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Prognostic Factors in Acute-on-Chronic Pancreatitis: Insights from a Romanian Tertiary Center Cohort

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Rezumat

Factorii de prognostic în pancreatita cronică acutizată: perspective dintr-o cohortă dintr-un centru terțiar din România

Context/Obiective: Acest studiu a avut ca scop evaluarea şi compararea severității pancreatitei acute (PA) la pacienții cu şi fără pancreatită cronică (PC) subiacentă.
Metode: Am inclus pacienți diagnosticați cu PA şi i-am clasificat în PC şi fără PC. Severitatea bolii a fost definită prin prezența insuficienței de organ, a internării în unitatea de terapie intensivă (UTI) sau a mortalității.
Rezultate: PC a reprezentat 25.85% din toate cazurile de PA din studiu. Pacienții cu PC au fost mai frecvent bărbați fumători cu IMC scăzut, niveluri mai scăzute de albumină şi scoruri Balthazar mai mari. În schimb, pacienții cu PA (fără PC) au avut frecvențe cardiace (FC), scoruri Balthazar şi scoruri CTSI semnificativ mai mari. Durata spitalizării şi ratele de mortalitate au fost mai mari la pacienții cu PA, care au fost asociați cu o rată ridicată de disfuncție organică. Factorii de prognostic care au influențat supraviețuirea la 72 de ore au fost insuficiența respiratorie, raportul creatinină/albumină, BISAP, nivelurile de albumină şi injurie renală acută. Între timp, supraviețuirea la 30 de zile a fost influențată de insuficiența respiratorie, raportul creatinină/albumină şi azotul ureic din sânge.
Concluzii: Comparativ cu PA fără PC, ACP este asociată cu o evoluție a bolii mai puțin severă, mortalitate mai mică, insuficiență de organ redusă şi şederi mai scurte la ATI. Cu toate acestea, ACP este observată mai frecvent la fumătorii de sex masculin cu valori IMC şi albumină mai mici şi scoruri CTSI şi Balthazar mai mari.

Cuvinte cheie: pancreatită acută, pancreatită acută pe pancreatită cronică, severitate, mortalitate

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Abstract

Background/Aims: This study aimed to assess and compare the severity of

acute pancreatitis (AP) in patients with and without underlying chronic pancreatitis (CP).
Methods: We included patients diagnosed with AP and categorized them into those with CP and those without CP. Disease severity was defined by the presence of organ failure, intensive care unit (ICU) admission, or mortality.
Results: ACP accounted for 25.85% of all AP cases in the study. Patients with ACP were more commonly male smokers with low BMI, lower albumin levels, and higher Balthazar scores. In contrast, patients with AP (without CP) had significantly higher heart rates (HR), Balthazar, and CTSI scores. Length of hospitalization and mortality rate were higher in those patients with AP, who were associated with a high rate of organ dysfunction. Prognostic factors influencing survival at 72 hours were respiratory failure, creatinine/albumin ratio, BISAP, albumin levels, and AKI. Meanwhile, survival at 30 days was influenced by respiratory failure, the creatinine/albumin ratio, and blood urea nitrogen.
Conclusions: Compared to AP without CP, ACP is associated with a less severe disease course, lower mortality, reduced organ failure, and shorter ICU stays. However, ACP is more frequently observed in male smokers with lower BMI and albumin and higher CTSI and Balthazar scores.

Keywords: acute pancreatitis, acute on chronic pancreatitis, severity, mortality

Introduction

Acute pancreatitis (AP) and chronic pancreatitis (CP) are common gastrointestinal disorders necessitating hospitalization, with increased incidence in the U.S. and Western Europe linked to rising medical costs (1,2). Acute pancreatitis (AP) involves sudden pancreatic inflammation with severity ranging from mild, manageable cases to severe ones with high morbidity and mortality rates (1,2). Clinical features, biochemical markers, and various imaging techniques, including abdominal ultrasound and computed tomography, are instrumental in accurately diagnosing the condition. While several scoring systems have been developed to aid in this assessment, none can truly address all relevant aspects of acute pancreatitis to determine severity and prognosis accurately (1,2). Thus, early detection and prompt treatment are crucial to reduce potential complications. Following an initial episode of acute pancreatitis (AP), 10% to 30% of individuals may experience recurrent acute pancreatitis (RAP), characterized by two or more distinct AP episodes that fully resolve in between, separated by at least three months (3,4). Approximately 35% of RAP cases may evolve into chronic pancreatitis (CP), a permanent disorder featuring abdominal pain and exocrine and endocrine dysfunction(3-6). Notably, some patients may develop CP without prior AP episodes. Both RAP and CP are associated with significant morbidity, mortality, healthcare utilization, and disability rates (3,4). A new occurrence of acute pancreatitis in an individual suffering from chronic pancreatitis could be as severe as the episodes of acute pancreatitis that present de novo, which some researchers named acute on chronic pancreatitis (ACP)(6). In 2023, Tiago et al. tried to find a universally accepted definition for ACP(6). Still, their systematic literature review revealed a paucity of evidence relating specifically to ACP, and it highlights several knowledge gaps that require further research (6). Another conclusion of their research was to propose diagnostic criteria and severity scores specific to ACP to improve the accuracy of diagnosis, the clinical course, and the prognosis (6).

