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Risk factors for intensive care unit admission in hospitalized patients with acute pancreatitis

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SUMMARY

Background: Acute pancreatitis (AP) is afflicted by substantial morbidity and mortality. Besides local/systemic complications and pancreatic necrosis, patients' comorbidities might be underrated as risk factor for intensive care unit (ICU) admission in AP.

Methods: We screened the German nationwide inpatient statistics identifying patients admitted due to AP (ICD-code K85) 2005–2019. AP hospitalizations were stratified for necessity of ICU admission and risk-factors for ICU admission were investigated.

Results: Overall, 797,364 patient-hospitalizations due to AP (median age 56.0 [IQR 44.0–71.0] years, 39.2% females) were detected in Germany 2005–2019. Among these, 78,437 (9.8 %) were treated at an ICU. AP patients admitted to an ICU were significantly older (59.0 [46.0–73.0] vs. 56.0 [44.0–71.0], $P < 0.001$), less often female (35.4 % vs. 39.6 %, $P < 0.001$), showed an aggravated comorbidity-profile and higher case-fatality than those without ICU admission (13.7 % vs. 1.6 %, $P < 0.001$). ICU admission was independently associated with increased in-hospital case-fatality (OR 9.82 [95%CI 9.54–10.12], $P < 0.001$).

Strongest independent risk factors for ICU admission regarding patient-characteristics were male sex (OR 1.26 [95%CI 1.23–1.28], $P < 0.001$), obesity (OR 1.53 [95%CI 1.49–1.57], $P < 0.001$), diabetes mellitus (OR 1.35 [95%CI 1.33–1.38], $P < 0.001$), heart failure (OR 2.43 [95%CI 2.37–2.49], $P < 0.001$) and atrial fibrillation/flutter (OR 1.87 [95%CI 1.82–1.91], $P < 0.001$).

Conclusions: Approximately 10 % of the hospitalized AP patients had to be admitted on an ICU. Besides AP complications, male sex, obesity, diabetes mellitus, heart failure and atrial fibrillation/flutter were associated with ICU admission.

1. Introduction

Acute pancreatitis (AP) is one of the leading causes for gastrointestinal disease admissions with increasing incidence worldwide [1–5]. The population-based incidence in western industrialised countries varies with regional differences between 13 and 100 per 100,000 population [6]; in Germany, the incidence ranges between 13 and 43 individuals with AP per 100,000 population [7,8]. The main etiology of AP is alcohol and gallstone (30–50 % depending on regional differences, as well as on sex and age) followed by rarer causes such as hypertriglyceridemia (10 %), post-ERCP AP (3–5 %), and medication associated AP (0.1–2.0 %), but AP is also related to smoking as an independent or at least as an important cofactor [6,9–11]. Approximately 80 % of the AP events are of a mild character and resolve with supportive treatment, whereas moderate and especially severe AP, stratified to the revised Atlanta classification (RAC), leads to substantially increased morbidity and mortality

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[12–19]. Therefore, over the past decades several prognostic scoring systems based on imaging, clinical and laboratory chemical tests were developed to predict the severity of AP [20–22]. The Revised Atlanta Classification (RAC) and the Determinant-based Classification (DBC) of AP are established scoring tools to evaluate the severity of AP and estimate the prognosis of AP [12–14,16,23]. Important risk factors for poor outcome are organ failure, local and systemic complications such as peritonitis, venous thromboembolism, systemic inflammatory response syndrome (SIRS), sepsis and particularly pancreatic necrosis [20,21,24]. The AP-related mortality increases from 0.1 % in mild cases to 54.1 % in critical AP manifestations [14–19]. Risk stratification scores like the Harmless Acute Pancreatitis Score (HAPS) [8], the Bedside Index of Severity in Acute Pancreatitis (BISAP) [25] or the Acute Physiology and Chronic Health Examination II (APACHE II) [26] were developed to predict short-term mortality and to identify patients, who benefit from an admission on an ICU and expanded therapeutic measures [8,25,26]. However, the commonly used risk stratification and scoring tools in AP tend to underestimate the impact of patients' comorbidity burden, which often plays a crucial role in determining the need for ICU treatment. The presence of comorbidities significantly influences the outcome of these patients [14,27]. In this context, the established AP risk stratification approaches revealed only low positive predictive values and moderate accuracy [20,28].

ICU treatment is a very important cornerstone in the treatment of severe AP to withstand impending deterioration and to avert patients' death. Since ICU capacities are expensive and limited, ICU treatment is a critical bottleneck in the hospitals, patient care and health care planning. Thus, evaluation of ICU as a primary outcome is important for health care planning in the different health care systems [6,20,29–32].

Therefore, we aimed to investigate risk factors and drivers for AP patients' ICU admission in these very large German nationwide inpatient statistics with real-world data in order to specify and draw conclusions on further important individual risk factors besides the aforementioned.

2. Methods

In Germany, a new remuneration system for the inpatient health care system was implemented and started during the year 2004. In this remuneration system, for all treated patients coexisting conditions, surgeries, interventions, treatments and procedures have to be coded by the German hospitals and afterwards the codes have to be transferred to the Institute for the Hospital Remuneration System as well as the Federal Statistical Office of Germany (Statistisches Bundesamt) in order to receive the remuneration for the provided and rendered services [33]. Coding of the aforementioned diagnoses has to be done according to ICD-10-GM (International Classification of Diseases, 10th Revision with German Modification) and surgical, diagnostic and interventional procedures according OPS codes (Operationen-und Prozedurenschlüssel) [33]. Besides the remuneration, the Federal Statistical Office of Germany gathers all mentioned coded treatment data from the hospitalized patient-cases, generating the German nationwide inpatient statistics for research purposes (diagnosis related groups [DRG] statistic), which was used for our present study-analysis [33].

