Original Article

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Outcome of elderly patients after acute biliary pancreatitis

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Summary **The specific management and outcome of acute biliary pancreatitis in elderly patients is not well established. The aim of this study was to assess the outcome of elderly compared to younger patients after acute biliary pancreatitis. Retrospective analysis of consecutive patients admitted with acute biliary pancreatitis between January 2006 and December 2012. Elderly patients (≥ 70 years) were compared to younger patients (< 70 years) in a case-control study. Comorbidities were assessed according to the Charlson score. Clinical (Atlanta score) and radiological (Balthazar and computed tomography severity index scores) severity were analyzed, as well as clinical outcome. Among 212 patients admitted with acute biliary pancreatitis, 76 were > 70 years (35.8%). Elderly patients had a higher Charlson comorbidity index score at admission ($p < 0.001$). No difference was observed in terms of clinical and radiological severity of acute pancreatitis. The median hospital stay was longer in elderly (11 days, interquartile range 7-15) than in younger patients (7 days, interquartile range 5-11) ($p < 0.001$). No difference was observed regarding in-hospital 90-day mortality (3 *vs*. 1 patients, $p = 0.133$). Elderly patients had similar clinical and radiological severity of acute biliary pancreatitis compared to younger patients.**

Keywords: Pancreatitis, aged, gallstones

1. Introduction

Acute pancreatitis is a common cause of surgical admission with an annual incidence that varies between 4.0-45.3 /100,000 and an overall mortality risk of 3-20% (*1*). Gallstone is the most frequent cause of acute pancreatitis (24 to 71%) and its incidence increase with age (*1-4*).

Different studies addressing the relation between age and prognosis of acute pancreatitis displayed conflicting results (*4-6*). A study published in 1988 found higher mortality in patients over 75 years, but complication rate and the proportion of patients with severe disease was not different (*4*). On the other hand, more recent studies observed that acute pancreatitis was more severe in elderly patients without increased mortality (*5,6*). However, none of these studies focused exclusively on biliary pancreatitis.

This present study aimed to evaluate the clinical severity, radiological presentation, and outcome of acute biliary pancreatitis in elderly patients over 70 years compared to younger patients.

2. Materials and Methods

2.1. *Study design*

Case-control study comparing patients over 70 years (study group) to younger patients (control group).

A retrospective analysis was performed of all consecutive patients admitted or secondarily referred with acute biliary pancreatitis to our institution, a tertiary referral center, between January 2006 and December 2012. The Institutional Review Board approved the study (119/13). The study was registered on www.researchregistry.com (UIN 2363). The study was conducted in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) criteria (*http://strobe-statement.org/*). Data

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was collected in 2014. All consecutive patients (> 18 years) with a diagnosis of acute biliary pancreatitis were included. The diagnosis of acute pancreatitis required 2 of the following 3 features: abdominal pain consistent with acute pancreatitis, serum lipase (or amylase) higher than at least 3 times the upper limit of normal, and characteristic findings of acute pancreatitis on contrast-enhanced computed tomography or magnetic resonance imaging or transabdominal ultrasonography (*7*). A biliary etiology of acute pancreatitis was determined by the presence of gallstone or sludge in the gallbladder or in the common bile duct, with neither evidence for alcohol abuse nor for another cause. Patients with pancreatitis secondary to endoscopic retrograde cholangio-pancreatography, were not included.

2.2. *Outcome measures*

Demographics data included age at the time of admission, gender, previous episode of acute biliary pancreatitis before the study period, and previous cholecystectomy. Patients' comorbidities were assessed including arterial hypertension, obesity (defined as a Body Mass Index (BMI) > 30 kg/m^2), diabetes, hypercholesterolemia, hypertriglyceridemia, ischemic heart disease, congestive heart failure, chronic obstructive pulmonary disease and chronic renal failure. The Charlson comorbidity index was calculated for every patient (*8*).