This study aims to assess and compare the severity of acute pancreatitis (AP) in patients with and without underlying chronic pancreatitis (CP) and their clinical outcomes.

Materials and Methods

Study Design and Population Selection

This study was conducted in a tertiary center in southern Romania. It was cross-sectional, observational, and retrospective. It included 321 hospitalized patients with a diagnosis of AP and, respectively, AP in the setting of chronic pancreatitis (CP) between January 2022 and May 2024. All patients that could be followed in our unit were included in the study. Since there is still no standard definition for ACP in the literature, we used the term ACP to define patients who presented with AP based on the Atlanta criteria classification, required hospitalization, and had abdominal imaging evidence of CP.

Data collected included demographic informa-

tion, etiology, and clinical and laboratory parameters collected from the medical records of enrolled patients. Clinical parameters included information about blood pressure, heart rate, and respiratory rate. Laboratory parameters included blood cell count values, glucose, liver and renal function, electrolytes, and arterial blood gas. All patients performed abdominal ultrasound and contrast-enhanced computer tomography (CT) scan, except those with contraindications for contrast substances. We recorded severity prognostic scores such as BISAP and Ranson at the admission and 48 hours after admission and the Balthazar/ CT severity index (CTSI) for specific features such as collections and vascular complications. In addition, we collected data about neutrophile-lymphocyte ratio (NLR), platelets-lymphocyte ratio (PLR), and C-reactive protein (CRP) 48 hours after admission.

Severe pancreatitis involves persistent organ failure (OF), while moderately severe pancreatitis includes local/systemic complications without persistent OF, and mild pancreatitis has no complications. We also collected data on length of hospital stay (days), need for intensive care (ICU), organ failure (OF), in-hospital mortality, and survival at 30 days after admission.

Ethical

This research followed ethical guidelines and received approval from the Local Ethics Committee (Protocol No. 78173/ 25 November 2024).

Statically Analysis

The statistical analysis included descriptive statistics (frequency, percentage, mean, standard deviation, median) and inferential statistics. We applied univariate and multivariable logistic regression because it is explicitly designed for dependent variables with binary classification (Yes or No). The Enter selection method was used for multivariable logistic regression, where all predictors were included simultaneously. To investigate the effect of several variables on the time a specified event takes to happen, we used multivariable Cox regression with a Forward Stepwise (Likelihood Ratio) selection method for survival analysis, and to estimate the survival, we used Kaplan-Meier curves. The significance threshold chosen for the p-value was 0.05. The statistical analysis was performed using SPSS software version 29.0 (SPSS, Chicago, IL, USA).

Results

The study included 321 patients, divided into two groups: 238 individuals with acute pancreatitis (AP) and 83 with acute-on-chronic pancreatitis (ACP). Age distribution analysis showed no significant differences between the groups. However, a statistically significant association was found between male gender and ACP, indicating that males had higher odds of developing ACP than females (*Table 1*). Additionally, smoking was significantly associated with ACP. Lower BMI was linked considerably to ACP (*Table 1*). Regarding the causes of AP episodes, alcohol was the most common etiology in both groups, followed by gallstone disease (lithiasis) and pancreatic cancer. Hypertriglyceridemia was more frequently observed in AP cases than in ACP. Notably, AP following ERCP (endoscopic retrograde cholangiopancreatography) was reported exclusively in patients with AP (*Fig. 1*).

Clinical parameters such as systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), and temperature were recorded on admission to the hospital. The AP group had higher HR values than those with ACP (*Table 1*). In addition, a group with AP was associated with lower albumin values more frequently than the group with ACP (*Table 1*).

All patients have been evaluated by prognostic scores, including creatinine/albumin ratio, neutrophil / lymphocyte ratio at 48 hours, PLT / lymphocyte ratio at 48 hours, C-reactive protein, BISAP, RANSON, and imagistic scores such as Balthazar and CTSI. In our study, Balthazar scores were significantly higher in the ACP group compared to the AP group (*Table 1*). Also, a statistically significant association was observed between higher CTSI scores and ACP (*Table 1*). Regarding local complications, pseudocysts were more frequently associated with ACP (*Table 1*).

Local complications, especially pseudocysts, were more frequently associated with patients with AP than ACP (*Table 1*).

Multivariable analysis showed that male gender, smoking, and lower albumin values are statistically associated with the development of ACP. Meanwhile, increasing heart rate is statistically associated with AP (*Table 2*).

