

The degree of obesity correlates with the severity of acute pancreatitis: An international multicenter cohort analysis of 2244 patients

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ABSTRACT

Introduction: Acute pancreatitis (AP) is a potentially severe or fatal gastrointestinal disease. Obesity is a major risk factor for chronic comorbidities and for a worse outcome in acute inflammatory conditions. We aimed to investigate the characteristics and role of the degree of obesity in the course and outcome of AP.

Methods: In total, 2244 AP cases from 13 countries and 29 centers of the Acute Pancreatitis Registry run by the Hungarian Pancreatic Study Group were included in our analysis. Patient groups were formed based on body mass index (BMI) categories according to the World Health Organization definitions. Anamnestic, admission, and outcome parameters were analyzed. We used logistic regression and multivariable logistic regression to model the relationship between BMI and AP outcomes. Odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Results: In our cohort, 2.8% of patients were underweight, 30.0% normal, 35.0% overweight, and 20.0%, 8.2%, and 3.7% were in the obesity class I, II, and III groups.

Examining the graded association in a multivariable logistic regression model, we found that the odds of organ failure increase with the degree of obesity (obesity class I: OR = 2.12, CI:1.29–3.46, p = 0.003;

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obesity class II: OR = 2.57, CI: 1.40–4.71, $p = 0.002$; obesity class III: OR = 2.71, CI: 1.25–5.89, $p = 0.012$). The three obesity groups had higher odds for severe AP as well (OR = 3.16, CI: 1.71–5.83, $p < 0.001$; OR = 3.98, CI: 1.95–8.15, $p < 0.001$; OR = 2.80, CI: 1.05–7.48, $p = 0.040$, respectively).

Conclusion: Obesity dose-dependently elevates the odds of pre-existing comorbidities and complications. Gradual weight loss may also have a positive effect and the impact of patient education should be investigated.

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1. Introduction

Acute pancreatitis (AP) is a potentially severe or even fatal gastrointestinal disease that requires hospitalization [1]. The incidence of AP has been increasing in the last decades. The average annual percent change was 3.8% in North America, while it was 2.8% in Europe, a great economic burden in most countries in the Western world [2]. AP severity is categorized into three groups: mild without any complications, moderately severe with local complications and/or transient organ failure, and severe complicated with permanent organ failure with or without local complications [3].

In 2020, across the 18 countries of Organization for Economic Co-operation and Development (OECD) where Body Mass Index (BMI) data were based on measurement, 26% of the population was obese, and a further 34% was overweight [4]. The proportion of the population with a BMI above 30 has doubled since the 1990s. What is more, the increasing prevalence is common among children and adolescents [4,5], which suggests an even darker future in obesity trends. The prevalence of obesity is expected to grow to 1.53 billion by 2035 [6]. Consequently, overweight and obesity-related diseases are anticipated to claim up to 92 million lives in the OECD over the next thirty years, with these conditions potentially reducing life expectancy by nearly 3 years by 2050 [7]. Besides its numerous public health consequences, obesity places a substantial economic burden on healthcare systems as well. Individuals who are clinically overweight require more frequent and complex healthcare services: they undergo more surgical interventions and have more than twice as many prescriptions as those with a healthy weight [7].

Besides alcohol consumption, smoking, unhealthy diet, and sedentary lifestyle, obesity is also a major risk factor for chronic comorbidities such as diabetes, cardiovascular diseases, and cancers, and it is associated with worse outcomes in acute inflammatory conditions and infectious diseases as well [8–10]. Earlier investigations showed that there is a correlation between obesity and AP outcome. A BMI above 25 is a risk factor for severe AP, while a BMI above 30 increases mortality risk [9]. According to our previous cohort analysis, obesity is an independent risk factor for renal failure and a longer hospital stay [11]. Other recent cohort analyses also found that obesity increases the risk of mortality and morbidity in AP [12,13]. Despite extensive studies on obesity in AP, the dose-dependent relationship between BMI categories and disease severity has not been fully explored.

We hypothesize that patients with higher BMI have an increased risk of an unfavorable outcome in AP. As AP can be severe or even fatal, identifying patients at a higher risk is crucial. Also, knowing that even a smaller weight loss might improve the outcome, motivating patients would become easier. While obesity may also influence the risk of developing AP, the present study specifically focuses on its association with disease severity and outcomes after onset. Therefore, we aimed to investigate the characteristics and the role of the degree of obesity in the course and outcome of AP.

2. Methods

2.1. Data collection and ethical permissions

Clinical data of 2461 AP cases were collected prospectively in the international Acute Pancreatitis Registry (APR) run by the Hungarian Pancreatic Study Group between 2012 and 2019. The study was approved by the Scientific and Research Ethics Committee of the Medical Research Council and the National Public Health Centre (reference numbers: 22254-1/2012/EKU and 17787-8/2020/EÜIG). Local ethical approval was obtained by the participating centers. All participants in this study provided written informed consent prior to enrolment. Clinical data sources were patient interviews conducted by trained clinical research administrators and electronic and paper-based medical records. A four-level monitoring system ensured the quality. Data completeness and the description of the monitoring system can be found in the Supplementary Appendix (Table S1). BMI was calculated using body weight and height recorded at hospital admission. Whenever feasible, measurements were performed directly by clinical staff; in cases where this was not possible due to the patient's clinical condition, values were obtained from patient interviews or recent medical records.

