Evaluation of the clinical course and prognostic indices of acute pancreatitis in elderly patients : a prospective study

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Abstract

Background and aim **: Acute pancreatitis (AP) is a life-threatening condition across all age groups. In this study, it was aimed to investigate the severity of the disease and associated mortality in the geriatric population.**

Methodology **: This single-center, prospective study elderly (≥65 years of age) and younger (18-65 years of age) total 147 patients with AP are enrolled To diagnose and asses the severity of AP Atlanta classification was used. Baseline and 12-months follow-up data included Ranson, Imrie, BISAP, APACHE-II, SOFA, Modified Marshall, Balthazar, and Computed Tomography Severity Index (CTSI) as prognostic tools.**

Results **: 6 (15%) patiens in elderly and 5 (6,7%) patients in non elderly group had modarete-severe AP . Patients were followed up 1 year and during this time no systemic complications were seen , 8 (20%) patients in elderly group and 10 (13,6%) patients in younger group had local complications. 1 patients in elderly and 2 patients in non elderly group had acute necrotic collection whereas 1 patient developed walled of necrosis in non elderly group. The elderly patients with any of the following index characteristics would not be expected to have a mild disease course: Imrie score ≥ 3, BISAP score ≥ 3, APACHE-II ≥ 11, CRP ≥ 195 mg/dl**

Conclusions **: AP caused a prolonged hospitalization in the elderly compared to younger patients but its severity and clinical outcomes were not different in the two groups.** (Acta gastroenterol. belg., **2020**, 83, **413-417**).

Keywords : Acute pancreatitis, APACHE, Blood urea nitrogen, C-reactive protein, elderly patients, prognosis.

Introduction

Acute pancreatitis (AP) can be associated with severe complications and mortality despite treatment. Around 80% of patients have edematous pancreatitis, which usually resolves within days without causing complications whereas one-fifth of patients develop necrotizing pancreatitis (1). Prediction of the severity of AP has been a crucial part of patient management as it can facilitate the decision-making in the selection of high-risk patients who might require transfer to the intensive care units.

Although older adults are at increased risk of having a more complicated course in certain disease conditions, the data related to AP is controversial (2-5). In a small sample of patients aged 80 years or older, AP was associated with increased mortality (3). Investigation of a larger population, 14322 patients with AP in an administrative database from Japan, showed that severe comorbidity was significantly associated with higher in-hospital mortality and longer length of stay (2). Moreover, cardiovascular and renal diseases were the most significant comorbidities affecting outcomes of older patients with AP. However, in a cohort of 227 patients, the duration of the hospital stay and the rate of mortality were not different in patients aged above and below 65 years (5). Others found a positive correlation between age and organ failure but the rate of complications was not dependent on age or presence of comorbidities (4). On the other hand, these studies are all retrospective and no targeted assessment and comparison of complications have been reported to date in older and younger adults.

In this study, we evaluated the clinical, biochemical and prognostic characteristics of elderly and younger patients with AP. We also analyzed the utility of the available prognostic indices in the prediction of a more severe AP in this group of patients.

Methodology

In this single-center study, patients who were diagnosed with AP at a tertiary care unit of a university hospital in the period between August 2014 and August 2016 were enrolled consecutively. The inclusion criteria were physician diagnosis of AP based on Atlanta criteria (6) (typical pain and /or elevated lipase and/or specific imaging), newly diagnosed disease with no previous history of pancreatitis and within two days of symptoms starting), and the ability to give consent to participate in the study. Exclusion criteria were having a diagnosis of chronic pancreatitis, being bed-bound elders and having a diagnosis of malignant diseases.

At study entry, we collected demographic data, comorbidities, current medical treatments, and surgical history using a standard questionnaire. The study protocol did not include any procedure outside the usual laboratory workup and imaging techniques required for AP management. The revised Atlanta classification to diagnose AP was used (6) in the presence of two of the following three features : 1) abdominal pain consistent with AP ; 2) serum lipase activity (or amylase activity)

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Submission date : 26/05/2019
Acceptance date : 02/03/2020

at least three times greater than the upper limit of normal range ; and 3) characteristic findings of AP on abdominal imaging (preferably CT, less commonly MRI or the US).