For this research project and to investigate our hypotheses, we generated the statistical syntaxes and sent them to the Research Data Center (RDC) of the Federal Statistical Office and the Statistical Offices of the federal states (in Wiesbaden, Germany), which computed the study results on our behalf based (by the statistical syntaxes) on delivered syntaxes. For the present study, we selected all inpatients hospitalized due to an AP (all inpatients with a main diagnosis of AP [ICD code K85]) (source: RDC of the Federal Statistical Office and the Statistical Offices of the federal states, DRG Statistics 2005–2019, own calculations). The main diagnosis of a patient is defined as that diagnosis, which was mainly responsible for hospitalization documented by the discharging physician. The AP (ICD code K85) patients were divided in those with and without need of an ICU admission and both groups were compared.

2.1. Study endpoints

The primary study endpoint was admission on an ICU. In addition, we investigated the impact of a necessity of ICU admission on death of all-causes during in-hospital stay (in-hospital death) as a secondary study endpoint.

2.2. Definitions

Obesity was defined as body mass index $\geq$30 kg/m^2 according to the recommendations of the WHO (World Health Organization) [34]. Shock as well as cardio-pulmonary resuscitation were defined according to current European guidelines [35–37]. Major adverse cardiovascular and cerebrovascular events (MACCE) was defined as composite of all-cause in-hospital death, acute myocardial infarction [ICD-code I21], and/or ischemic stroke [ICD-code I63] [38].

The VTE entities of pulmonary embolism (PE, ICD code I26) and deep vein thrombosis and/or thrombophlebitis (DVT, ICD codes I80, I81, I82) were subsumized as VTE. Pancreas specific surgeries comprised the OPS code 5-52.

2.3. Ethical aspects and study oversight

Since the present study did not contain direct access by us as the investigators to data of individual patients, but in contrast only to aggregate results provided by the RDC, approval by an ethics committee and informed consent were not required, in compliance with German law.

2.4. Statistics

Descriptive statistics for the comparison of AP patients with and without necessity of ICU admission were provided with median and interquartile range (IQR), or absolute numbers and corresponding percentages; continuous variables were compared with the use of the Wilcoxon-Whitney U test, while the comparisons of categorical variables were computed with Fisher's exact or chi test, as appropriate.

Logistic regression models were calculated to investigate the impact of patients' characteristics, different conditions and comorbidities as well as adverse in-hospital events on the necessity of an ICU admission. Results were presented as odds ratios (OR) and related 95 % confidence intervals (CI). In order to ensure that the results of these logistic regression analyses are not substantially biased by age, sex and important comorbidities the multivariate logistic regressions were adjusted for these aforementioned parameters. The logistic regressions were calculated with all parameters in one model and the adjustment comprised the following parameters: age, sex, obesity, cancer, heart failure, essential arterial hypertension, chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/1.73 m^2), diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

Temporal trends on total numbers of AP hospitalizations, the necessity of ICU admission, and the in-hospital case-fatality over time and with age were illustrated as figures and estimated by means of linear regression analyses. Results were presented as β-estimates and related 95 % CI.

We used the software of SPSS® (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp) for the computerised data analysis. Only P values lower than 0.05 (two-sided) were considered to be statistically significant.

3. Results

3.1. Study overview and temporal trends

In total, 797,364 hospitalization-cases of patients admitted due to AP (median age 56.0 [IQR 44.0–71.0] years, 39.2 % females) were counted in Germany between the years 2005 and 2019. Among them, 78,437 (9.8 %) had to be treated on an ICU. While total numbers of hospitalizations due to AP increased from 50,760 in the year 2005 to 53,345 in 2019, the rate of ICU admission did not change substantially over time (2005: 8.9 % vs. 2019: 7.6 %, maximum 2011: 10.9 %, β −0.001 [95%CI -0.001 to 0.001], P < 0.001). However, highest ICU demand was seen in the years 2010–2012 (Fig. 1). In contrast, the necessity for ICU admission increased significantly with age-decade (β 0.006 [95%CI 0.006 to 0.007], P < 0.001) (Fig. 2). Whereas the in-hospital case-fatality in AP patients with need of ICU was widely stable over time (Fig. 1), the case-fatality rate increased substantially with rising age (Fig. 2).

3.2. AP patients admitted to an ICU have primarily an aggravated cardiovascular profile

AP patients admitted to ICU were slightly older (59.0 [46.0–73.0] vs. 56.0 [44.0–71.0], P < 0.001) and less often females (35.4 % vs. 39.6 %, P < 0.001). All investigated cardiovascular risk factors were more prevalent in AP patients with need of ICU admission than in those treated without ICU (Table 1). In particular, cardiovascular diseases such as heart failure (14.9 % vs. 5.4 %, P < 0.001), coronary artery disease (11.8 % vs. 8.7 %, P < 0.001) and atrial fibrillation/flutter (15.1 % vs. 6.8 %, P < 0.001) were more often detected in AP patients, who had to be treated on an ICU. In addition, also other diseases such as renal failure and chronic obstructive pulmonary disease were more often found in patients treated on an ICU. In addition, AP patients admitted to an ICU were more often treated with general or pancreatic surgeries. As expected, length of in-hospital stay is prolonged if patients have to be admitted to an ICU (16.0 [10.0–28.0] vs. 7.0 [5.0–11.0] days, P < 0.001 (Table 1).