The length of hospitalization was higher in those with AP than in those with ACP. Organ dysfunction and the need for an intensive care unit (ICU) were more frequent in patients with AP. The mortality rate was higher in those

Table 1. General characteristics of patients with AP and ACP on admission

	ACP (n=83)	AP (n=238)	Univariate		
			Exp(B)	95% CI	p-value
Age (Mean±SD, median)	55.99±15.43 (59.00)	54.31±16.90 (54.00)	1.006	0.991-1.022	0.42
Gender (Males/ Females)	**70 (84.34%)**	**154 (64.71%)**	**2.937**	**1.535-5.620**	**0.001**
Smoker (Yes/No)	54 (65.06%)	101 (42.44%)	2.526	1.503-4.245	<0.0001
Alcohol (Yes/No)	58 (69.88%)	139 (58.40%)	1.652	0.968-2.822	0.06
BMI	23.87±4.253 (24.20)	25.14±4.422 (24.55)	0.934	0.881-0.991	0.02
CVD (Yes/No)	43 (51.81%)	100 (42.02%)	1.483	0.898-2.450	0.12
DM (Yes/ No)	9 (10.84%)	43 (18.07%)	0.552	0.256-1.187	0.12
CLD (Yes/ No)	17 (20.48%)	31 (13.03%)	1.720	0.895-3.305	0.10
Clinical parameters					
SBP (mmHg)	128.8±22.29 (130.0)	131.2±23.66 (130.0)	0.995	0.985-1.006	0.41
HR (beats/min)	84.08±14.57 (80.00)	90.02±17.93 (89.00)	0.978	0.962-0.994	0.007
RR (resp/min)	21.40±3.534 (21.00)	21.48±3.531 (21.00)	0.993	0.925-1.067	0.85
Temperature	36.45±0.541 (36.40)	36.51±0.617 (36.50)	0.837	0.539-1.302	0.83
Laboratory parameters					
WBC	9.587±4.381 (8.700)	9.787±4.346 (9.200)	1.002	0.943-1.065	0.94
Neutrophil/lymphocyte ratio at 48h	6.656±6.616 (4.310)	6.048±5.269 (4.350)	1.018	0.976-1.062	0.40
PLT/lymphocyte ratio at 48h	196.4±115.0 (170.0)	202.8±139.4 (174.0)	1.000	0.998-1.002	0.70
CRP (mg/dL)	7.108±8.004 (3.910)	8.790±9.890 (4.800)	0.980	0.952-1.008	0.16
Glucose (mg/dl)	123.1±63.50 (98.00)	138.8±80.51 (106.0)	0.997	0.993-1.001	0.11
BUN (mg/dL)	38.16±36.55 (29.00)	42.54±38.03 (31.50)	0.996	0.989-1.004	0.36
Calcium (mg/dL)	8.764±0.898 (8.790)	8.650±1.004 (8.780)	1.131	0.869-1.474	0.35
LDH (U/L)	216.0±90.57 (201.0)	239.9±172.4 (201.0)	0.999	0.996-1.001	0.23
Hemoglobin (g/dl)	11.93±2.796 (12.50)	12.25±2.268 (12.45)	0.946	0.854-1.048	0.28
Albumin (g/dl)	3.582±0.850 (3.560)	3.832±1.039 (3.900)	0.770	0.592-1.000	0.0504
Lactate (mmol/l)	1.778±0.896 (1.700)	1.948±1.110 (1.830)	0.834	0.626-1.111	0.21
Triglyceride (mg/dl)	127.7±131.8 (100.0)	257.1±696.9 (111.5)	0.998	0.996-1.000	0.10
Cr/Alb	0.3165±0.2796 (0.220)	0.3979±0.9221 (0.230)	0.877	0.556-1.382	0.57
Prognostic scores					
BISAP	1.000±0.950 (1.00)	0.9370±0.886 (1.00)	1.080	0.820-1.422	0.58
RANSON admission	0.8795±0.8322 (1.00)	0.8613±0.7361 (1.00)	1.032	0.744-1.432	0.85
RANSON at 48h since admission	1.361±0.8776 (1.00)	1.391±0.9016 (1.00)	0.964	0.728-1.276	0.79
Balthazar	1.614±1.257 (2.00)	1.193±1.189 (1.00)	1.320	1.078-1.617	0.007
CTSI	0.1928±0.5050 (0.00)	0.0756±0.2951 (0.00)	2.140	1.151-3.979	0.016
Local and distance complications					
Peripancreatic collections	32 (38.55%)	117 (49.16%)	0.649	0.390-1.080	0.09
Necrosis	15 (18.07%)	67 (28.15%)	0.563	0.301-1.053	0.07
Pseudocysts	36 (43.37%)	54 (22.69%)	2.610	1.537-4.432	0.0004
Pleural effusion (Yes/ No)	7 (8.43%)	22 (9.24%)	0.904	0.371-2.202	0.82

BMI - body mass index; CVD – cardiovascular disease; DM - diabetes mellitus; CLD – chronic liver disease; SBP – systolic blood pressure; HR – heart rate; RR – respiratory rate; WBC - white blood count; PLT/LF ratio – platelets/lymphocytes ratio; NF/LF ratio – neutrophils/lymphocytes ratio; CRP – C-reactive protein; BUN-blood urea nitrogen; LDH – lactate dehydrogenase; Cr/Alb- creatinine/albumin ratio; BISAP-Bedside index of severity in acute pancreatitis; CTSI- modified CT severity index.

patients with AP at 72 hours and 30 days (*Table 3*).