The Atlanta classification was also used to define the severity of AP as "mild", "moderately severe", and "severe"(6). Additionally, clinical severity was assessed by the following scoring systems: Acute Physiology and Chronic Health Examination (APACHE) II (7) Bedside Index of Severity in Acute Pancreatitis (BISAP) (8), Ranson's (9) and Imrie's (10) scoring systems within 48 hours, Sequential Organ Failure Assessment (SOFA) score (11) the modified Marshall scoring system (6) Balthazar scoring (12) and modified CT severity index (CTSI) (13). For geriatric patients Geriatric Index of Comorbidity (GIC) was used (14).

Biliary etiology is recorded if gallstones or sludge could be demonstrated. Patients who had a history of regular alcohol intake (more than 40 g ethanol per day (20 g in female)) for at least 5 years were diagnosed with alcoholic AP (15). or the presence of a periampullary tumor along with the exclusion of other etiologies were accepted as the hyperlipidemic and malignant etiology, respectively. We made a diagnosis of idiopathic pancreatitis when no relevant cause was identified.

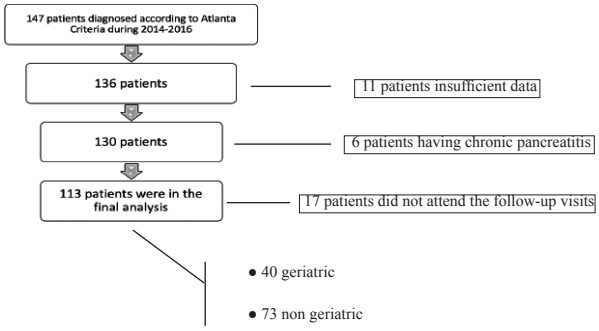
A follow-up visit was performed at one month and three months after discharge. All patients were re-evaluated by clinical examination, laboratory assessment and ultrasonography to monitor the local complications as well as mortality. Local complications are described according to Atlanta classification criteria and as follows peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst and walled-off necrosis (sterile or infected).Informed consent was obtained from all the participants and the study was approved by the ethics committee of Gazi University (26-01-2015/52)

Patients were managed as follows: nothing by mouth, proton pump inhibitor to inhibit pancreatic secretion and to prevent stress ulcers, efficient pain control and intravenous restoration of fluid and electrolytes. Antibiotics were used in patients with infected necrosis or cholangitis. Oral intake was resumed as soon as pain ceased and the placement of nasoenteral feeding tube was performed for a starvation period of longer than 5-7 days. An endoscopic sphincterotomy was done to extract co-existing common bile duct stone. Computerized tomography (CT) was ordered in patients with clinical deterioration to search for necrosis (16). The patients who develop organ failure were transferred to the intensive care unit and followed there until restoration of organ functions was observed. The severity of AP was determined according to the abovementioned revised Atlanta classification (6). Clinical severity was also evaluated by several scoring systems (Table 2).

Statistical analyses

Continuous data were presented as mean ± SD. Categorical variables were provided as percentages. In univariate analysis, Student's t-test / Mann–Whitney test were used to compare continuous variables while chi-square and Fisher's exact test were used for categorical variables. ROC analysis was used to determine the cut-off values of several prognostic scoring systems to predict AP with the moderately severe/severe course. A two-sided P-value of 0.05 or less was considered statistically significant. The study was conducted between 2014-2016 and all patients diagnosed with AP were included. During study intermittant power analysis was done and at the end of the study with a power of 91,8 % wtih the 95% confidance interval.

Diagram 1 : Study design scheme



Results

A total of 147 patients with AP was enrolled in the study. Eleven patients had insufficient follow-up data during hospitalization and seventeen patients did not attend the follow-up visit. Six patients who were diagnosed as acute pancreatitis at admission later were appeared to have chronic pancreatitis were also excluded. The final analysis included 113 individuals (Diagram 1).