3.3. Need for ICU admission was afflicted by poorer outcome

AP patients who had to be treated on an ICU had an 8.5-fold Risk Ratio to die during the hospitalization in comparison to those patients admitted due to AP without necessity of ICU admission (Table 1). This result was confirmed in the logistic

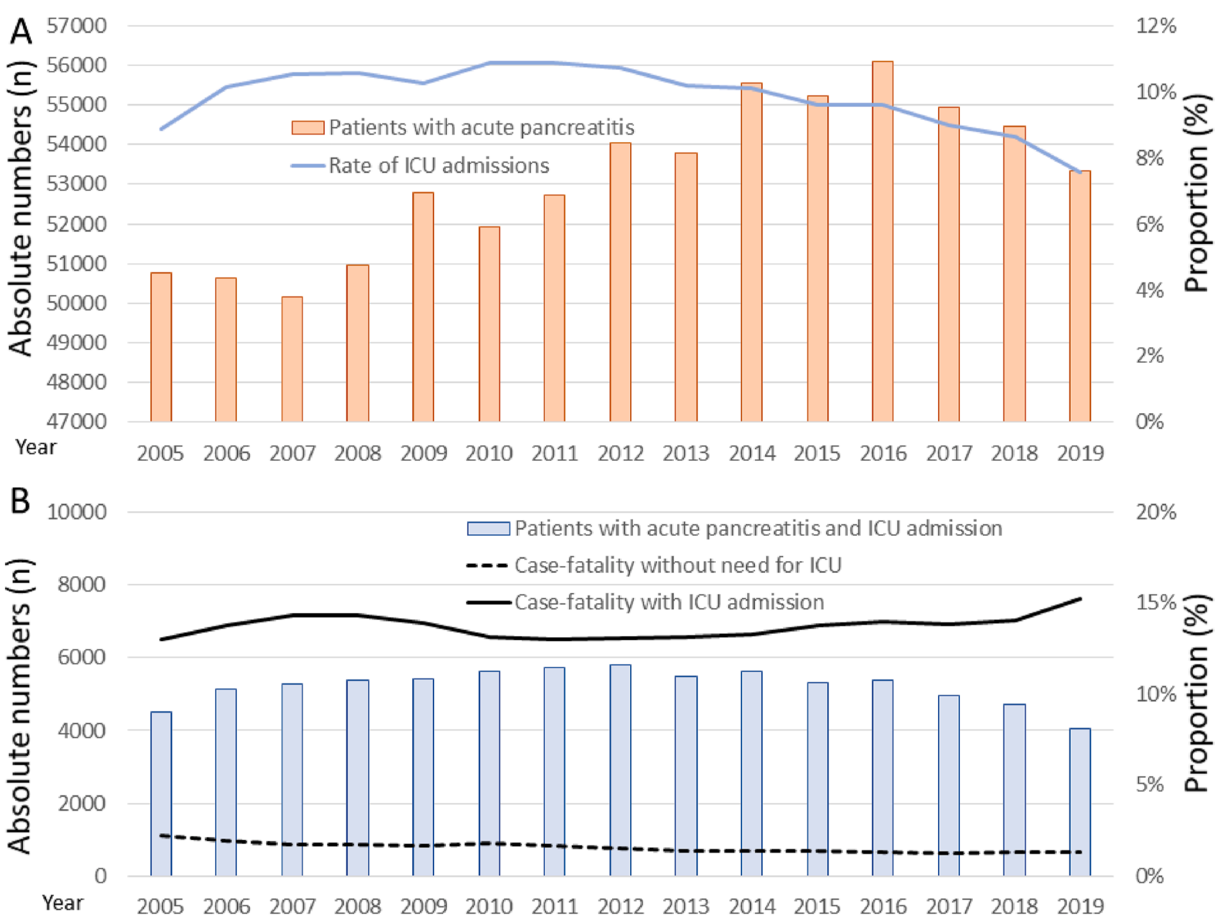

Fig. 1. Time trends in patients with acute pancreatitis and ICU admission.
Panel A: Annual time trends of absolute numbers of patients admitted due to acute pancreatitis (orange bars) and proportion of these patients, who had to be admitted to an intensive care unit (ICU, blue line) during the observational period 2005-2019
Panel B: Annual numbers of patients admitted due to acute pancreatitis, who had to be admitted to an intensive care unit (ICU, blue bars) and case-fatality rate of patients treated on ICU (solid black line) or without ICU (dashed black line) during the observational period 2005–2019.