For 72-hour survival, the dominant prognostic factor was respiratory failure. The next significant prognostic factor was the creatinine/albumin ratio, followed by BISAP, albumin levels, and AKI. All factors included had a statistically significant improvement in the fit of the previous model. Respiratory failure, high creatinine/albumin ratio, BISAP, and albumin values are associated with shorter survival time (*Table 4*).

The most important prognostic factor for 30 days of survival was respiratory failure. The next significant prognostic factor was the creatinine/albumin ratio, followed by blood urea nitrogen and respiratory rate. All factors included had statistically significant improvement in the fit of the previous model: respiratory failure, high

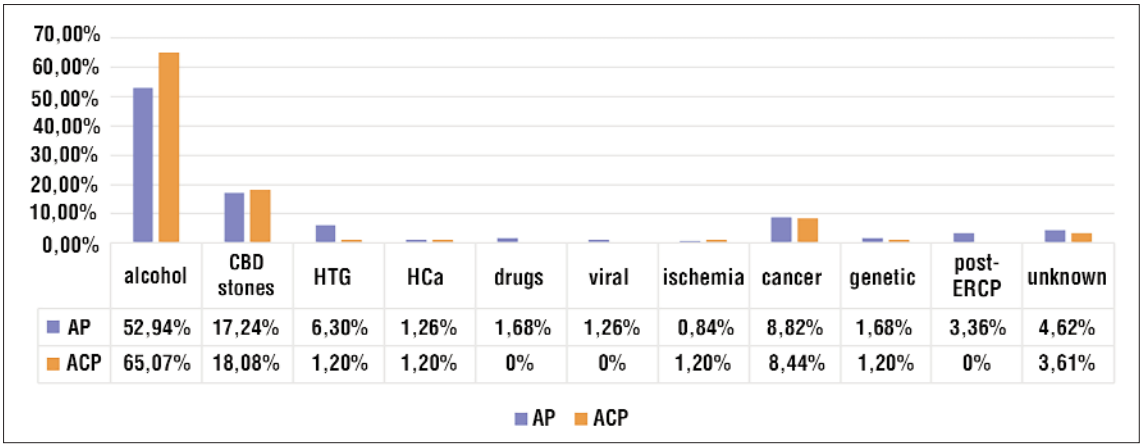

Figure 1. Etiology of the acute pancreatitis episode in both groups

Table 2. Predictor factors associated with the development of ACP

Parameters	Exp(B)	95% C.I.		p-value
		Lower	Upper	
Age (years)	1.015	0.991	1.039	0.2262
Gender	3.010	1.436	6.309	0.0035
Smoker (Yes vs No)	3.013	1.558	5.826	0.0010
Alcohol (Yes vs No)	0.956	0.454	2.012	0.9058
HR (beats/min)	0.980	0.963	0.998	0.0267
RR (resp/min)	1.026	0.935	1.125	0.5901
Temperature	0.897	0.548	1.470	0.6673
PLT/ LF ratio at 48h	1.000	0.997	1.002	0.7754
NF/LF ratio at 48h	1.029	0.978	1.084	0.2679
CRP (mg/dL)	0.968	0.933	1.004	0.0783
Calcium	1.326	0.926	1.900	0.1238
Albumin (g/dl)	0.603	0.414	0.878	0.0082
AKI	0.370	0.117	1.176	0.0921
Cr /Albumin	0.707	0.375	1.333	0.2837
Ranson on admission	0.983	0.678	1.427	0.9289
Ranson 48h	1.109	0.806	1.526	0.5251
BISAP	1.087	0.728	1.623	0.6831
Balthazar	1.242	0.929	1.660	0.1436
CTSI	2.296	0.931	5.663	0.0713

HR – heart rate; RR – respiratory rate; PLT/LF ratio – platelets/ lymphocytes ratio; NF/LF ratio – neutrophils/lymphocytes ratio; CRP – C-reactive protein; AKI – acute kidney injury; Cr/Alb - creatinine/albumin ratio; BISAP-Bedside index of severity in acute pancreatitis; CTSI - modified CT severity index.

Table 3. The presence of organ dysfunction and mortality in both groups of patients with AP and ACP.