Baseline evaluation

Table-1 shows the basic characteristics of the study population. 40 elderly patients and 73 non elderly patients were included in the study. Population age (mean±SD): 73.7±7.0 and 45.2±11, respectively].Geriatric Index of Comorbidity (GCI) score's were 0 in 5 (12,5%) patients, 1 in 8 (20%) patients, 2 in 24 patients (60%) and 3 in 3 (7,5% patients). Intensive care unit admission , hospital staying length, pancreatitis severity scores were similar between GCI scores. Male sex ratio was higher in non elderly group, this differannce not significant though (p:0.169). The number of major comorbidities (diabetes mellitus, coronary heart disease, hypertension) was significantly higher in the elderly group. The two groups were similar for complete blood count and renal functions but BUN was higher and albumin was lower in the elderly individuals. Interestingly, younger patients had significantly higher CRP levels compared to the elderly group (p:0,045). The probable causes of AP were also listed in the Table-1. Biliary etiology (n:29, 72,5%) was identified more frequently in the elderly group,

Table 1. — **Baseline demographics and clinical characteristics of the patients, mean±SD, n(%)**

Variable	Elderly (n=40)	Non-elderly (n=73)	P Value
Age (years)	73.7±7	45.2±11	<0.001
Male sex	16 (40)	40 (54.8)	0.169
Smoker	11 (27.5)	25 (34.2)	0.530
Heavy drinker	3 (7.5)	9 (12.3)	0.534
Comorbidity	32 (82.5)	32 (43.8)	0.0003
Diabetes mellitus	12 (30)	10 (13.6)	0.048
Coronary heart disease	14 (35)	6 (8.2)	0.0001
Hypertension	27 (67.5)	16 (21.9)	0.0001
Malignant disease	2 (5)	5 (6.8)	1.000
Laboratory findings			
Hematocrit (%)	39±5.2	39.2±5	0.803
Blood urea nitrogen (mg/dl)*	18 (14.75)	13 (7)	0.018
Creatinine (mg/dl)*	0.77 (0.31)	0.80 (0.49)	0.117
Albumin (g/dl)	3.4±0.6	3.9±0.5	<0.001
C-reactive protein (0-6 mg/dl)*	78 (116)	120 (135)	0.045
Etiology			
Biliary	29 (72.5)	30 (41.1)	0.017
Alcohol	-	3 (4.1)	0.551
Idiopathic	6 (15)	19 (26)	0.237
Miscellaneous	5 (12.5)	21 (28.7)	0.062

Creatinine, C-reactive protein and blood urea nitrogen expressed as median (IQR).

Table 2. — **Severity, local complications, clinical course and outcome of acute pancreatitis in the elderly patients and non-elderly control group and comparison with respect to prognostic scoring systems,n(%), median (IQR)**

Variable	Elderly (n=40)	Non-elderly (n=73)	P Value
Severity of AP			
Mild	34 (85)	68 (93.2)	
Moderately severe	5 (12.5)	3 (4.1)	0.251
Severe	1 (2.5)	2 (2.7)	
Ranson	3 (1.5)	2 (3)	<0.001
Imrie	3 (2)	1 (2)	<0.001
BISAP	2 (1)	1 (1)	<0.001
APACHE-II	11 (4)	2 (8)	<0.001
Balthazar	1 (2.5)	2 (2)	0.273
CTSI	4 (2)	2 (2)	0.881
Local complications	8 (20)	10 (13.6)	
APFC	3 (7.5)	9 (12.3)	
Pseudocyst	5 (12.5)	4 (5.4)	0.346
ANC	1 (2.5)	2 (2.7)	
WON	-	1 (1.4)	
Transfer to ICU	1 (2.5)	3 (4.1)	0.555
Median hospital stay, days	10 (4-31)	6 (2-36)	<0.001
Median ICU stay, days	2	6 (2-11)	0.346

Values are expressed as the n (%). AP, acute pancreatitis ; APFC, acute peripancreatic fluid collection ; ANC, acute necrotic collection ; WON, walled-off necrosis. ICU : Intensive care unit. Severity was assessed according to revised Atlanta classification.BISAP, bedside index of severity in acute pancreatitis ; APACHE-II, Acute Physiology and Chronic Health Evaluation-II ; SOFA, Sequential Organ Failure Assessment score ; CTSI, computed tomography severity index.

which was significantly lower in the younger group (n:30, 41,1%) (p:0.017). Miscellaneous etiologic factors such as hyperlipidemia, infection, malignancy, idiopathic were more commonly seen in non elderly group as shown in table 1.