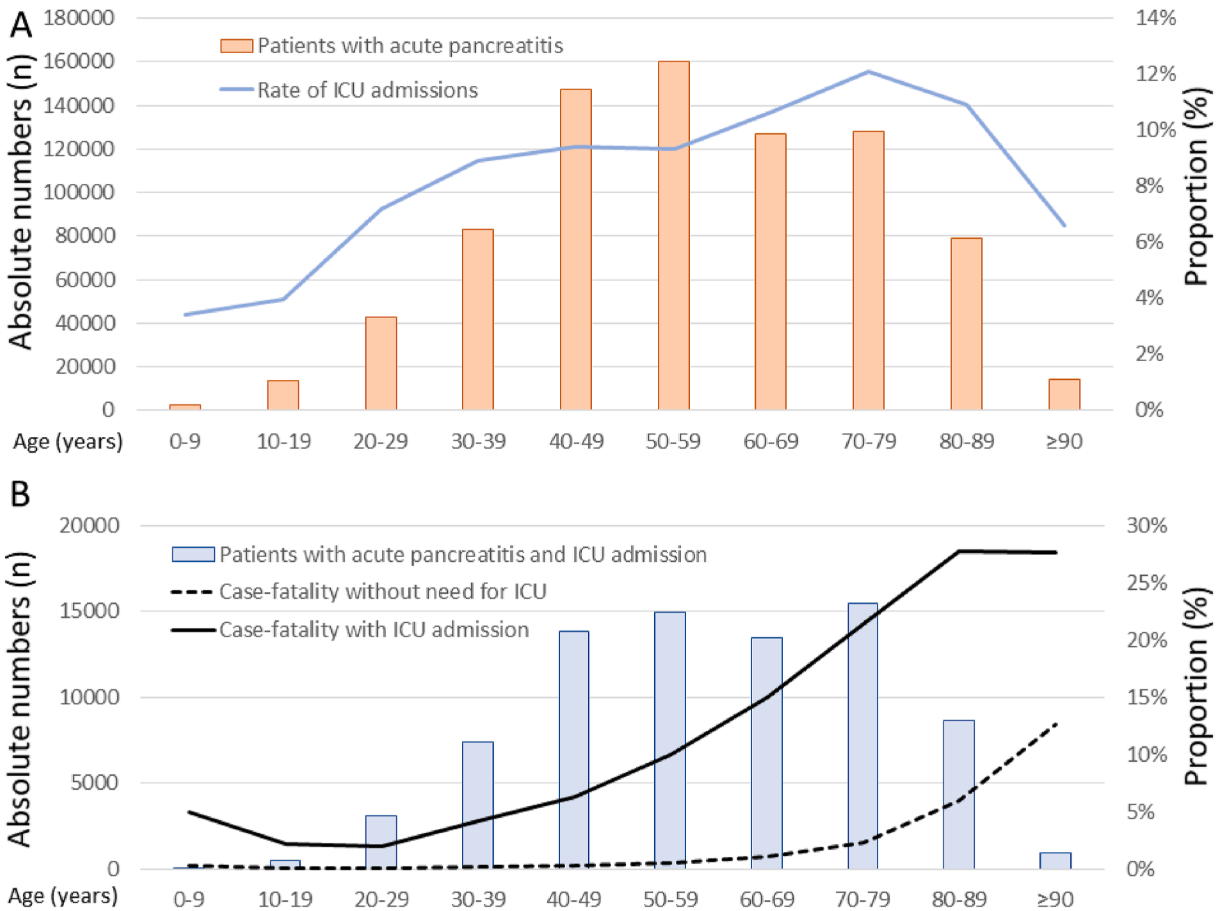

Fig. 2. Age trends in patients with acute pancreatitis and ICU admission.
Panel A: Age trends of absolute numbers of patients admitted due to acute pancreatitis (orange bars) and proportion of these patients, who had to be admitted to an intensive care unit (ICU, blue line) during the observational period 2005-2019
Panel B: Decade-dependent numbers of patients admitted due to acute pancreatitis, who had to be admitted to an intensive care unit (ICU, blue bars) and case-fatality rate of patients treated on ICU (solid black line) or without ICU (dashed black line) during the observational period 2005–2019.

regression analysis: ICU admission was independently associated with a nearly 10-fold increased in-hospital case-fatality (univariate logistic regression: OR 9.95 [95%CI 9.68–10.23], P < 0.001; multivariate logistic regression: OR 9.82 [95%CI 9.54–10.12], P < 0.001).

In addition, MACCE was also more often detected in patients who were admitted to an ICU (15.1 % vs. 1.8 %, P < 0.001). Venous thromboembolism (5.1 % vs. 1.4 %, P < 0.001), sepsis (6.0 % vs. 0.3 %, P < 0.001) and pneumonia (19.6 % vs. 2.6 %, P < 0.001) were more often diagnosed in patients who had to be admitted on ICU (Table 1). It is of further importance that all investigated bleeding events were more prevalent in patients with ICU treatment. Especially, transfusions of blood constituents (28.1 % vs. 2.3 %, P < 0.001) were more often needed in those patients on ICU (Table 1).

3.4. Risk factors for ICU admission

Focusing on the patient characteristics, male sex was an independent risk factor for ICU admission (OR 1.26 [95%CI 1.23–1.28], P < 0.001) (Table 2). Regarding the investigated traditional cardiovascular risk factors, obesity (OR 1.53 [95%CI 1.49–1.57], P < 0.001) and diabetes mellitus (OR 1.35 [95%CI 1.33–1.38], P < 0.001) were also independent risk factors for ICU admission (Table 2).

Among the assessed and analysed comorbidities, heart failure (OR 2.43 [95%CI 2.37–2.49], P < 0.001) and atrial fibrillation/flutter (OR 1.87 [95%CI 1.82–1.91], P < 0.001) were the strongest independent risk factors for ICU admission. Chronic obstructive pulmonary disease was a moderate predictor regarding the need of ICU setting (OR 1.34 [95%CI 1.30–1.38], P < 0.001) (Table 2).

In addition and as expected, surgery in general (OR 3.77 [95%CI 3.68–3.85], P < 0.001) and pancreatic surgery in particular (OR 5.27 [95%CI 5.15–5.39], P < 0.001) were strong predictors of ICU admission (Table 2).

The logistic regressions demonstrated that all of the adverse in-hospital events were independently associated with ICU admission. Strongest independent associations with OR >15 were found between shock and ICU (OR 20.30 [95%CI 19.42–21.22], P < 0.001), sepsis and ICU (OR 16.25 [95%CI 15.44–17.10], P < 0.001) as well as transfusion of blood constituents and ICU (OR 15.38 [95%CI 15.03–15.73], P < 0.001) (Table 2). These conditions are of course also circumstances that require an ICU admission and therefore are also risk factors of ICU admission, but the need for ICU admission in these conditions are in most cases self-explanatory.