Status	ACP	AP	p-value
Days of hospitalization	5.506±4.112 (5.00)	5.836±4.458 (5.00)	0.59
AKI (Yes/ No)	6 (7.23%)	27 (11.34%)	0.40
Admission in ICU (Yes/ No)	0 (0.00%)	9 (3.78%)	
Respiratory failure (Yes/No)	0 (0.00%)	8 (3.36%)	
POF (Yes/No)	0 (0.00%)	8 (3.36%)	
Mortality at 72 hours (Yes/No)	2 (2.41%)	8 (3.36%)	0.99
Mortality at 30 days (Yes/ No)	2 (2.41%)	22 (9.24%)	0.05

AKI – acute kidney injury; ICU – intensive care unit; RF - respiratory failure; POF - persistent organ failure

creatinine/albumin ratio, and blood urea nitrogen values (*Table 5*).

Although the estimated mean survival time was higher in the ACP group at 72 hours and 30 days, a statistically significant difference in survival distribution between the AP and ACP groups was observed only at 30 days (*Table 6, Figs. 2, 3*).

Discussion

This study evaluated the etiological factors, severity, and outcome of patients admitted to our department with AP and AP with CP. Most patients have AP, and just 25.85% have ACP. In our cohort study, patients with ACP were more frequently males, smokers, and had low BMI. Regarding the etiology in both groups, alcohol was the most common etiology, which is similar to the observations of Sharma et al. and Akshintala et al. (1,7,8) but in contrast with other data from the literature, where alcohol represented the second cause of AP (1). Males are associated more frequently with ACP, maybe because of increased alcohol consumption. In the literature, it is the exact opposite situation; gallstones represent the most common cause (40-70%) worldwide because of associated metabolic disorders, and are more frequent in women (1). Gallstone pancreatitis represents an acute event and is rapidly managed by removing or passing. Still, it is mandatory to

Table 4. Multivariable Cox regression for 72-hour survival

		Exp(B)	95.0% CI for Exp(B)		p-value
			Lower	Upper	
Step 1	Respiratory failure	33.915	9.527	120.739	<0.0001
Step 2	Creatinine/Albumin ratio	1.561	1.248	1.952	<0.0001
	Respiratory failure	35.182	9.523	129.981	<0.0001
Step 3	Creatinine/Albumin ratio	1.620	1.247	2.104	0.0003
	BISAP	3.292	1.542	7.025	0.002
	Respiratory failure	38.142	9.672	150.418	<0.0001
Step 4	Albumin	1.657	1.055	2.603	0.02
	Creatinine/Albumin ratio	2.075	1.455	2.960	<0.0001
	BISAP	3.890	1.755	8.620	0.0008
	Respiratory failure	60.953	13.479	275.644	<0.0001
Step 5	Albumin	1.705	1.094	2.658	0.01
	Creatinine/Albumin ratio	2.346	1.610	3.419	<0.0001
	BISAP	4.510	1.937	10.499	0.0005
	AKI	0.116	0.015	0.890	0.03
	Respiratory failure	363.036	35.936	3667.510	<0.0001
Variable(s) Entered at Step Number 1: Respiratory failure					
Variable(s) Entered at Step Number 2: Creatinine/Albumin ratio					
Variable(s) Entered at Step Number 3: BISAP					
Variable(s) Entered at Step Number 4: Albumin					
Variable(s) Entered at Step Number 5: AKI					

AKI – acute kidney injury

Table 5. Multivariable Cox regression for 30 days of survival

		Exp(B)	95.0% CI for Exp(B)		p-value
			Lower	Upper	
Step 1	Respiratory failure	36.270	14.131	93.096	<0.0001
Step 2	Creatinine/Albumin ratio	1.442	1.179	1.763	0.0004
	Respiratory failure	32.166	12.381	83.564	<0.0001
Step 3	Blood urea nitrogen	1.008	1.003	1.014	0.0033
	Creatinine/Albumin ratio	1.350	1.091	1.672	0.0058
	Respiratory failure	16.051	5.142	50.099	<0.0001
Step 4	Respiratory rate	1.124	1.043	1.211	0.0023
	Blood urea nitrogen	1.009	1.003	1.015	0.0016
	Creatinine/Albumin ratio	1.336	1.084	1.647	0.0066
	Respiratory failure	9.061	2.649	30.988	0.0004
Variable(s) Entered at Step Number 1: Respiratory failure					
Variable(s) Entered at Step Number 2: Creatinine/Albumin ratio					
Variable(s) Entered at Step Number 3: Blood urea nitrogen					
Variable(s) Entered at Step Number 4: Respiratory rate					

Table 6. Means for Survival Time for 72h and 30 days survival

	Events (Death) n	Censored n (%)	Mean for Survival time		
			Estimate	95% Confidence Interval	
		72h Survival			
Acute pancreatitis	8	230 (96.6%)	70.286	69.112	71.460
Acute chronic pancreatitis	2	81 (97.6%)	71.133	69.879	72.386
Overall	10	311 (96.9%)	70.505	69.575	71.434
		30 days Survival			
Acute pancreatitis	22	216 (90.8%)	27.685	26.751	28.618
Acute chronic pancreatitis	2	81 (97.6%)	29.313	28.373	30.254
Overall	24	297 (92.5%)	28.106	27.368	28.844

