigation on this is necessary.

Conflict of interest The authors have no potential conflict of interest

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