Clinical severity of acute pancreatitis was defined according to the revised Atlanta criteria (*7*). Radiological severity of acute pancreatitis was assessed using the Balthazar grade (*9*), the Computed Tomography Severity Index (CTSI) (*10*) and the modified CTSI (*11*). Local complications such as pseudocyst formation, portal venous thrombosis, pleural effusion, and intra-abdominal pseudoaneurysmal bleeding were assessed.

Patients underwent abdominal MultiDetector Computed Tomography (MDCT) scans which were performed 48 hours following the appearance of symptoms. MDCT scans were performed on a 64-detector row scanner (Lightspeed VCT; 64 Pro, GE Healthcare; Milwaukee, WI, USA). The imaging protocol included the whole abdomen and pelvis (120 kV, 300-400 mA, pitch 1.375). After an unenhanced phase (2.5/2 mm reconstructed axial slices), iodinated contrast medium was injected (Accupaque®, 300 mgI/mL; GE Healthcare; volume in mL = body weight+30 mL) at a flow rate of 4 mL/s, followed by an arterial phase (25 s, 1.25/1mm reconstructed axial slices) and a venous phase (80 s, 2.5/2mm reconstructed axial slices) scans. Image analysis was performed by 2 board-certified radiologists (R.D. and S.H, with 9 and 6 years of experience in abdominal imaging, respectively) during a consensus reading. The Balthazar grading and CTSI score were assessed. Radiologists were blinded to clinical outcomes.

The different treatments performed were assessed, including: antibiotics, Endoscopic Retrograde CholangioPancreatography (ERCP), percutaneous or transgastric drainage of intra-abdominal fluid collections and surgical necrosectomy. Hospital and intensive care unit length of stay, as well as in- hospital 90-day mortality was noted. Patient's discharge destination (home or nursing home) was collected. The rate of cholecystectomy (excluding patients with previous cholecystectomy) as well as the interval between admission for acute pancreatitis and cholecystectomy was measured. The recurrence of acute biliary pancreatitis during the study period was also recorded.

2.3. *Statistical analysis*

Descriptive statistics for categorical variables were reported as numbers and percentages, while continuous variables were reported as medians and interquartile ranges for non-normally distributed data or means and standard deviations for normally distributed data. The Student *t* test or the Mann-Whitney *U* test were used to compare continuous variables. Fisher's exact test or Chi-Square test were used for the comparison of categorical variables. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA).

3. Results

During the study period, 481 patients were hospitalized for acute pancreatitis (Figure 1). Among them, a total of 212 patients (aged 18 - 99 years) with acute biliary pancreatitis were included in the analysis. Seventy-six patients were 70 years or over (study group) and 136 were younger than 70 years (control group).

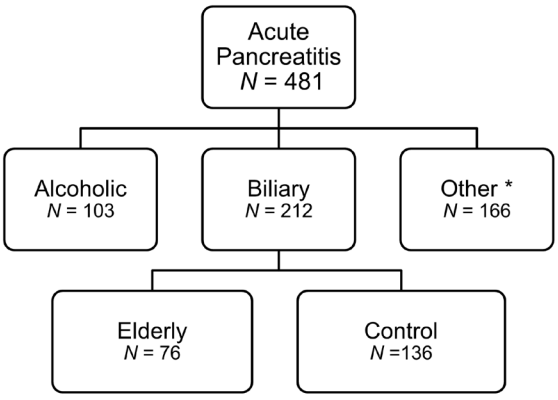

Figure 1. Flow diagram of patients admitted with acute pancreatitis. *Others: idiopathic (*N* = 110), traumatic or following endoscopic retrograde cholangiopancreatography (*N* = 26), drug-induced (*N* = 12), tumoral (*N* = 7), hypertriglyceridemia-induced (*N* = 3), mucoviscidosis (*N*= 2), pancreas divisum (*N* = 1), duodenal diverticula (*N* = 1), perforated ulcus (*N* = 1), hemobilia (*N* = 1), auto-immune (*N* = 1), hypercalcemia (*N* = 1). Elderly: ≥ 70 years ; Control < 70 years.