Based on the initial evaluation using the Atlanta Classification, the severity of AP was mild in the majority of the patients, which was similar in the two groups (85% versus 93,2% respectiveley) (Table-2). Moreover, only a few cases were classified as having severe disease. However, we observed significant differences between the older and younger groups concerning the prognostic systems including Ranson, Imrie, BISAP, and APACHE-II that showed a severe disease in the elderly group (Table 2). Balthazar and CTSI scores showed no difference between the two groups.

Follow-up Evaluation

No patient died during hospitalization and within a three-month follow-up period. The most frequent local complication in the elderly group was the pseudocysts which were detected by 12.5%, whereas acute peri-pancreatic fluid collection (APFC) was the primary complication in the younger group (Table-2). The overall proportion of subjects having local complications was similar between the two groups (Table 2). The rate of transfer to the intensive care unit (ICU) was low and did not differ in the two groups. However, median days of hospitalization was significantly longer in the elderly group compared to nonelderly patients (Table 2).

Performance of Scoring Systems and Parameters on Predicting Bad Prognosis

The validity of the various prognostic systems and individual parameters to predict the AP cases without a mild course in the elderly and nonelderly groups are tested separately. Accordingly, Imrie, BISAP, APACHE-II, and CRP levels were found to be different between mild and moderately severe/severe AP groups in the elderly population($P < 0.05$). The cut-off values of the relevant parameters to differentiate two above-mentioned subgroups of AP in the elderly are shown in table 3. Receiver operating characteristics curve demonstrating the predictive performance of the parameters with a P value < 0.05 is shown in Figure 1. The age (mean±SD) of the patients in the moderately severe/severe (57±19.7) and mild (55.1±16.6) pancreatitis groups was not significantly different (P=0.724).

At baseline, the elderly group had more comorbidities, gallstone disease, worse laboratory data, and higher Ranson, Imrie, BISAP, APACHE-II, and SOFA scores. The severity of AP at baseline and the rates of local complications and transfer to ICU during follow-up were similar in the two groups. Days of hospitalization were sigficantly higher in the elderly group. Imrie score ≥ 3, BISAP score ≥ 3, APACHE-II score ≥ 11, and CRP ≥ 195 mg/dl were the predictors of moderately severe/severe disease course in the elderly group.

Table 3. — **Moderately severe/severe versus mild acute pancreatitis classification performance of blood urea nitrogen, C-reactive protein and various prognostic systems in elderly patients**

Parameter	Mod Sev/Sev vs Mild	Cut-off	AUC	Pp	Ssens	Ssps
Imrie	2.8±0.4 vs 1.6±1.3 P=0.027	3	0.770 (0.571-0.969)	0.037	883.3	770.6
BISAP	3±0.6 vs 2.1±0.6 P=0.006	3	0.814 (0.622-1.000)	0.015	883.3	779.4
APACHEII	11.3±2 vs 8.6±2.9 P=0.024	11	0.770 (0.571-0.969)	0.037	883.3	770.6
CRP	227.5 (121.5) vs109 (107) P=0.007	195	0.839 (0.676.-1.000)	0.009	883.3	884.3

BISAP, bedside index of severity in acute pancreatitis ; APACHE-II, Acute Physiology and Chronic Health Evaluation-II ; CTSI, computed tomography severity index, CRP, C-reactive protein (mg/dl) ; BUN, blood urea nitrogen. Expressed as value (95% Confidence Interval). Sensitivity (Sens), Specificity (Sps). Cut off as ≥. Parameter values expressed as mean±SD or median (IQR).

Discussion

Our findings showed that people older than 65 years old with AP do not have increased mortality and morbidity compared to younger patients. And BISAP, APACHE-II, Imrie, and CRP serve to identify elderly patients who will not have a mild disease course.