2.2. Population and definitions

AP were enrolled in the APR based on the recommendation of the IAP/APA guideline [14,15]. Two out of the following three conditions had to be fulfilled for the diagnosis: 1) acute abdominal pain, 2) amylase and/or lipase levels at least three times higher than the upper normal limit, and 3) imaging signs characteristic to AP. Severity and complications of AP were defined according to the revised Atlanta classification [3].

Out of the 2461 cases in the APR, BMI data were available in 2244 cases from 13 countries and 29 centers. The center distribution of the analyzed population is presented in Table S2. The analyzed cohort was representative of the total cohort (Table S3).

Patient groups were formed based on BMI categories according to the World Health Organization (WHO) guidelines [16].

Clinical data of 2461 AP cases were collected prospectively in the international Acute Pancreatitis Registry (APR) run by the Hungarian Pancreatic Study Group between 2012 and 2019 [17]. The population of the current investigation partially overlaps with the former cohort analysis; 1226 cases are included in both [11]. In the former analysis, we grouped patients into obese and non-obese groups, while in the current analysis, we formed six BMI groups to examine the correlation between the degree of obesity and AP outcome. Anamnestic, admission, and outcome parameters were analyzed.

2.3. Statistical analysis

To determine whether the “analyzed cohort” is a good representation of the “total cohort”, i.e., whether the data distribution is similar, we used the Kolmogorov-Smirnov test for continuous

variables and the Chi-square Goodness-of-fit test for categorical variables.

Descriptive statistical summaries of our data were presented as mean, standard deviation (SD), median, interquartile range (IQR), minimum/maximum values for continuous variables, and frequencies and percentages for categorical variables.

We used binary logistic regression to model the relationship between outcomes, BMI groups and multiple predictors (age, gender, and comorbidities). The coefficients were transformed to odds ratios (OR) and their corresponding confidence intervals (CI). In the case of on-admission laboratory parameters, we applied Analysis of Variance (ANOVA) with Dunnett's post hoc test to compare the differences between the BMI group categories and the normal weight groups. The Spearman rank correlation was calculated to handle the correlation between BMI and continuous variable. No data imputation was used.

All results were considered significant only if our p-value was less than 0.05.

All analyses were performed in the R statistical environment (R version 4.4.2, R Core Team (2024). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria).

2.4. Reporting

We followed the “Strengthening the Reporting of Observational Studies in Epidemiology” (STROBE) guidelines [18] in reporting this investigation (Table S4).

3. Results

3.1. General characteristics of the total cohort

In our cohort, 2.8% of the patients were underweight, 30% were normal weight, 35% were in the pre-obesity, 20% in obesity class I, 8.2% in obesity class II, and 3.7% were in the obesity class III groups. General characteristics of the cohort are presented in Table 1.

3.2. General characteristics of the BMI groups

While female patients had a 42.7% and males had a 57.3% share in the total cohort, there was a 56.5% female share in the underweight, 41.0% in the normal, 38.8% in the overweight, and 47.3%, 47.8% and 48.2% in the obesity class I, II and III patient groups, respectively (Fig. S1).

The median age increases with BMI until obesity class I, and it is lower again in obesity class II and III groups (50, 52, 58, 60, 56, 57, in the underweight, normal weight, overweight, and obesity class I, II, and III groups respectively). Details are shown in Fig. S2.

3.3. Univariable analyses

3.3.1. Alcohol consumption and smoking

Compared to the normal BMI group, there is less alcohol consumption and smoking in the overweight and obesity I, II, and III groups (Fig. 1). Increasing obesity categories were associated with lower odds of smoking and alcohol consumption (Table 2, Table S5/A1).

There are also lower odds of smoking (OR:0.92, CI:0.91-0.94, p < 0.001) and alcohol consumption (OR:0.97, CI:0.95-0.98, p < 0.001) when the BMI increased with 1. Further details of the statistical analysis are shown in Table S5/A2.

3.3.2. Comorbidities

The odds for comorbidities, among them diabetes,

Table 1

General clinical characteristics of the acute pancreatitis cohort. Other etiologies include anatomical malformation, tumor, virus, drug-induced, trauma, chronic or autoimmune pancreatitis exacerbation, and hypercalcemia. BMI: body mass index; SD: standard deviation; IQR: interquartile range; ERCP: endoscopic retrograde cholangiopancreatography.