3.1. *Patients demographics and comorbidities*

Patients demographics and comorbidities are listed in Table 1. The study group had a mean age of 81 years, and the control group a mean age of 45 years. There was no significant difference in the number of acute episodes of pancreatitis before admission ($p = 1.000$) and history of cholecystectomy between both groups ($p = 0.491$). Elderly patients had a significantly higher Charlson comorbidity score ($p < 0.001$), with a higher rate of hypertension ($p = 0.001$), diabetes ($p = 0.012$), ischemic heart disease ($p = 0.001$), chronic obstructive pulmonary disease ($p = 0.026$), and chronic renal disease ($p = 0.001$), than the control group.

3.2. *Clinical and radiological severity*

According to the Atlanta classification, the clinical severity of pancreatitis was similar in elderly and young patients with most mild acute pancreatitis in both groups (67% *vs*. 65%, respectively), as shown in Table 2. The radiological extent of pancreatitis assessed by the Balthazar grading was similar between elderly and young patients ($p = 0.172$). No significant differences were observed between the study and control groups in terms of median CTSI score (2 *vs*. 2, $p = 0.160$) or modified CTSI score (2 *vs*. 2, $p = 0.693$). The CTSI could not be established in 31 elderly patients (41%) and in 34 in the control group (25%). Among these patients with unknown CTSI, 11 *vs* 1 had a computed tomography without intravenous contrast, 12 *vs* 21 had an abdominal ultrasound or magnetic resonance imaging, and 8 *vs.* 12 had no imaging in the study *vs.*

Table 1. Patients demographics and comorbidities

N (%)	Elderly, *N* = 76	Control, *N* = 136	*p* value
Age, years, median (IQR)	79 (75-85)	47 (30-57)	< 0.001
Sex ratio, M:F	26 : 50	56 : 80	0.378
Previous pancreatitis (%)	4 (5.3)	8 (5.9)	1.000
Previous cholecystectomy (%)	10 (13.2)	13 (9.6)	0.491
Charlson score, median (IQR)	1 (0-3)	0 (0-0)	< 0.001
Hypertension (%)	49 (64.5)	33 (24.3)	< 0.001
Obesity (%)	8 (10.5)	11 (8.1)	0.619
Diabetes (%)	20 (26)	16 (12)	0.012
Hypercholesterolemia (%)	13 (17.1)	18 (13.2)	0.544
Hypertriglyceridemia (%)	4 (5.3)	5 (3.7)	0.725
Ischemic heart disease (%)	22 (28.9)	7 (5.1)	< 0.001
Chronic obstructive pulmonary disease (%)	6 (7.9)	2 (1.4)	0.026
Congestive heart failure	4 (5.3)	1 (0.7)	0.057
Chronic renal disease (%)	20 (26.3)	3 (2.2)	< 0.001
Dialysis (%)	0 (0)	0 (0)	1.000

IQR, interquartile range.

Table 2. Clinical and radiological severity of acute biliary pancreatitis

N (%)	Elderly, *N* = 76	Control, *N* = 136	*p* value
Atlanta classification			0.210
Mild	51 (67.1)	88 (64.7)	
Moderately severe	21 (27.6)	46 (33.8)	
Severe	4 (5.3)	2 (1.5)	
Balthazar grade			0.172
A (%)	16 (21.1)	25 (18.4)	
B (%)	8 (10.5)	10 (7.4)	
C (%)	21 (27.6)	26 (19.1)	
D (%)	5 (6.6)	23 (16.9)	
E (%)	10 (13.2)	27 (19.9)	
Unknown (%)	16 (21.1)	25 (18.4)	
CTSI, median (IQR)	2 (1-3)	2 (1-4)	0.160
Mild (0-3)	35 (46.1)	66 (48.5)	
Moderate (4-6)	6 (7.9)	33 (24.3)	
Severe (7-10)	4 (5.3)	3 (2.2)	
Unknown	31 (40.8)	34 (25.0)	
Modified CTSI, median (IQR)	2 (2-4)	2 (0-6)	0.693
Mild (0-2)	26 (34.2)	51 (37.5)	
Moderate (4-6)	15 (19.7)	39 (28.7)	
Severe (8-10)	4 (5.3)	12 (8.8)	
Unknown	31 (40.8)	34 (25.0)	

CTSI: Computed tomography severity index.

control group, respectively ($p = 0.089$).