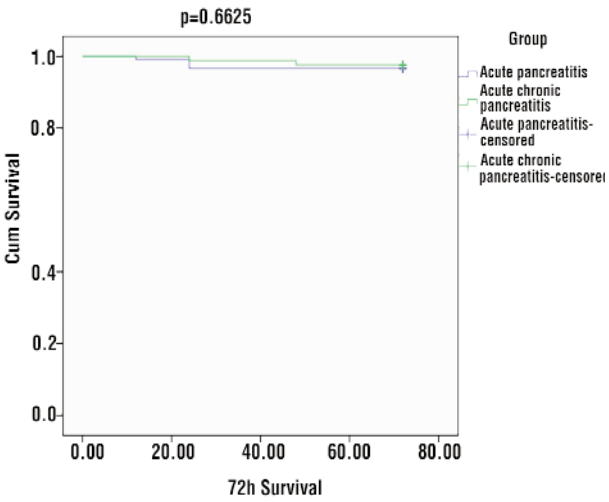

Figure 2. Survival at 72 hours since admission in the study groups

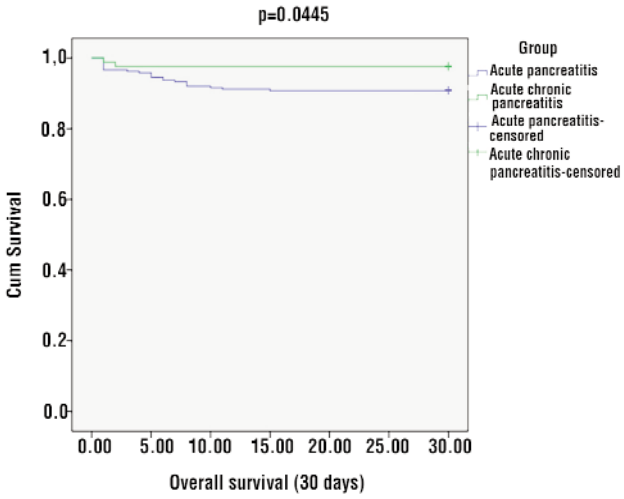

Figure 3. Survival at 30 days since admission in the study groups

refer the patient to cholecystectomy to prevent the recurrence of attacks and potential biliary sepsis (1,9,10).

Pancreatic cancer is represented in our groups as the third cause of episodes of AP. It is well known that AP could be an early symptom of pancreatic cancer; 1% of AP admissions are due to pancreatic cancer (11,12). The majority of these patients are diagnosed with pancreatic cancer after some months from the AP episode or are misdiagnosed, impairing survival (11,13,14).

In our study groups, low BMI values were associated with patients with ACP. Meanwhile, patients with AP had higher values. Data from the literature show that a higher BMI is correlated with severe AP if it is above 25 and with increased mortality if it is higher than 30 or lower than 18.5 (15). Unfortunately, the literature doesn't have much data about ACP because this condition is not defined. In a Danish cohort that included 642 patients, of 290 with CP, those with a BMI less than 20 and CP had a poor prognosis compared with those with CP and a BMI>25 (16).

All patients have been evaluated by prognostic scores, including creatinine/albumin ratio, neutrophil/lymphocyte ratio at 48 hours, PLT/lymphocyte ratio at 48 hours, C-reactive protein, BISAP, RANSON, and imagistic scores such as Balthazar and CTSI. In our study, both CTSI and Balthazar scores were significantly higher in the ACP group compared to the AP group.

About 3.38% of patients had persistent organ failure needing ICU care. Patients with AP develop more frequent acute kidney injury (AKI) and have higher HR compared to those with ACP. Statistical analysis revealed that survival at 72 hours was influenced by prognostic factors such as respiratory failure, high creatinine/albumin ratio, followed by BISAP, albumin levels, and AKI. Meanwhile, respiratory failure was the most important prognostic factor for 30 days of survival, followed by high creatinine/albumin ratio and blood urea nitrogen values.

In a recent prospective, multicenter study, it was discovered that the mortality of patients with AP is significantly higher, with ≥ two organs failing, especially when a combination of cardiovascular (CV) and respiratory failure is present, and when the first organ to fail is the respiratory or CV system (17). In addition, this study reveals a higher risk of developing POF when SIRS occurs early, becomes persistent, or has high scores (17). The authors also showed that persistent MOF is linked to higher mortality than single POF, highlighting the need to refine the severity classification systems to distinguish between persistent single OF and persistent MOF (17) Previous studies suggest that the mortality rate is higher in early POF (the first 48 hours) than in later-onset POF (17–21). However, this study's results contradict this, showing no association between the onset and duration of POF and mortality, maybe because of the improvement in critical care for POF during this time and the less invasive approach of necrotizing pancreatitis (17,22). In ACP, because of the fibrosis in CP, the systemic inflammatory

response syndrome and organ failure are less common than in patients with AP. Some data suggest that patients with ACP are not obese, with less peripancreatic fat compared to those with AP and obesity (8).