Characteristic	Value
BMI groups	
Underweight (n, %)	62 (2.8)
Normal weight (n, %)	681 (30.3)
Overweight (n, %)	788 (35.1)
Obesity class I (n, %)	446 (19.9)
Obesity class II (n, %)	184 (8.2)
Obesity class III (n, %)	83 (3.7)
Sex	
Female (n, %)	959 (42.7)
Male (n, %)	1285 (57.3)
Age	
Mean (SD)	56.1 (16.7)
Median (IQR)	57 (44, 69)
Minimum; Maximum	18; 95
Etiology, n (%)	
Biliary (n, %)	949 (42.7)
Alcoholic (n, %)	541 (24.4)
Hypertriglyceridaemia (n, %)	142 (6.6)
Post-ERCP (n, %)	70 (4.1)
Idiopathic (n, %)	406 (18.3)
Other (n, %)	403 (18.1)
Outcome	
Mild, n (%)	1606 (71.6)
Moderate, n (%)	520 (23.2)
Severe, n (%)	118 (5.2)
Mortality, n (%)	64 (2.9)
Length of stay in days, median (IQR)	8.0 (6.0, 11.5)
Patients with local complication, n (%)	593 (26.6)
Acute pancreatic fluid collection, n (%)	495 (22.2)
Pseudocyst, n (%)	163 (7.3)
Acute necrotic collection, n (%)	187 (8.4)
Patients with organ failure, n (%)	188 (8.4)
Respiratory failure, n (%)	131 (5.9)
Heart failure, n (%)	51 (2.3)
Renal failure, n (%)	80 (3.6)
New-onset diabetes, n (%)	72 (3.2)

hypertension, liver steatosis, and hyperlipidemia, are higher, and for recurrent AP (RAP) and chronic pancreatitis (CP) are lower in the overweight and obesity groups compared to the normal BMI group (Table 2, Fig. 1, Table S5/B1).

When BMI was treated as a continuous variable in the analysis, increases in BMI were associated with higher rates of diabetes, hypertension, liver steatosis, and hypertriglyceridemia, while RAP and CP decreased (Table S5/B2).

3.3.3. On-admission laboratory parameters

On-admission liver parameters such as total bilirubin, gamma-glutamyl transferase (GGT), aspartate transaminase (AST) levels, glucose, and HbA1c median values are all higher in the higher BMI groups, while the renal function parameter and the estimated glomerular filtration rates (eGFR) are lower in the higher BMI groups (Fig. 1). Details and further laboratory parameters are shown in Table S5/C1. Calculating the effect of BMI as a continuous variable, we found that BMI is correlated with on-admission laboratory parameters (Table S5/C2).

3.3.4. Etiology

Compared to the normal BMI group, biliary and hypertriglyceridemia-induced etiology was more common in the overweight and obesity groups, while alcohol-induced etiology was less common. The highest and lowest odds ratios were present in the obesity III group (Fig. 1, Table 2). Further details can be found

