Original Article

Course of Acute Pancreatitis Patients with Renal Failure According to Balthazar Classification

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ABSTRACT

Background and Aim: There are criteria that include many organ systems to predict the prognosis in acute pancreatitis (AP) patients. In this study, we aimed to show how the course of the disease changes according to the Balthazar classification in AP patients presenting with renal failure. **Methods and Materials:** Our study included 352 patients who were admitted to the Emergency Service of our hospital and were diagnosed and hospitalized with AP. According to the Balthazar score, patients with scores of 0–2, 4–6, and 8–10 were evaluated as mild, moderate, and severe AP, respectively. Demographic data (age, gender) of all patients were documented. The etiology of AP was determined in all patients. Biliary, drug/toxic, alcohol, infections, hyperlipidemia, post-endoscopic retrograde cholangiopancreatography (ERCP), genetics, hypercalcemia, structural anomalies, and malignancy were evaluated as the etiology. Those without any underlying pathology were evaluated as idiopathic AP. The patients were divided into two groups as those with and without renal insufficiency. All patients underwent helical computed tomography (section 64, Aquilion; Toshiba Medical Systems, Tokyo) within the first 12 hours and between days 3 and 7. Pancreas, peripancreatic and extrapancreatic findings, and complications were examined. "The Statistical Package for the Social Sciences 19.0 (SPSS Armonk, NY: IBM Corp.)" was used for all analyses. Kolmogorov–Smirnov test and histograms were used to determine whether there was a normal distribution. The non-parametric data of the groups were compared using the Mann–Whitney U test and the parametric data using the ındependent *t* test. Chi-square test was used to test categorical data. Cases with $P < 0.05$ were considered statistically significant. **Results:** While 22 (6.2%) patients had renal insufficiency, 332 (95.8%) patients did not have renal insufficiency. In the evaluation made in terms of AP severity; according to Balthazar classification at admission, there was no difference in mild and moderate pancreatitis for kidney insufficiency in both groups, but it was significantly higher in the group with severe pancreatitis [2 (9.1%) versus 1 (0.3%), $P < 0.001$]. In the evaluation made after 72 hours; renal failure was significantly lower in the group with mild pancreatitis [11 (50.0%) versus 245 (73.8%), *P*: 0.016] and severe renal failure was significantly higher in severe pancreatitis [7 (31.8%) versus 13 (%) 3.9), $P < 0.001$]. **Conclusions:** Early intensive care unit admission and close follow-up and early treatment in AP patients change the course of the disease. In

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our study, we showed that serum creatinine level is an important parameter in the course of AP and has a predictive value for the course of the disease.

Keywords: *Acute pancreatitis, Balthazar classification, kidney failure*

Introduction

Acute pancreatitis (AP) is the leakage of proteolytic enzymes into the parenchyma and the activation of these enzymes and the development of widespread inflammation in the pancreas and surrounding tissues.[1]

Imaging methods also play an important role in determining the cause, diagnosis, staging, and complications of AP.[2]

There are few studies investigating changes in imaging findings during the course of AP and evaluating renal function and radiological examinations together.[3] Our study aims to evaluate how the course of the disease changes according to the Balthazar classification in patients with AP presenting with renal failure.

Subjects and Methods

Study design

Our study included 352 patients who were admitted to the Emergency Service of Van Training and Research Hospital between 2013 and 2019, diagnosed with AP and hospitalized. The diagnosis of AP was made based on the American College of Gastroenterology guidelines.[2] Those with chronic pancreatitis, pregnant women, those with contrast allergy, and those who did not want to participate were excluded from the study.

Demographic data (age, gender) of all patients were documented. The etiology of AP was determined in all patients. Biliary, drug/toxic, alcohol, infections, hyperlipidemia, post-endoscopic retrograde cholangiopancreatography (ERCP), genetics, hypercalcemia, structural anomalies, and malignancy were evaluated as the etiology. Those without any underlying pathology were evaluated as idiopathic AP.

Glomerular filtration rate

The glomerular filtration rate was calculated using the chronic kidney disease epidemiology collaboration (CKD-EPI) formula, instead of the modification of diet in renal disease (MDRD) now recommended for routine use. It is known that the CKD-EPI formula gives more accurate results than the MDRD equation in clinical diseases.[4] The patients were divided into two groups as those with and without renal insufficiency.