In recent years, the incidence of ACP has been increasing, probably due to the widespread access to advanced imaging tools (7,23,24). Until now, there have been just two studies available in the literature that studied the clinical profile and outcome of patients with ACP (7,8).

In our study, we observed that patients with ACP were more frequently associated with hypoalbuminemia and a poor outcome. In 2017, Hong et al. published a paper regarding hypoalbuminemia in the first 24 hours since hospital admission and its independent role in the development of persistent organ failure (POF) and death in acute pancreatitis (25). Since then, many researchers have proven that this biomarker is an independent predictor of the outcome of patients with AP (26-28). In addition, they demonstrated that early detection of hypoalbuminemia and early infusion of albumin improve the course of the disease (25-28). There is a lack of research in this domain regarding ACP and the role of albumin in the outcome of these patients. Therefore, our result cannot be compared with data from the literature, and it is essential to continue the research and demonstrate the important role of hypoalbuminemia in the evolution of patients with ACP.

Regarding the imagistic prognostic scores, the Balthazar score was the only score significantly higher in patients with severe forms of AP. The imaging revealed local complications that were more significant in patients with AP, except the pseudocysts, which were more frequently present in those with ACP. The data from our study are similar to those from the literature; recent research from a Hungarian cohort of patients that included 2275 patients with an episode of AP de novo and patients with CP showed that the development of pseudocysts is associated with a more severe course of the disease and increased length of hospital stay (29). Also, patients with CP are more frequently associated with pseudocysts that require closer attention after an episode of AP (29).

Clinical parameters such as systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), and temperature were recorded on admission to the hospital. The AP group had higher HR values than those with ACP (*Table 1*). In addition, a group with AP was associated with lower albumin values more frequently than the group with ACP (*Table 1*).

Our study has strengths and limitations. The strength of our research is that no data have been published about the prognostic role of biomarkers in the outcomes of patients with ACP since 2013, and there is no comparison between the evolution of AP and ACP (8). Akshintala et al. showed that patients with AP-on-CP generally have mild disease severity compared to AP without CP (8). As a risk factor, they discovered that advanced age, an increased number of comorbidities, and weight loss increase the risk for severe disease in patients with AP on CP (8).

One limitation of our study is that it was conducted in a unicentric tertiary center with a small number of patients, and there may be a bias in the selection of the patients. Usually, patients with severe forms of the disease are referred. Another limitation is that the study is retrospective, and we couldn't follow the evolution of the biomarkers over a well-established period of time. Future observational studies are needed to evaluate the prognostic role of biomarkers in ACP.

Conclusion

Compared to AP without CP, ACP is associated with a less severe disease course, lower mortality, reduced organ failure, and shorter ICU stays. However, ACP is more frequently observed in male smokers with lower BMI and albumin and higher CTSI and Balthazar scores.

Although there is no international consensus on the definition of acute on chronic pancreatitis (ACP), distinguishing it from acute pancreatitis (AP) without chronic pancreatitis (CP) is essential; these findings may serve as a foundation for future research in this field to improve the outcome of those patients.

Author's Contributions

Conceptualization, P.V.F., L.S.D. and C.S.P.; Methodology, C.S.P, F.E.T and P.V.P.; Software, FET.; Validation, S.L.D. and D.G.M.; Formal Analysis, F.E.T.; Investigation, P.V.F; Resources, P.V.F., N.T. and L.S.D.; Data Curation, C.S.P. and N.T.; Writing – P.V.F. and N.T.; Writing – Review & Editing, L.S.D and D.G.M; Visualization, D.G.M.; Supervision, C.S.P. and R.T. e; Project Administration, C.S.P.

Conflict of Interest

The authors report no conflicts of interest.