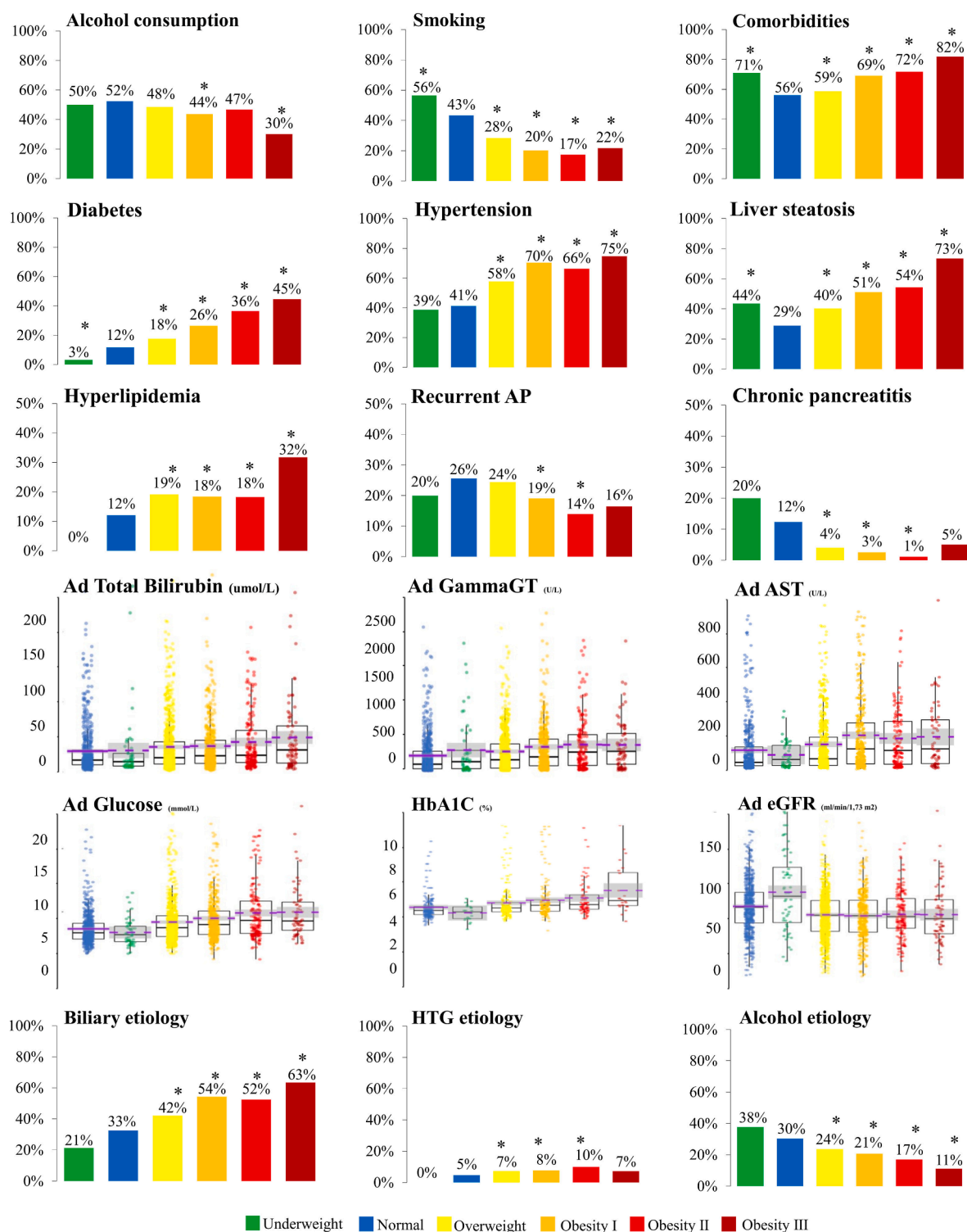


Fig. 1. Prevalence of anamnestic factors, admission parameters and etiology in the body mass index groups. AP: acute pancreatitis; Ad: admission; GammaGT: gamma-glutamyl transferase; AST: aspartate transaminase (AST); HbA1c: hemoglobin A1c; eGFR: estimated glomerular filtration rate; HTG: hypertriglyceridemia. *statistically significant difference compared to the normal body mass index group.

in Table S5D1.

We found also the increase of odds in biliary and hypertriglyceridemia-induced AP and the decrease of odds in alcohol-induced AP when treating BMI as a continuous variable (Table S5/D2).

3.3.5. Outcome of AP

The three obesity groups had higher odds for severe AP than the normal BMI group (Table 2, Fig. 2).

Patients in the obesity I group have higher odds of mortality. The median length of hospitalization was significantly higher in the overweight (8, IQR: 6–12, $p = 0.007$), obesity I (8, IQR: 6–13, $p < 0.001$) and obesity III (8, IQR: 6–13, $p < 0.001$) groups compared

Table 2

The odds ratio for alcohol consumption, smoking, comorbidities, etiologies and acute pancreatitis outcomes compared to the normal BMI group, univariable analysis. OR: odds ratio; CI: confidence interval; AP: acute pancreatitis; HTG: hypertriglyceridemia.

	Overweight	Obesity I	Obesity II	Obesity III
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Alcohol consumption	0.84 (0.68, 1.04)	0.69 (0.54, 0.87)	0.79 (0.57, 1.10)	0.39 (0.23, 0.63)
Smoking	0.52 (0.41, 0.64)	0.33 (0.25, 0.44)	0.28 (0.18, 0.42)	0.37 (0.21, 0.63)
Comorbidities	1.28 (1.01, 1.63)	2.00 (1.49, 2.68)	2.11 (1.40, 3.19)	4.63 (2.18, 9.81)
Diabetes	1.61 (1.20, 2.17)	2.71 (1.98, 3.72)	4.32 (2.95, 6.32)	6.15 (3.75, 10.07)
Hypertension	1.76 (1.35, 2.31)	3.23 (2.28, 4.57)	3.00 (1.85, 4.88)	4.38 (2.05, 9.39)
Liver steatosis	1.70 (1.36, 2.13)	2.76 (2.12, 3.58)	2.93 (2.07, 4.15)	7.05 (4.06, 12.26)
Hyperlipidemia	1.72 (1.23, 2.42)	1.64 (1.12, 2.40)	1.62 (1.00, 2.63)	3.38 (1.87, 6.12)
Recurrent AP	0.94 (0.74, 1.19)	0.68 (0.51, 0.92)	0.47 (0.30, 0.74)	0.57 (0.31, 1.06)
Chronic pancreatitis	0.30 (0.19, 0.46)	0.19 (0.10, 0.35)	0.08 (0.02, 0.33)	0.38 (0.13, 1.06)
Biliary etiology	1.51 (1.22, 1.87)	2.46 (1.92, 3.16)	2.29 (1.64, 3.19)	3.59 (2.23, 5.79)
HTG etiology	1.58 (1.00, 2.48)	1.68 (1.01, 2.79)	2.23 (1.20, 4.13)	1.57 (0.63, 3.87)
Alcohol etiology	0.71 (0.56, 0.89)	0.60 (0.45, 0.79)	0.47 (0.31, 0.71)	0.29 (0.14, 0.58)
Severe AP	1.46 (0.80, 2.64)	3.73 (2.11, 6.58)	4.24 (2.18, 8.26)	3.39 (1.37, 8.38)
Mortality	1.06 (0.51, 2.23)	2.54 (1.26, 5.12)	2.34 (0.95, 5.72)	1.27 (0.28, 5.72)
Newly diagnosed diabetes	2.41 (1.20, 4.85)	2.56 (1.20, 5.48)	2.77 (1.10, 6.99)	3.90 (1.32, 11.53)
Local complications	1.32 (1.04, 1.67)	1.44 (1.10, 1.89)	1.18 (0.81, 1.72)	1.02 (0.59, 1.76)
Organ failure	1.60 (1.04, 2.47)	2.51 (1.60, 3.94)	2.85 (1.64, 4.94)	3.53 (1.78, 7.00)
Renal failure	2.66 (1.19, 5.96)	5.64 (2.55, 12.49)	5.34 (2.12, 13.48)	7.74 (2.73, 21.93)
Respiratory failure	1.27 (0.82, 2.29)	2.30 (1.36, 3.89)	3.37 (1.84, 6.17)	2.79 (1.21, 6.41)
Heart failure	1.75 (0.70, 4.37)	2.89 (1.14, 7.31)	5.52 (2.07, 14.73)	6.16 (1.91, 19.88)