3.3. *Complications*

As shown on Table 3, a higher rate of portal vein thrombosis was observed in the elderly patients compared to young patients (12% *vs*. 2%, respectively; p=0.018). There was no significant difference in terms of occurrence of pseudocysts (8 *vs*. 6, p = 0.146), pseudoaneurysmal bleeding (0 *vs*. 2, p = 0.538), and pleural effusion (19 *vs*. 30, p =0.616).

3.4. *Management*

Elderly patients required more ERCP (38% *vs*. 21%, respectively; $p = 0.009$) and endoscopic drainage of infected intra-abdominal collections (4% *vs*. 0%, respectively; $p = 0.045$) compared to younger patients. No statistically significant differences were observed for antibiotherapy, percutaneous drainage, or the need for surgical necrosectomy or bowel resection (Table 4).

3.5. *Outcome*

In comparison to the control group, elderly patients had a longer hospital length of stay (median, 11 *vs*. 7 days, in study and control groups, respectively; $p < 0.001$), with a higher proportion (26% *vs*. 2%, $p < 0.001$) of them being discharged to a nursing home or another hospital as they needed further nursing care due to their advanced age and comorbidities (Table 5). Three elderly and one younger patients were dead within 90 days. Three patients died from multiorgan failure and one patient died from septic shock. Seven elderly patients (9%) required admission to the intensive care unit (ICU) compared to 5 younger patients (4%) ($p = 0.103$) with a similar median ICU length of stay (8 *vs*. 6 days, $p = 0.870$). No difference was observed between the two groups regarding in-hospital 90-day mortality (3 *vs*. 1 patients, $p = 0.133$). Following recovery, the control group underwent significantly more elective laparoscopic cholecystectomy than the study group (109/123 patients (88.6%) and 35/66 patients (53.0%), respectively ($p = 0.041$)).

4. Discussion

The present study is, to our knowledge, the largest study focusing on elderly patients with acute biliary pancreatitis. The results suggest that despite higher pre-existing comorbidites in elderly patients, clinical and radiological severity of acute biliary pancreatitis

Table 3. Local complications during in-hospital stay

N (%)	Elderly, *N* = 76	Control, *N* = 136	*p* value
Pseudocyst (%)	8 (11.8)	6 (4.4)	0.146
Portal venous thrombosis (%)	8 (11.8)	3 (2.2)	0.018
Pseudoaneurysmal bleeding (%)	0 (0)	2 (0.7)	0.538
Pleural effusion (%)	19 (25.0)	30 (22.1)	0.616

Table 4. Management of acute biliary pancreatitis

N (%)	Elderly, *N* = 76	Control, *N* = 136	*p* value
Antibiotherapy (%)	19 (25.0)	30 (22.1)	0.616
ERCP (%)	29 (38.2)	28 (20.6)	0.009
Percutaneous drainage (%)	6 (7.9)	5 (3.7)	0.207
Endoscopic drainage (%)	3 (3.9)	0 (0)	0.045
Surgical necrosectomy (%)	2 (2.6)	3 (2.2)	1.000
Bowel resection	2 (2.6)	0 (0)	0.127

ERCP: Endoscopic retrograde cholangiopancreatography.