3.4.1. Impact of nutritional status of the patients with pancreatitis on the admission rate to an intensive care unit

The majority of patients with acute pancreatitis treated on an ICU were of normal weight or had an overweight (72,844; 92.6 %).

Table 1
Patients' characteristics, medical history, presentation and outcomes of the included 797,364 patients with acute pancreatitis stratified according the necessity of intensive care unit admission.

Parameters	Hospitalizations of acute pancreatitis patients without ICU admission (n = 718,927; 90.2 %)	Hospitalizations of acute pancreatitis patients with ICU admission (n = 78,437; 9.8 %)	P-value
Age	56.0 (44.0–71.0)	59.0 (46.0–73.0)	**<0.001**
Age ≥70 years	196,381 (27.3 %)	25,052 (31.9 %)	**<0.001**
Female sex	284,558 (39.6 %)	27,778 (35.4 %)	**<0.001**
In-hospital stay (days)	7.0 (5.0–11.0)	16.0 (10.0–28.0)	**<0.001**
Prolonged in-hospital stay >14 days	98,435 (13.7 %)	43,813 (55.9 %)	**<0.001**
Traditional cardiovascular risk factors			
Obesity	49,763 (6.9 %)	8847 (11.3 %)	**<0.001**
Essential arterial hypertension	278,956 (38.8 %)	35,976 (45.9 %)	**<0.001**
Diabetes mellitus	128,253 (17.8 %)	20,391 (26.0 %)	**<0.001**
Hyperlipidaemia	78,910 (11.0 %)	10,119 (12.9 %)	**<0.001**
Surgery			
Any surgery	463,844 (64.5 %)	68,758 (87.7 %)	**<0.001**
Pancreatic surgery	25,404 (3.5 %)	12,953 (16.5 %)	**<0.001**
Comorbidities			
Coronary artery disease	62,194 (8.7 %)	9285 (11.8 %)	**<0.001**
Heart failure	39,095 (5.4 %)	11,654 (14.9 %)	**<0.001**
Peripheral artery disease	10,185 (1.4 %)	1740 (2.2 %)	**<0.001**
Atrial fibrillation/flutter	48,839 (6.8 %)	11,879 (15.1 %)	**<0.001**
Chronic obstructive pulmonary disease	27,891 (3.9 %)	5172 (6.6 %)	**<0.001**
Chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/ 1,73 m^2)	34,149 (4.7 %)	5944 (7.6 %)	**<0.001**
Cancer	15,901 (2.2 %)	2043 (2.6 %)	**<0.001**
Adverse events during hospitalization			
In-hospital death	11,281 (1.6 %)	10,741 (13.7 %)	**<0.001**
MACCE	13,285 (1.8 %)	11,826 (15.1 %)	**<0.001**
Myocardial infarction	1686 (0.2 %)	1133 (1.4 %)	**<0.001**
Shock	3015 (0.4 %)	7103 (9.1 %)	**<0.001**
Cardio-pulmonary resuscitation	2163 (0.3 %)	3180 (4.1 %)	**<0.001**
Peptic ulcer	7633 (1.1 %)	1481 (1.9 %)	**<0.001**
Venous thromboembolism	10,105 (1.4 %)	3967 (5.1 %)	**<0.001**
Deep venous thrombosis or thrombophlebitis	9300 (1.3 %)	3351 (4.3 %)	**<0.001**
Pulmonary embolism	988 (0.1 %)	813 (1.0 %)	**<0.001**
Sepsis	2377 (0.3 %)	4716 (6.0 %)	**<0.001**
Pneumonia	18,370 (2.6 %)	15,410 (19.6 %)	**<0.001**
Acute kidney injury	18,140 (2.5 %)	16,095 (20.5 %)	**<0.001**
Stroke (ischemic or hemorrhagic)	1059 (0.1 %)	667 (0.9 %)	**<0.001**
Gastro-intestinal bleeding	6631 (0.9 %)	2367 (3.0 %)	**<0.001**
Intracranial bleeding	80 (0.01 %)	82 (0.10 %)	**<0.001**
Transfusion of blood constituents	16,421 (2.3 %)	22,066 (28.1 %)	**<0.001**

Only 0.3 % of these patients were underweight, whereas 7.1 % were obese (Table 3). In total, 7.5 % of the underweight patients had to be admitted to an ICU and in obese patients the rate was 11.3 %.

While underweight was not an independent risk factor for ICU admission, all obesity classes were independently associated with ICU admission (Table 4). The risk for ICU admission increased with obesity class and thus, was highest in obesity class III with 1.7-fold increased risk for ICU admission (OR 1.70 (1.61–1.80), $P < 0.001$) (Table 4).

3.4.2. *Impact of nutritional status on outcomes in patients with pancreatitis, who were admitted on an intensive care unit*

We detected a strong influence of nutritional status on the outcomes of patients with pancreatitis. While peptic ulcer, deep venous thrombosis or thrombophlebitis, pulmonary embolism and bleeding events as well as pancreatic surgery were more often observed in underweight patients, infections such as pneumonia and sepsis occurred more frequently in obese patients with an increase over the obesity classes (Table 3). In contrast, case-fatality rate as well as MACCE rate showed an U-shaped curve with lowest rates in the normal weight, overweight and obesity class I patients and an increase regarding case-fatality and MACCE rates at both ends of the curve (underweight and severe obesity) (Fig. 3, Table 3). This was in part confirmed by the logistic regressions elucidating an independent association of obesity class I with reduced case-fatality and class III with increased case-fatality (Table 5).