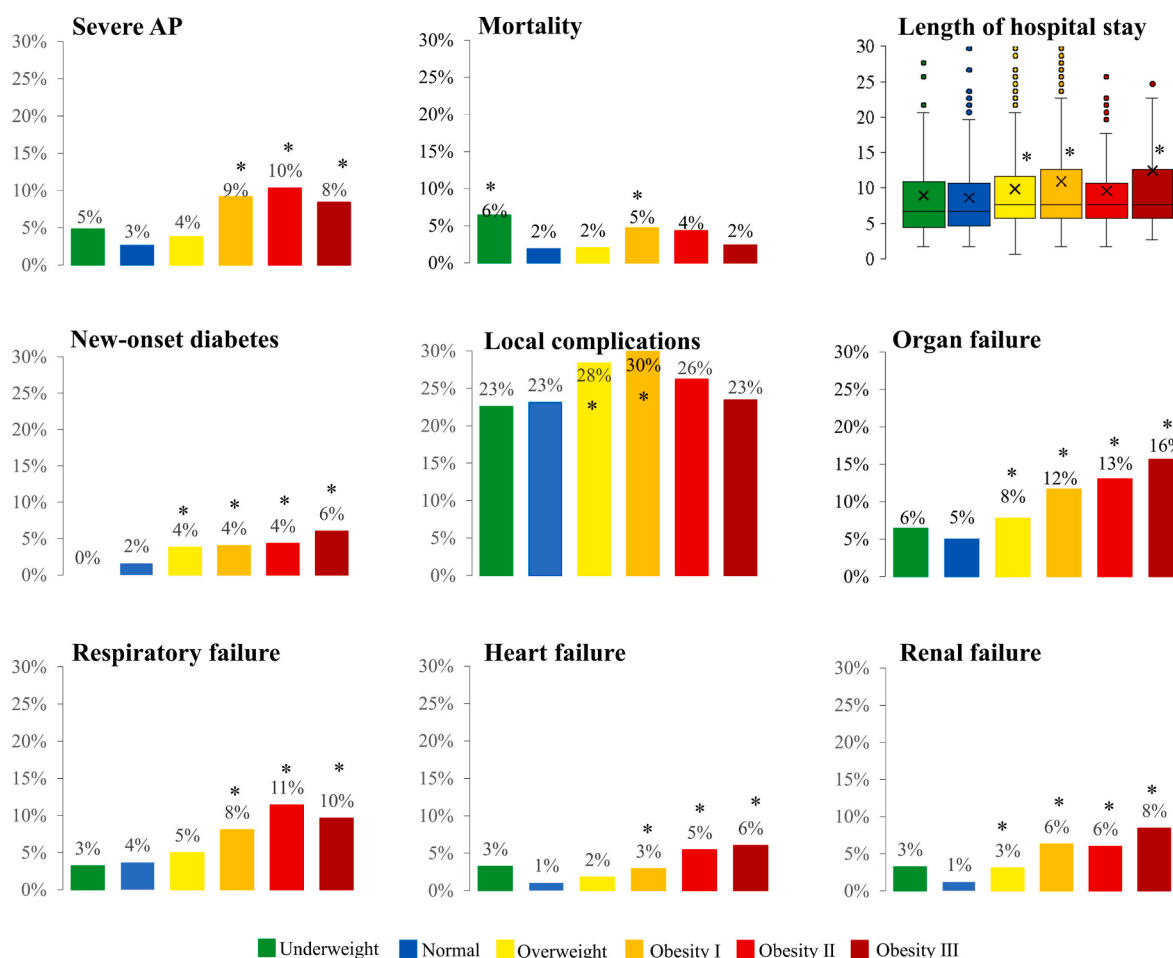


Fig. 2. Prevalence of acute pancreatitis in-hospital outcomes in the different body mass index groups. *statistically significant difference compared to the normal body mass index group.