Table 5. Outcome following acute biliary pancreatitis

N (%)	Elderly, *N* = 76	Control, *N* = 136	*p* value
Hospital length of stay, median (IQR)	11 (7-15)	7 (5-11)	< 0.001
ICU length of stay, median (IQR)	8 (2-11)	6 (4-30)	0.870
In-hospital 90-day mortality (%)	3 (3.9)	1 (0.7)	0.133
Discharged home (%)	52 (68.4)	132 (97.1)	< 0.001
Recurrence of acute pancreatitis (%)	8 (10.5)	16 (11.8)	1.000

IQR, Interquartile range ; ICU : Intensive care unit.

is comparable to younger patients. However, a longer length of hospital stay was observed, with a higher proportion of elderly patients requiring secondary transfer to nursing home or another hospital.

Despite multiple comorbidities and higher Charlson index in the elderly group at admission, the present study suggests that age did affect neither mortality nor severity of acute biliary pancreatitis. These results are supported by data from previous studies showing that only 6% of patients older than 65 years developed severe acute pancreatitis (*12*), while others found no link between age and the risk of mortality from pancreatitis (*2*). There was no significant difference in the radiological severity between elderly and younger patients as assessed by both CTSI and modified CTSI. Both CTSI indexes were evaluated as being more accurate than the APACHE II score to diagnose clinically severe disease and did better correlate with pancreatic infection and the need for intervention (*13*). Furthermore, the modified CTSI seemed to correlate better with clinical outcome compared to the CTSI (*14*).

On the other hand, the complications and management of acute biliary pancreatitis seemed to be different between young and elderly patients. Elderly had a significantly higher rate of portal vein thrombosis. According to a recent systematic review, the prevalence of portal vein thrombosis in acute pancreatitis is 6% (*15*). The later study suggested that the risk of extrahepatic portal vein thrombosis was increased in patients with pseudocysts (*16*). Although the present study was not designed to address this issue, there was no difference between the young and elderly patients in the rate of pseudocyst formation. In addition, elderly patients needed more invasive procedures like percutaneous or endoscopic transgastric drainage of infected collections. This more invasive approach may result from a higher susceptibility of elderly to infection, and hence a lower threshold to initiate invasive treatment of intra-abdominal fluid collections in this group.

In case of mild biliary pancreatitis, early or same-admission cholecystectomy is recommended to avoid recurrent gallstone-related complications as confirmed by a recent randomized trial (*17*). The present study suggests that laparoscopic cholecystectomy is safe in elderly patients with a similar timing between acute pancreatitis and surgery when compared to young patients. Of note, more ERCP were performed in elderly during their hospital stay due to higher rate of obstructive cholangitis. According to a recent study including patients older than 65 years with acute biliary pancreatitis and acute cholangitis, 25% of elderly patients presented relapsed biliary complications after discharge (*12*). According to a previous study where ERCP in older patients with no cholecystectomy reduced the risk of developing further episode of biliary pancreatitis, ERCP with sphincterotomy should be considered when cholecystectomy is postponed or contra-indicated following an episode of biliary pancreatitis in elderly patients (*18*).

Several limitations to this study need to be addressed. First, this is a retrospective study from a single center, but data were collected prospectively what could decreases selection bias. As a direct consequence of the retrospective study design, no systematical follow-up could be performed. Therefore, cholecystectomy rate needs to be cautiously interpreted, as this operation could have been performed in another hospital. The number of severe pancreatitis was low in both group and no specific conclusion could be drawn for severe pancreatitis. A significant proportion of patients (41% in the elderly patients and 25% in the control group) had no injected computed tomography to establish the radiological severity based on validated scores. This was mainly due to contraindications to the injection of soluble contrast medium (such as previous contrast medium allergic reaction or renal failure), and the use of another imaging modality such as magnetic resonance imaging. However, this reflects daily management of patients out of a specific clinical trial what would have led to a "study-effect". Nonetheless, all available imaging was systematically reviewed by two experienced radiologists.

In conclusion, the results of this study suggest that radiological and clinical severity of acute biliary pancreatitis is similar between young and elderly patients. However, elderly patients required more invasive procedures to treat intraabdominal infected collections and developed more extrahepatic portal vein thrombosis compared to young patients. This data should be considered to be proactive in the management of acute biliary pancreatitis among elderly patients.

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