4. Discussion

The incidence of AP increased in the last decades [3,39,40]. The global pooled incidence of AP was estimated as 34 cases per 100,000 population per year [39]. In line with previously published studies, the annual hospitalizations of AP increased over time in Germany [40,41]. Although the reasons for this increase are still not fully understood, it has to be hypothesized that temporal changes of the most common causes of AP such as gallstones and alcohol abuse might have significantly influenced the incidence of AP [3,19,42]. In particular, the increasing prevalence of obesity and its resulting related complications like gallstones, hypertriglyceridemia and diabetes mellitus contribute to higher incidence of AP [42–45]. However, the proportion of obesity in our study was lower than the expected prevalence of obesity in the German population [46].

Pathophysiologically, AP is initially characterized by a localized inflammation, including cytokine release, leukocyte activation, and increased oxidative stress. This can lead to a complicated course, potentially progressing to systemic inflammatory response

Table 2
Risk factors for necessity of admission on an intensive care unit in patients with pancreatitis (univariable and multivariable logistic regression models).

	Univariable regression model		Multivariable regression model[a]	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Age	1.007 (1.007–1.008)	**<0.001**	0.997 (0.997–0.998)	**<0.001**
Age ≥70 years	1.25 (1.23–1.27)	**<0.001**	0.87 (0.86–0.89)	**<0.001**
Female sex	0.84 (0.82–0.85)	**<0.001**	0.79 (0.78–0.81)	**<0.001**
Traditional cardiovascular risk factors				
Obesity	1.71 (1.67–1.75)	**<0.001**	1.53 (1.49–1.57)	**<0.001**
Essential arterial hypertension	1.34 (1.32–1.36)	**<0.001**	1.19 (1.17–1.21)	**<0.001**
Diabetes mellitus	1.62 (1.59–1.65)	**<0.001**	1.35 (1.33–1.38)	**<0.001**
Hyperlipidemia	1.20 (1.18–1.23)	**<0.001**	0.95 (0.93–0.97)	**<0.001**
Surgery				
Any surgery	3.91 (3.82–3.99)	**<0.001**	3.77 (3.68–3.85)	**<0.001**
Pancreatic surgery	5.40 (5.28–5.52)	**<0.001**	5.27 (5.15–5.39)	**<0.001**
Comorbidities				
Coronary artery disease	1.42 (1.39–1.45)	**<0.001**	0.94 (0.92–0.96)	**<0.001**
Heart failure	3.04 (2.97–3.10)	**<0.001**	2.43 (2.37–2.49)	**<0.001**
Peripheral artery disease	1.58 (1.50–1.66)	**<0.001**	1.16 (1.10–1.22)	**<0.001**
Atrial fibrillation/flutter	2.45 (2.40–2.50)	**<0.001**	1.87 (1.82–1.91)	**<0.001**
Chronic obstructive pulmonary disease	1.75 (1.70–1.80)	**<0.001**	1.34 (1.30–1.38)	**<0.001**
Chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/1,73 m^2)	1.64 (1.60–1.69)	**<0.001**	1.06 (1.02–1.09)	**0.001**
Cancer	1.18 (1.13–1.24)	**<0.001**	1.12 (1.07–1.18)	**<0.001**
Adverse events during hospitalization				
Myocardial infarction	6.24 (5.78–6.73)	**<0.001**	4.40 (4.06–4.76)	**<0.001**
Shock	23.64 (22.64–24.69)	**<0.001**	20.30 (19.42–21.22)	**<0.001**
Venous thromboembolism	3.74 (3.60–3.88)	**<0.001**	3.55 (3.42–3.69)	**<0.001**
Deep venous thrombosis or thrombophlebitis	3.41 (3.27–3.55)	**<0.001**	3.30 (3.17–3.44)	**<0.001**
Pulmonary embolism	7.61 (6.93–8.35)	**<0.001**	6.46 (5.86–7.11)	**<0.001**
Sepsis	19.28 (18.35–20.27)	**<0.001**	16.25 (15.44–17.10)	**<0.001**
Pneumonia	9.32 (9.11–9.54)	**<0.001**	7.85 (7.67–8.04)	**<0.001**
Acute kidney injury	9.97 (9.75–10.20)	**<0.001**	8.47 (8.27–8.68)	**<0.001**
Stroke (ischemic or hemorrhagic)	5.81 (5.28–6.41)	**<0.001**	4.60 (4.15–5.08)	**<0.001**
Gastro-intestinal bleeding	3.34 (3.19–3.51)	**<0.001**	3.04 (2.90–3.19)	**<0.001**
Intracranial bleeding	9.40 (6.91–12.80)	**<0.001**	8.45 (6.14–11.62)	**<0.001**
Transfusion of blood constituents	16.75 (16.38–17.12)	**<0.001**	15.38 (15.03–15.73)	**<0.001**

[a] Adjusted for age, sex, obesity, cancer, heart failure, essential arterial hypertension, chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/1,73 m^2), diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

syndrome (SIRS) and further deterioration into severe AP, which may result in hypovolemic and distributive shock and multi-organ failure or damage [47]. Thus, the early and timely identification of these indications of a severe AP course is crucial to treat targeted and optimize early management, to prevent aggravation and further complications and avoid an (early) AP-related death. Consecutively, identification of risk factors for an aggravated course of AP and early risk stratification in AP is of crucial interest. Although severity assessment tools with clinical and radiological scoring systems and in part with incorporated assessments of additional laboratory markers already have been established [6,20,29], the search for new and especially simple as well as easily assessable scores with a favorable effectiveness is still ongoing [48]. These simple risk stratification tools are of key interest, since some of the established scores, like the Ranson criteria or the Acute Physiology and Chronic Health Evaluation II (APAChE-II), are

Table 3
Patients' outcomes of the included 78,437 patients with acute pancreatitis treated on an ICU stratified according nutritional status (underweight vs. normal weight or overweight vs. obesity).