Severity of AP

All patients included in the study underwent abdominal computed tomography (CT). In addition to pancreatic necrosis and peripancreatic fluid accumulation, extrapancreatic findings such as ascites, pleural fluid, extrapancreatic parenchymal abnormalities (subcapsular fluid accumulation, hemorrhage, or infarction), gastrointestinal tract involvement (inflammation, intramural fluid accumulation, or perforation), and vascular complications (arterial hemorrhage, venous thrombosis or pseudoaneurysm) were evaluated. According to Balthazar score, patients with 0–2, 4–6, and 8–10 scores were evaluated as mild, moderate, and severe AP, respectively.[3]

Imaging analysis

All patients underwent helical CT (section 64, Aquilion; Toshiba Medical Systems, Tokyo) within the first 12 hours and between days 3 and 7. Contrast-enhanced CT scan (collimation, 4 × 2.5 mm; slice thickness, 5 mm; reconstruction interval, 5 mm) was obtained 65 seconds after administration of 100 ml of Iohexol (Omnipaque 300), at a rate of 3 ml/sec. All images were analyzed by a radiologist. Pancreas, peripancreatic and extrapancreatic findings, and complications were examined.

Ethics statement

Written consent was obtained from all participants of the study. Ethical approval for this study was obtained from the Ethics Committee of our hospital (Van, Turkey) (2021/21 document number, date: 24.11.2021). All procedures were in accordance with the ethical standards of our institution's human experimentation committee and the Declaration of Helsinki.

Statistical analysis

"The Statistical Package for the Social Sciences 19.0 (SPSS Armonk, NY: IBM Corp.)" was used for all analyses. Kolmogorov–Smirnov test and histograms were used to determine whether there was a normal distribution. The non-parametric data of the groups were compared using the Mann–Whitney U test and the parametric data using the ındependet *t* test. Chi-square test was used to test categorical data. Cases with $P < 0.05$ were considered statistically significant.

Results

The number of patients included in the study with the diagnosis of AP was 354. Of the patients included in the study, 206 (58.2%) were female, with a mean age of 54.8 ± 17.9 years (age range: 18-100).While 22 (6.2%)

Table 1: Baseline clinical data of patients included in the study

	With renal failure *N*: 22 (%6.2)	without renal failure *N*: 332 (%95.8)	Total *N*: 354	*P*
Age (year)	71.1±9.4	53.7±17.8	54.8±17.9	<0.001
(Mean, SD, Range)	(55-88)	(18-100)	(18-100)	
Sex				0.002*
Male	16 (72.7%)	132 (39.8%)	148 (41.8%)	
Female	6 (27.3%)	200 (60.2%)	206 (58.2%)	
Balthazar classification (At time of admission)				<0.001
Mild	12 (%54.5)	239 (%72.0)	251 (%70.9)	0.081
Moderate	8 (%36.4)	92 (%27.7)	100 (%28.2)	0.383
Severe	2 (%9.1)	1 (%0.3)	3 (%0.8)	<0.001
Balthazar classification (72 hours after admission)				<0.001
Mild	11 (%50.0)	245 (%73.8)	256 (%72.3)	0.016*
Moderate	4 (%18.2)	74 (%22.3)	78 (%22.0)	0.653
Severe	7 (%31.8)	13 (%3.9)	20 (%5.6)	<0.001
CT changes				0.010*
Regression	4 (18.2%)	73 (22.0%)	77 (21.8%)	0.675
Progression	10 (45.5%)	62 (18.7%)	72 (20.3%)	0.003*
No change	8 (36.4%)	197 (59.3%)	205 (57.9%)	0.035*

*: $P<0.05$, CT: Computed tomography

Table 2: Evaluation of the changes in CT scan performed on the 3th–7th day compared to the one performed within the first 12 hours in a patient with renal insufficiency

CT after 72 hours of admission	CT at the time of admission					
	Stage A *n* (%)	Stage B *n* (%)	Stage C *n* (%)	Stage D *n* (%)	Stage E *n* (%)	Total *n* (%)
Stage A	0 (0%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)	2 (9.1%)
Stage B	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stage C	0 (0%)	2 (100%)	6 (60%)	1 (33.3%)	0 (0%)	9 (40.9%)
Stage D	0 (0%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)	2 (9.1%)
Stage E	0 (0%)	0 (0%)	0 (0%)	2 (66,7%)	7 (100%)	9 (40.9%)
Total	0 (100%)	2 (100%)	10 (100%)	3 (100%)	7 (100%)	22 (100%)

Table 3: Evaluation of the changes in CT scan performed on the 3th–7th day compared to the one performed within the first 12 hours in patients without renal insufficiency