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References

1. Tenner S, Vege SS, Sheth SG, Sauer B, Yang A, Conwell DL, et al. American College of Gastroenterology Guidelines: Management of Acute Pancreatitis. Am J Gastroenterol. 2024;119(3):419-437.
2. Hu JX, Zhao CF, Wang SL, Tu XY, Huang WB, Chen JN, et al. Acute pancreatitis: A review of diagnosis, severity prediction and prognosis assessment from imaging technology, scoring system and artificial intelligence. World J Gastroenterol. 2023;29(37):5268-91.
3. Strand DS, Law RJ, Yang D, Elmunzer BJ. AGA Clinical Practice Update on the Endoscopic Approach to Recurrent Acute and Chronic Pancreatitis: Expert Review. Gastroenterology. 2022;163(4):1107-14.
4. Sankaran SJ, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS. Frequency of Progression From Acute to Chronic Pancreatitis and Risk Factors: A Meta-analysis. Gastroenterology. 2015;149(6):1490-1500.e1.
5. Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. Am J Gastroenterol. 2020;115(3): 322–39.
6. Bouça-Machado T, Bouwense SAW, Brand M, Demir IE, Frøkjșr JB, Garg P, et al. Position statement on the definition, incidence, diagnosis and outcome of acute on chronic pancreatitis. Pancreatology. 2023;23(2):143–50.
7. Sharma D, Mallick B, Samanta J, Gupta V, Sinha SK, Kochhar R. Acute-on-Chronic Pancreatitis: Analysis of Clinical Profile and Outcome. Cureus. 2021;13(4):e14242.
8. Akshintala VS, Hutfless SM, Yadav D, Khashab MA, Lennon AM, Makary MA, et al. A Population-Based Study of Severity in Patients With Acute on Chronic Pancreatitis. Pancreas. 2013;42(8):1245–50.
9. McAlister VC, Davenport E, Renouf E. Cholecystectomy deferral in patients with endoscopic sphincterotomy. Cochrane Database Syst Rev. 2007;2007(4): CD006233.
10. Yadav D, O'Connell M, Papachristou GI. Natural History Following the First Attack of Acute Pancreatitis. Am J Gastroenterol. 2012;107(7):1096-103.
11. Kirkegtrd J, Gaber C, Lund JL, Hinton SP, Ladekarl M, Heide-Jørgensen U, et al. Acute pancreatitis as an early marker of pancreatic cancer and cancer stage, treatment, and prognosis. Cancer Epidemiol. 2020;64:101647.
12. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet. 2015;386(9988):85–96.
13. Munigala S, Kanwal F, Xian H, Scherrer JF, Agarwal B. Increased Risk of Pancreatic Adenocarcinoma After Acute Pancreatitis. Clin Gastroenterol Hepatol Actions. 2014;12(7):1143-1150.e1.
14. Li S, Tian B. Acute pancreatitis in patients with pancreatic cancer. Medicine. 2017; 96(3):e5908.
15. İnce AT, Seven G, Koçhan K, Kiremitçi S, Yıldız K, Şentürk H. The course of acute pancreatitis in patients with different BMI groups. Pancreatology. 2022; 22(3):348–55.
16. Nøjgaard C. Prognosis of acute and chronic pancreatitis - a 30-year follow-up of a Danish cohort. Dan Med Bull. 2010;57(12):B4228.
17. Machicado JD, Gougol A, Tan X, Gao X, Paragomi P, Pothoulakis I, et al. Mortality in acute pancreatitis with persistent organ failure is determined by the number, type, and sequence of organ systems affected. United European Gastroenterol J. 2021;9(2):139–49.
18. Lytras D, Manes K, Triantopoulou C, Paraskeva C, Delis S, Avgerinos C, et al. Persistent Early Organ Failure. Pancreas. 2008;36(3):249-54.
19. Johnson CD. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut. 2004;53(9):1340-4.
20. Johnson CD. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut. 2004;53(9):1340-4.
21. Schepers NJ, Bakker OJ, Besselink MG, Ahmed Ali U, Bollen TL, Gooszen HG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut. 2019;68(6):1044–51.
22. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis. N Engl J Med. 2010;362(16):1491-502.
23. Parakh A, Tirkes T. Advanced imaging techniques for chronic pancreatitis. Abdom Radiol (NY). 2020;45(5):1420-1438.
24. Kamat R, Gupta P, Rana S. Imaging in chronic pancreatitis: State of the art review. Indian J Radiol Imaging. 2019;29(2):201-210.
25. Hong W, Lin S, Zippi M, Geng W, Stock S, Basharat Z, et al. Serum Albumin Is Independently Associated with Persistent Organ Failure in Acute Pancreatitis. Can J Gastroenterol Hepatol. 2017;2017:5297143.
26. Ocskay K, Vinkó Z, Németh D, Szabó L, Bajor J, Gódi S, et al. Hypoalbuminemia affects one third of acute pancreatitis patients and is independently associated with severity and mortality. Sci Rep. 2021;11(1):24158.
27. Amri F, Rahaoui M, Aissaoui H, Elmqaddem O, Koulali H, Zazour A, et al. Is serum albumin a pivotal biomarker in anticipating acute pancreatitis outcomes? BMC Gastroenterol. 2024;24(1):234.
28. Xu H, Wan J, He W, Zhu Y, Zeng H, Liu P, et al. Albumin infusion may decrease the mortality of hypoalbuminemia patients with severe acute pancreatitis: a retrospective cohort study. BMC Gastroenterol. 2023;23(1):195.
29. Szakó L, Gede N, Váradi A, Tinusz B, Vörhendi N, Mosztbacher D, et al. Early occurrence of pseudocysts in acute pancreatitis – A multicenter international cohort analysis of 2275 cases. Pancreatology. 2021;21(6):1161–72.