Parameters	Hospitalizations of acute pancreatitis patients with ICU admission and …					P-value
	… underweight (n = 257; 0.3 %)	… normal weight or overweight (n = 72,844; 92.9 %)	… obesity class I (n = 2349; 3.0 %)	… obesity class II (n = 1592 2.0 %)	… obesity class III (n = 1652 2.1 %)	
In-hospital death	37 (14.4 %)	9971 (13.7 %)	239 (10.2 %)	198 (12.4 %)	296 (17.9 %)	**<0.001**
MACCE	39 (15.2 %)	10,987 (15.1 %)	268 (11.4 %)	224 (14.1 %)	308 (18.6 %)	**<0.001**
Shock	32 (12.5 %)	6415 (8.9 %)	203 (8.6 %)	186 (11.7 %)	267 (16.2 %)	**<0.001**
Pancreatic surgery	111 (43.2 %)	11,942 (16.5 %)	378 (16.1 %)	260 (16.3 %)	262 (15.9 %)	0.823
Peptic ulcer	11 (4.3 %)	1374 (1.9 %)	32 (1.4 %)	30 (1.9 %)	34 (2.1 %)	0.280
Deep venous thrombosis or thrombophlebitis	24 (9.3 %)	3079 (4.3 %)	107 (4.6 %)	73 (4.6 %)	68 (4.1 %)	0.809
Pulmonary embolism	4 (1.6 %)	726 (1.0 %)	29 (1.2 %)	24 (1.5 %)	30 (1.8 %)	**0.002**
Sepsis	22 (8.6 %)	4211 (5.8 %)	186 (7.9 %)	139 (8.7 %)	158 (9.6 %)	**<0.001**
Pneumonia	45 (17.5 %)	14,183 (19.5 %)	475 (20.2 %)	335 (21.0 %)	372 (22.5 %)	**0.009**
Gastro-intestinal bleeding	15 (5.8 %)	2222 (3.1 %)	49 (2.1 %)	35 (2.2 %)	46 (2.8 %)	**0.009**
Transfusion of blood constituents	122 (47.5 %)	20,489 (28.3 %)	572 (24.4 %)	404 (25.4 %)	479 (29.0 %)	**<0.001**

Table 4
Nutritional status as risk factor for necessity of admission on an intensive care unit in patients with pancreatitis (univariable and multivariable logistic regression models).

	Univariable regression model		Multivariable regression model[a]	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Underweight	0.74 (0.65–0.84)	**<0.001**	0.72 (0.63–0.81)	**<0.001**
Obesity class I	1.46 (1.40–1.52)	**<0.001**	1.29 (1.23–1.35)	**<0.001**
Obesity class II	1.63 (1.55–1.72)	**<0.001**	1.41 (1.33–1.487)	**<0.001**
Obesity class III	2.00 (1.89–2.11)	**<0.001**	1.70 (1.61–1.80)	**<0.001**

[a] Adjusted for age, sex, cancer, heart failure, essential arterial hypertension, chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/1,73 m^2), diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

Table 5
Nutritional status as risk factor for in-hospital death in patients with pancreatitis, who were admitted on an ICU (univariable and multivariable logistic regression models).

	Univariable regression model		Multivariable regression model[a]	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Underweight	1.06 (0.75–1.50)	0.743	1.17 (0.82–1.68)	0.389
Obesity class I	0.71 (0.62–0.81)	**<0.001**	0.73 (0.64–0.84)	**<0.001**
Obesity class II	0.90 (0.77–1.04)	0.157	0.98 (0.84–1.15)	0.817
Obesity class III	1.30 (1.22–1.58)	**<0.001**	1.68 (1.46–1.92)	**<0.001**

[a] Adjusted for age, sex, cancer, heart failure, essential arterial hypertension, chronic renal insufficiency (chronic renal insufficiency stages 3–5 with glomerular filtration rate <60 ml/min/1,73 m^2), diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

complex and therefore not designed for prompt bed-side use in clinical routine [6,20,30]. Regarding laboratory assessment, also several serum biomarkers like hypertriglyceridemia or early hypophosphatemia were already studied for risk factors regarding ICU admission [49,50]. Beyond that, gut microbiota analysis might additionally be helpful for prediction of AP severity [51].

In the risk assessment of different other acute diseases it is well established that patients' baseline parameters and especially patients' comorbidities summed up as patient's comorbidity burden are important for the patients‘ outcome, but receive only little attention and their impact is frequently underestimated [52–55]. In this context, it should not be forgotten that the individual comorbidity burden and nutritional status affects patients' capacities to encounter the strain, stress and occurrence of complications due to AP to avoid organ failure and in-hospital death [43,56,57]. For health care planning in the different health care systems, risk factors for ICU admission of patients with severe AP are of particular interest to monitor patients with severe AP and to optimize the management of these critical ill patients in order to improve their prognosis [58–60]. Approximately 20 % of the patients with AP develop a severe course (according to the RAC) [12,42], which is often accompanied by ICU admission [30,61].