CT after 72 hours of admission	CT at the time of admission					
	Stage A *n* (%)	Stage B *n* (%)	Stage C *n* (%)	Stage D *n* (%)	Stage E *n* (%)	Total *n* (%)
Stage A	48 (77.4%)	8 (22.2%)	22 (15.6%)	11 (26.2%)	3 (5.9%)	11 (22%)
Stage B	4 (6.5%)	22 (61.1%)	10 (7.1%)	1 (2.4%)	1 (2.0%)	1 (2%)
Stage C	8 (12.9%)	6 (16.7%)	87 (61.7%)	9 (21.4%)	5 (9.8%)	11 (22%)
Stage D	2 (3.2%)	0 (0%)	12 (8.5%)	13 (31.0%)	3 (5.9%)	9 (18%)
Stage E	0 (0%)	0 (0%)	10 (7.1%)	8 (19.0%)	39 (76.5%)	18 (36%)
Total	62 (100%)	36 (100%)	141 (100%)	42 (100%)	51 (100%)	332 (100%)

patients had renal insufficiency, 332 (95.8%) patients did not have renal insufficiency.

In the demographic comparison between the two groups; it was determined that the ratio of male gender was significantly higher in the group with renal failure and the mean age was significantly higher in this group ($P < 0.01$ and $P < 0.001$, respectively). Considering the causes of AP, respectively, 193 (54.5%) patients were biliary, 50 (14.1%) patients were drug or toxic substances related, 28 (7.9%) patients were secondary

to ERCP, 10 (2.8%) patients were hyperlipidemia, and 8 (2.3%) patients were alcohol-related AP, while 32 (9.0%) patients had AP due to other causes (structural pathologies such as the annular pancreas and pancreatic divisium, malignancy, hypercalcemia, etc.) and no cause was found in 33 (9.3%) patients (idiopathic AP). According to the Balthazar classification, in which the tomographies taken after the 3rd day was evaluated, it was observed that the rate of mild AP was significantly lower and the rate of severe AP was significantly higher in the renal failure group ($P < 0.05$ and $P < 0.001$, respectively). In addition, in the comparison made in terms of changes in the severity of the disease (regression, progression, or no change) at the time of admission and later on; the rate of those who had disease progression was found to be significantly higher in the renal failure group ($P < 0.01$) [Table 1].

The course of AP severity in both groups was analyzed in detail. In the group with renal insufficiency; while there was no patient with stage A, it was observed that 2 (100%) of 2 patients with stage B remained stage B in the images taken after 72 hours. In the images taken after 72 hours of 10 patients with stage C, 6 (60%) patients remained stage C, 2 (20%) patients regressed to stage A, and 2 (20%) patients progressed to stage D. In the images taken after 72 hours of 3 patients with stage D, it was seen that 1 (33.3%) patient regressed to stage B, and 2 (66.7%) patients progressed to stage E. It was observed that 7 patients with stage E remained stage E in 7 (100%) patients in the images taken after 72 hours [Table 2].

In the group without renal insufficiency; ın the images taken after 72 hours of 62 patients with stage A, it was seen that 48 (77.4%) patients remained at stage A, and 14 (22.6%) patients progressed to stages B, C, and D. In the images taken after 72 hours of 36 patients with stage B, 22 (61.1%) patients remained stage B, 8 (22.2%) patients regressed to stage A, and 6 (16.7%) patients progressed to stage C. In the images taken after 72 hours of 141 patients with stage C, 87 (61.7%) patients remained stage C, 32 (22.7%) patients regressed to stage A and B, and 22 (15.6%) patients appeared to have progressed to stage D and E. In the images taken after 72 hours of 42 patients with stage D, 13 (31.0%) patients remained stage D, 21 (50%) patients regressed to stages A, B, and C, and 8 (19.0%) patients progressed to stage E. In the images taken after 72 hours of 51 patients with stage E, 39 (76.5%) patients remained stage E, and 12 (23.5%) patients regressed to stages A, B, C, and D [Table 3].

Discussion

AP is a common disease of the pancreas. It is the most common cause of hospitalizations in gastroenterology and one of the leading causes of in-hospital deaths.[5] Its severity ranges from mild self-limiting disease to severe acute necrotizing pancreatitis characterized by systemic complications and multi-organ failure. While mild and moderate pancreatitis is locally self-limiting, multiple organ failure may develop in severe pancreatitis due to both local and systemic effects. It is known that morbidity and mortality in AP patients decrease with close monitoring and early initiation of treatment.[6] For this reason, it is important to determine the course of the disease using laboratory and radiological parameters.