The predominant etiological subgroup of AP was biliary pancreatitis in our elderly patients. We think that this finding is not surprising because it has been reported that the risk of gallstones tends to increase with age in all ethnic groups (17,18). Increase in the frequency of gallstone disease in the elderly may be explained by a positive correlation between age and an increased cholesterol secretion and saturation. After investigating with more precise technique such as endoscophic ultrasonography or magnetic resonance imaging, endoscopic sphincterotomy and/or cholecystectomy could be discussed with patient with recurrent AP of unknown origin. (19)

In the study population, elderly patients had a tendency to have higher baseline levels of BUN compared to younger patients (Table 1). Elevation in baseline BUN reflects intravascular volume loss and predicts outcome in AP. In fact, BUN can also be used to evaluate fluid resuscitation efficiency as well. The target for "controlled resuscitation" is to correct hypotension, to maintain effective mean arterial pressure and to reach urine output >0.5 mL/kg/hour (16,19,20). This fluid resuscitation should be carefuly managed to avoid hypervolemic complications especially in geriatric population. In fact in modarete-severe AP elderly patient can be admitted in ICU for better monitorization.

Elderly patients had lower baseline albumin levels compared to younger patients. The negative impact of systemic inflammation on albumin levels partially can be explained for this difference because CRP levels were different between elderly and non-elderly groups (Table 1).In fact non-elderly population had higher CRP levels. So it was attributed to have relatively decreased baseline albumin levels in our elderly patients in favor of malnutrition. Inappropriate prolongation of "nothing by mouth" period may deepen malnutrition in elderly patients. Enteral feeding reverses the mucosal injury of fasting and maintains epithelial integrity, and bacterial ecology, thereby helping to protect gut barrier function (21,22). For these reasons, the elderly patients with AP should be dynamically evaluated for the early resumption of oral intake.

Another result is that the elderly patients had a higher rate of comorbidity is consistent with the results of some other studies (5,23) . But the presence of comorbidity did not have a negative impact on the clinical course of AP in our series .On the other hand, considering the sample size and the rarity or absence of some co-existing disease entities (e.g. chronic renal disease, malignancy or chronic pulmonary disease) in elderly cohort prevent us from drawing a general conclusion regarding the lack of association between comorbidity and severity of AP.

Early studies suggested that AP has a more severe and life threatining course in the elderly patients (10,24,25). In this study elderly patients had a longer duration of hospital stay but they had a disease course similar to younger patients with no mortaliy. Although the number of moderately severe/severe AP patients was higher among the elderly than younger patients in our series (15 % vs 6.8 %); the difference was not statistically significant (P=0.112). The mean age was not also different between moderately severe/severe and mild AP. Changing attitudes in the management of AP over time, especially early enteral nutrition and efficient IV hydration, may have improved the clinical course of AP in elderly patients. In favour of this hypothesis, this conclusion is consistent with the results of recent studies in that chronological age had no significant influence on the clinical outcome of AP(5) and mortality rates (5, 26). But in subgroup analysis , regarding severe and moderate AP, no final conclusions can be drawn, due to the low number of patients with moderate severe AP.

The utility of various indices to predict prognosis of AP in the elderly was also tested (Table 2-3).And it was showed that the elderly patients with any of the following index characteristics would not be expected to have a mild disease course: Imrie score ≥ 3, BISAP score ≥ 3, APACHE-II ≥ 11, CRP ≥ 195 mg/dl (Table 3). In elderly patients other parametres were not different between

mild and moderate/severe course. In literature higher Ranson score was found in elderly patients with worse disease prognosis (27-29) APACHE- II was also high as it happened in our study(29). But as far as we know ,no information related to Imrie BISAP and CRP levels in elderly onset acute panreatitis patients evaulated in literature. Early identification of these risky patients with as many tools as may necessitate better closer follow up and effective triage to reduce morbidity and mortality.

Major limitations of the study was the low number of moderate-severe AP patients. Although it was possible to predict which patients had a worse prognosis in the light of our study findings, it was not possible to generalize this result in real life settings. Also geriatric patients mostly do not have serious comorbidities, thus this may effect the prognosis of AP in this population.

Conclusion

AP does not necessarily have a more severe course and/or worse clinical outcome in geriatric patients compared to younger individuals. Several prognostic indices (Imrie, BISAP, APACHE-II and CRP) may help early triage of the elderly patients with AP but the relevant cut off values to predict a more severe AP disease course in the elderly are to be determined and confirmed by future prospective studies with larger sample sizes.

Conflict of interest

The authors declare that they have no conflict of interest

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