to the normal BMI group (7, IQR: 5–11). There is a higher odds for newly diagnosed diabetes in all BMI groups higher than normal. The odds for local complications are higher only in the overweight and obesity I groups, while organ failure has higher odds in all four BMI groups higher than normal. Regarding the specific organ failures, the odds for renal failure were higher in all four elevated BMI groups compared to the normal BMI group, while only the three obesity groups had higher odds for respiratory failure and heart failure (Table 3, Fig. 2). Further details of the statistical analysis regarding outcomes can be found in Table S6/A.

We also found an increase of odds for all AP outcome parameters, except local complications, when BMI was a continuous variable in the analysis (Table S6/B).

3.4. Multivariable analyses

3.4.1. Organ failure

Examining the individual potential risk factors of organ failure in a model, higher age, male sex, comorbidities, and obesity are independent risk factors of organ failure. In obesity, odds ratios increase with the degree of obesity (Table 3A).

3.4.2. Severity of AP

Complications affect severity. Having comorbidities means a 2-fold increase in the risk of severe AP, while obesity is an independent risk factor for a 3–4-fold increase of severe AP risk (Table 3B).

3.4.3. Mortality

There is a 2-fold increase in risk of death for male sex and class 1 and 2 obesity (Table 3C).

When BMI was a continuous variable in the multivariable analyses, incremental increases in BMI were associated with higher rates of necrosis, organ failure, severe AP and mortality (Table S7).

4. Discussion

In our cohort analysis, we found that patients with higher BMI have more comorbidities, such as diabetes, and metabolic conditions like hypertension, hyperlipidemia, and liver steatosis and lower prevalence of recurrent acute and chronic pancreatitis. The proportion of female patients was higher in the higher BMI groups and median age increased across BMI categories up to obesity class I and decreased slightly in the higher obesity classes. Additionally, biliary and hypertriglyceridemia-induced etiology are more common, while alcohol-induced causes are less prevalent in the obese patient groups. The differences in age across BMI categories may partly explain the inverse association between BMI and recurrent acute or chronic pancreatitis. Patients with lower BMI tended to be younger and may more often reflect etiologies such as alcohol use, genetic predisposition, or early structural pancreatic disease, which are associated with recurrence and progression to chronic pancreatitis [19,20]. In contrast, patients with higher BMI were slightly older and more likely to have pancreatitis related to metabolic conditions such as gallstone disease, which typically presents as a single acute event. The higher proportion of female patients in the higher BMI groups, where alcohol consumption and smoking were less frequent, may further contribute to the lower prevalence of recurrent and chronic pancreatitis; both exposures have been shown to dose-dependently increase pancreatic injury and recurrence risk [21]. Additionally, recurrent and chronic pancreatitis may lead to pancreatic exocrine insufficiency with malabsorption and weight loss, contributing to lower BMI over time [22].

Obese patients had higher odds of severe AP, new-onset

diabetes, and organ failure. Organ failure also showed a linear correlation in the univariate and multivariable analyses. Earlier, obesity class III has been associated with a higher risk for inpatient mortality, increased costs of hospitalization, and overall worse clinical outcomes in acute pancreatitis [13]. In our analysis the increased mortality risk was observed for male sex and obesity class I and II in the multivariable analysis, while the association for class III obesity did not reach statistical significance. This may be related to the relatively low number of events in this subgroup. A meta-analysis investigating all BMI categories highlighted that a BMI above 25 increases the risk of severe AP but not mortality, while a BMI >30 raises the risk of mortality [9], which is broadly consistent with the current findings. The presence of obesity was an independent predictive factor for renal failure and a longer hospital stay in our earlier cohort analysis [11]. We observed similar results in the current analysis when evaluating obesity categories, whereas other studies reported complications, the need for interventional procedures, and mortality to be more frequent among obese patients [12].

Among possible reasons behind obesity being a risk factor for a worse outcome in AP we should mention 1) comorbidities: hypertension, hyperlipidemia, liver steatosis, and type 2 diabetes are common in patients with high BMI and can worsen AP outcomes [23–27], 2) higher risk of organ dysfunction: reduced lung compliance, and impaired microcirculation may exacerbate AP complications and increase the risk of organ failure [28], 3) increased risk of systemic inflammation: the metabolically active fat tissue releases pro-inflammatory cytokines like tumor necrosis factor- α (TNF- α), interleukin-1 (IL-1), and interleukin-6 (IL-6) that may amplify systemic inflammation and hormones secreted by fat cells (e.g., leptin, adiponectin) may influence immune response [29,30], 4) damaged intestinal mucosal barrier: impaired function in protecting the circulatory system from exposure to pro-inflammatory molecules, such as microorganisms, antigens and toxins, 5) delayed diagnosis and treatment: healthcare professionals face significant challenges when treating patients with obesity in finding the etiology, mobilization, interventions and interpretation of imaging findings as well [31].