It has been known for many years that acute kidney injury is a life-threatening complication in patients with AP.[7] In Ranson, APACHE-2, and BİSAP scores, in which the severity of AP is evaluated, the presence of renal failure predicts that the disease will have a severe course.[8] Many theories have been proposed regarding the pathophysiology of renal failure seen in AP. Hypoxemia-related damage to renal tubular epithelial cells, impaired renal microcirculation as a result of pancreatic amylase secretion, the effect of cytokines released from the pancreas, and ischemic damage due to compartment syndrome seen in severe pancreatitis are suggested theories.[9,10] The reason why severe pancreatitis is more common in the renal failure group may be due to the correlation with the increased level of cytokines such as IL-6, IL-8, IL-18, and TNF-a, as emphasized in the study of Malmstrøm *et al*.[10] In the same study, it was found that these cytokines were increased in other organ failures due to severe pancreatitis.

Although studies on kidney function in the course of AP have been reported to be closely related to the course of the disease, there are rare studies on the relationship between kidney function and radiological findings.[11,12] In studies conducted on AP patients, it has been reported that renal dysfunction develops in the range of 15.5%–42%.[6,13,14] In the study of Johnson *et al*.[12] 174 patients with early organ failure due to AP, the mortality rate was found to be 1% in the transient organ failure group (recovered within 48 hours) (n = 71), and local complications of AP were seen in 29% of these patients; mortality was found to be 35% in the group with permanent organ failure (n = 103) and a local complication was reported in 77% of the patients. In a prospective study conducted by Muddana *et al*., which included 129 patients who developed AP, it was shown that there was a significant relationship between creatinine level and the development of necrosis in patients. Pancreatic necrosis developed in 14 of 15 patients with creatinine level >1.8 mg/dl, while pancreatic necrosis developed in only 20 of 112 patients

with creatinine level ≤1.8 mg/dl. Pancreatic necrosis was found to be 35 times more likely to develop in patients with a creatinine level >1.8 mg/dl. The specificity of pancreatic necrosis development at high creatinine levels was 98.9 and its positive predictive value was 93.3.[11] Since the patients in our study were patients with mild, moderate, and severe AP, acute kidney injury was found to be 6.2% and was found to be relatively low compared to other studies in the literature.[3,4] The fact that the patients included in the studies mentioned in the literature have severe pancreatitis explains the higher incidence of renal failure.[15-17] In our study, renal failure was 35% in the group with severe pancreatitis, and it was within the range defined in the literature (15.5–42%). In addition, in our study, it was shown that AP disease course was more progressive according to the Balthazar classification in patients with renal dysfunction at the time of admission.

To differentiate interstitial pancreatitis from necrotizing pancreatitis when clinically and laboratory suggestive of severe pancreatitis 72. hour Contrast-enhanced CT is required. It is not recommended earlier as it may give false information due to pancreatic edema and/or vasoconstriction.[18-22] JD Casas *et al*. showed that 13.2% of patients without necrosis developed complications compared to 61.5% of patients with necrosis. In the same study, it was shown that complications occur 10 times more in the group of patients with stage D and stage E according to the Balthazar classification, compared to the group without necrosis. In this patient group, the sensitivity and specificity of detecting necrosis by CT in the early period to predict complications were found to be 53.3% and 90.2%, respectively.[23] In our study, it was observed that the rate of mild AP was significantly lower and the rate of severe AP was significantly higher compared to the Balthazar classification, in which the tomography taken after the 3rd day was evaluated in patients who were examined on the time of admission and who developed renal dysfunction. In addition, the rate of progression of the disease was higher in the group with renal dysfunction.

This study has some limitations and strengths. The important limitations of the study are that it is retrospective and other risk factors that play a role in the progression of the disease are not discussed in detail. In addition, since the data were obtained only from a single tertiary center, it may not include all patients hospitalized with a diagnosis of AP. Clearly revealing all patient etiologies, large sample size, and evaluation of all CT scans by the same person (radiology specialist) are the strengths of our study.

Close follow-up of AP patients in the early period and initiation of treatment change the course of the disease. In this respect, it is important to know the course of the disease at the time of admission.[18] In our study, we showed that serum creatinine level is an important parameter in the course of AP and has a predictive value for the course of the disease. Although CT is an important marker, it is not recommended due to its inability to show the severity of the disease in the early stages. However, the degree of kidney dysfunction gives us an idea about the course of the disease, since there is a correlation between the kidney function measured at the beginning and the severity of the disease according to the CT taken later.

Ethics approval

The study was conducted with the approval of our hospital Ethics Committee dated 24.11.2021 (2021/21 document number).

Key messages

In our study, we showed that serum creatinine level is an important parameter in the course of acute pancreatitis and has a predictive value for the course of the disease. Although CT is an important marker, it is not recommended due to its inability to show the severity of the disease in the early stages. However, the degree of kidney dysfunction gives us an idea about the course of the disease, since there is a correlation between the kidney function measured at the beginning and the severity of the disease according to the computed tomography taken later.

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Conflicts of interest

There are no conflicts of interest.

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