Behind dose-dependency, we can consider more comorbidities, higher amounts of fat tissue, higher levels of pro-inflammatory cytokines, and more difficulties in the diagnosis and treatment. Our earlier cohort studies also found a dose-dependent relationship between hypertriglyceridemia or glucose levels and AP in-hospital outcomes, strengthening our findings on BMI dose dependency [21,25]. Moreover, smoking and alcohol were found to be in a dose-dependent relationship with RAP and CP prevalence, which is in line with the current analysis as the higher the BMI, the less alcohol consumption, smoking, RAP, and CP were present [32]. However, sociocultural factors and reporting bias may partly influence these patterns, as alcohol use and smoking are often more prevalent and socially accepted among men, while women may underreport these behaviors due to stigma or concerns about social acceptability.

In our analysis, we did not find any signs of the obesity paradox [33], higher BMI was not associated with lower mortality or reduced disease severity. It would have been interesting, however, to evaluate the quality of fat tissue [34] and examine the associations with AP outcomes.

We used BMI in our analysis to measure the degree of obesity as this is an easily accessible and the most common tool in clinical practice. However, BMI does not distinguish between lean and fat mass and does not capture fat distribution, particularly visceral adiposity, which may be more closely related to metabolic and inflammatory complications. Visceral fat has also been suggested to play a role in the pathophysiology and severity of AP, potentially

Table 3

Risk factors of A) organ failure, B) severe AP, C) mortality. Multivariable analyses. OR: odds ratio; CI: confidence interval; BMI: body mass index. AP: acute pancreatitis.

A) Organ failure					
Variable	N	Event	OR	95% CI	p-value
Age	1933	152	1.03	1.02, 1.04	<0.001
Gender	1933	152			
Female	836	50	1.00	—	
Male	1097	102	1.87	1.30, 2.72	<0.001
BMI groups	1933	152			
Normal weight	589	30	1.00	—	
Underweight	56	2	0.76	0.17, 3.29	0.709
Overweight	655	47	1.29	0.80, 2.09	0.290
Obesity class I	391	43	2.12	1.29, 3.46	0.003
Obesity class II	166	20	2.57	1.40, 4.71	0.002
Obesity class III	76	10	2.71	1.25, 5.88	0.012
Comorbidities	1933	152			
No	541	21	1.00	—	
Yes	1392	131	1.68	1.02, 2.75	0.039
B) Severity of AP					
Variable	N	Severe	OR	95% CI	p-value
Age	1938	98	1.02	1.01, 1.04	0.001
Gender	1938	98			
Female	836	36	1.00	—	
Male	1102	62	1.52	0.98, 2.36	0.065
BMI groups	1938	98			
Normal weight	590	16	1.00	—	
Underweight	56	1	0.677	0.09, 5.25	0.709
Overweight	658	23	1.17	0.61, 2.24	0.643
Obesity class I	392	35	3.16	1.71, 5.83	<0.001
Obesity class II	166	17	3.98	1.95, 8.15	<0.001
Obesity class III	76	6	2.80	1.05, 7.48	0.040
Comorbidities	1938	98			
No	542	11	1.00	—	
Yes	1396	87	2.09	1.08, 4.05	0.028
C) Mortality					
Variable	N	Event	OR	95% CI	p-value
Age	1938	51	1.03	1.01, 1.05	0.003
Gender	1938	51			
Female	836	16	1.00	—	
Male	1102	35	2.11	1.13, 3.93	0.019
BMI groups	1938	51			
Normal weight	590	12	1.00	—	
Underweight	56	2	2.07	0.44, 9.66	0.356
Overweight	658	9	0.60	0.25, 1.44	0.250
Obesity class I	392	18	2.18	1.03, 4.62	0.042
Obesity class II	166	8	2.53	1.01, 6.36	0.049
Obesity class III	76	2	1.30	0.28, 6.01	0.738
Comorbidities	1938	51			
No	542	8	1.00	—	
Yes	1396	43	1.30	0.59, 2.88	0.519

through increased pro-inflammatory activity [35]. Several other, more accurate anthropometric tools exist to assess obesity [36]. Waist circumference and waist-hip ratio may help to evaluate central obesity more accurately and may better reflect visceral fat accumulation. Imaging-based methods such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Dual X-ray Absorptiometry (DXA) could be more accurate for measuring body composition, but they require expensive infrastructure, a technician and may involve radiation usage. Bioimpedance (BIA) analysis is a non-invasive and non-expensive tool to measure obesity. However, some limitations must be considered when evaluating accuracy and reliability. The BIA tool is not recommended currently for patients with extreme BMI and non-normal hydration status. Digital anthropometry [37] is a relatively new, promising, non-invasive, non-expensive measurement technique using three-dimensional optical imaging or two-dimensional digital photography. It can accurately predict total fat mass [38]

and total body composition [39], but currently, it still has some limitations [36].

It should also be considered that the obesity treatment landscape is rapidly evolving with the increasing use of pharmacological therapies, particularly GLP-1 receptor agonists and dual incretin agonists. Large, randomized trials have demonstrated substantial weight loss with agents such as semaglutide and tirzepatide, suggesting that wider uptake could influence future obesity prevalence and related disease burden [40,41]. However, the extent to which these therapies will modify population-level obesity trends remains uncertain and will likely depend on affordability, access, and long-term adherence. The potential association between GLP-1-based therapies and acute pancreatitis (AP) remain debated. Although product labels include warnings, meta-analyses of randomized trials have generally not demonstrated a clear increase in AP risk [42].

Although there are recommendations for counseling patients

with obesity or hypertriglyceridemia in AP to undergo lifestyle or pharmacological interventions [43], there are usually no follow-up plans and control visits regarding obesity after AP. Channeling patients to professionals who follow the comprehensive approach [37], including dietary changes, physical activity, and behavioral interventions in obesity treatment and follow-up, might improve AP outcomes [44] and would be important after AP.

4.1. Strengths and limitations

Besides characterizing the associations between the degree of obesity and AP outcome, our analysis is the first to show a dose-dependent effect between the obesity classes and organ failure in AP. In contrast to previous studies, we used a large international cohort with prospectively collected data and conducted multi-variable analyses to investigate whether the degree of obesity is independently associated with AP outcome.

We must consider some limitations as well. BMI is not the most accurate marker for obesity as it does not consider the body composition. In some critically ill patients, BMI could not be measured directly at admission, and values were based on patient-reported or previously recorded data, which may introduce measurement bias. We could not consider other confounding factors like genetic predisposition, physical activity, dietary or sleeping habits, which also greatly impact health and immune response or outcome of different diseases. Likewise, we could not evaluate the quality and quantity of adipose tissue or inflammatory markers such as IL-6, TNF- α , or C-reactive protein (CRP) levels either. Because AP etiology differed across BMI categories, we cannot exclude that part of the observed association between obesity and disease severity may be influenced by differences in etiologic distribution. Additionally, laboratory parameters were measured only at admission and may reflect both acute changes related to pancreatitis and underlying chronic conditions.

4.2. Implication for practice

Gradual weight loss may decrease the risk of organ failure and improve AP outcome. Obesity status reports and education should be part of patient care. Co-operating with psychologists, dietitians, and physiotherapists to elaborate a personalized obesity treatment and follow-up of patients would contribute to preventing further comorbidities [45]. However, as our findings are based on observational cohort data, these implications should be interpreted cautiously and require confirmation in prospective interventional studies. These actions are critical to translate scientific results for patients' benefit [46,47].

4.3. Implication for research

A more accurate measurement of body composition may improve the investigation of the associations between obesity and the outcome of AP, including post-discharge complications [48]. Randomized clinical trials are warranted to examine the efficacy of patient counseling and obesity treatment methods after AP. The Current data may also contribute to AI-supported personalized medicine in the future, considering the limitations of BMI as an anthropometric measurement tool. It is also an important question: what is the effect of obesity on post-discharge mortality and morbidity [49].

4.4. Implication for policymakers

Obesity is a worldwide epidemic, and addressing prevention and treatment challenges of obesity in other diseases as well

would help in follow-up planning and preventing further burden on healthcare systems and economies. Future research, including clinical trials, is needed to evaluate whether targeted weight management interventions can improve outcomes in patients with acute pancreatitis.

5. Conclusion

Obesity dose-dependently elevate the risk of pre-existing comorbidities and complications. Gradual weight loss may also have a positive effect and should be included in patient reports and education.

Patient and public involvement

Patients and/or the public were not involved in this research's design, reporting or dissemination plans.

Author contributions

AS: conceptualization, project administration, methodology, formal analysis, interpretation of results, visualization, writing-original draft; ZS: methodology, formal analysis, interpretation of results, visualization, writing - review and editing; NF: methodology, formal analysis, interpretation of results, writing - review and editing; DD, GC, ÁV, PS, SG, BCN, LC, BK, FI, LG, VDV, MP, JH, MV, IT, JN, AM, AP, MF, MI, BE, PJH, SV: data collection, writing - review and editing; PH: conceptualization, methodology, supervision, funding acquisition, writing - original draft.

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the manuscript's concept, design, analysis, writing, or revision.

Data sharing

Original raw data is available from the corresponding author upon reasonable request.

Ethical permission

The study was approved by the Scientific and Research Ethics Committee of the Medical Research Council and the National Public Health Centre (reference numbers: 22254-1/2012/EKU and 17787-8/2020/EÜIG). All participants in this study provided written informed consent prior to study enrolment.

Supplementary appendix

Hungarian Pancreatic Study Group, further contributors, data quality and the description of the monitoring system, center distribution, representativeness of the analyzed cohort, sex distribution and age by BMI groups, tables of statistical analysis.

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Competing interests

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pan.2026.07.016>.

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