Annual rates of ICU admissions in AP patients varied between 7.6 % and 10.9 % in Germany and was 9.8 % during the whole period of the years 2005–2019. Besides annual variation regarding ICU admission rate, the admission rates of AP patients to an ICU varied also substantially between different countries: While older trials indicate that ICU admission rates ranged higher than in Germany (between 15 % and 25 % of the AP patients) [47,59,62], a newer small retrospective single center analysis from Singapore reported that only 3.1 % of the AP patients required an ICU admission [58]. In the interventional trial from Lee et al., comparing administration of lactated Ringers vs. normal saline in mild AP, ICU admission occurred less frequently with lactated Ringers (9.8 %) compared to normal saline (25.0 %) [43]. Therefore, these differences regarding ICU rates might be explained by varying of admission criteria on

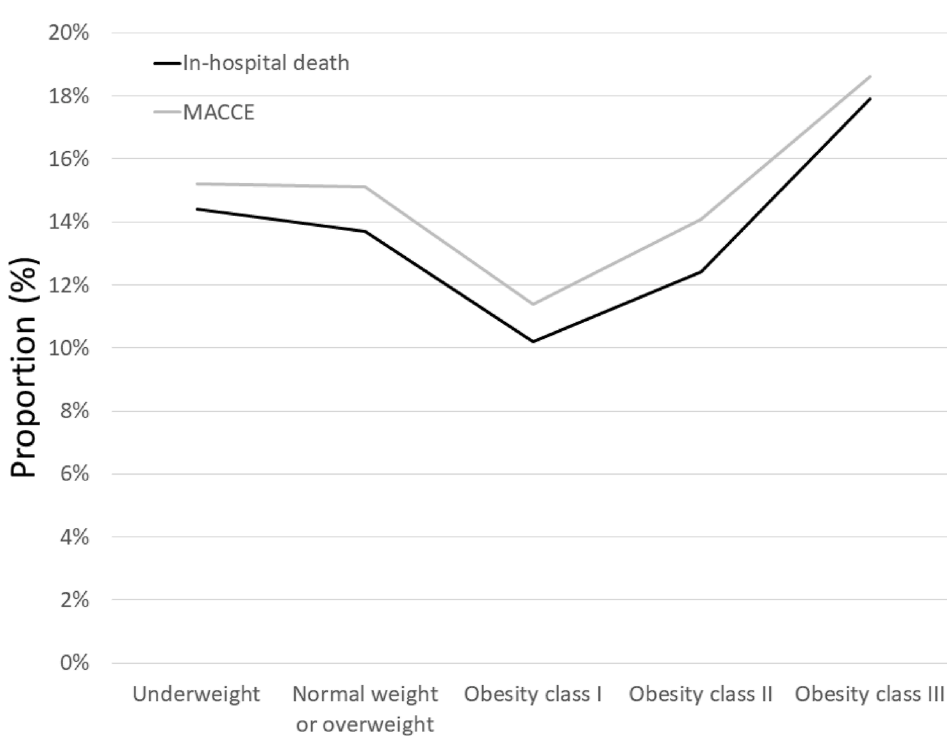

Fig. 3. Case-fatality and MACCE rate stratified according nutritional status (underweight vs. normal weight or overweight vs. obesity).

ICU and also as aforementioned by early treatment differences in the institutions and in the countries [43,47,58,59,62]. In this context, the latest German guidelines recommend a treatment on the ICU especially in presence of the following prognostic parameters: BISAP Score ≥3, APACHE II Score ≥8, Ranson-Score ≥3, haematocrit increase >44 %, blood urea nitrogen >25 mg/dl and sequential organ failure assessment (SOFA)-Score ≥2 [6]. In addition, our study confirmed that the necessity for ICU admission as well as the case-fatality rate of AP patients admitted to an ICU increased substantially with rising age in our study, which is in line with the literature [63–68]. Consequently, older age was already implemented in several risk scores such as BISAP (>60 years), RANSON (>55 years), APACHE II (>45 years) and the Japanese severity score (>70 years) [59,65]. However, age was not an independent risk factor for ICU admission after adjustment for comorbidities in our analysis of the German nationwide inpatient statistics. Pathophysiologically, several reasons like higher prevalence of comorbidities and imbalance of pro- and anti-inflammatory cytokine responses during AP in older patients might contribute to poor prognosis [41,43,56,57,63,66–69]. Besides AP related complications, exacerbation of pre-existing comorbidities might also influence the prognosis of AP substantially [12,58,59]. In this context, our study results demonstrated that cardiovascular diseases and their acute manifestations, but also metabolic deviations such as diabetes mellitus are key risk factors for poor prognosis and consecutively for ICU admission in AP patients in accordance with previously published studies [43,56–58]. While it is well established that diabetes mellitus contributes to higher incidence of AP [42–45], studies demonstrated in accordance with our results that diabetes mellitus negatively influences the outcome of AP in humans [70] confirmed by animal studies [71]. Remarkably, a previously published large meta-analysis reported that approximately 1/4 to 1/2 of the patients diagnosed with AP and diabetes mellitus developed kidney diseases with corresponding raised mortality [70]. In accordance with this meta-analysis, our study results showed that acute kidney injury was associated with 8-fold risk for ICU admission in all investigated AP patients of our study. Regarding cardiovascular diseases it is important that stable coronary artery disease was not an independent risk factor for ICU admission, while AP patients with heart failure, peripheral artery disease and atrial fibrillation/flutter were afflicted with an increased risk to be admitted on ICU. In addition and as expected, the acute atherosclerotic manifestations of myocardial infarction and stroke were strongly related to ICU admission. Early onset of organ dysfunction with especially concomitant cardiac manifestations is associated with poor outcome, which highlights the relevance of avoidance of exacerbations of cardiovascular disease in AP [72]. In accordance with the literature, cardiac arrhythmia contributes also as an important trigger for aggravated outcome and ICU admission [59].

Condensed, our study results indicate that cardiovascular diseases and AP seem to interact with each other. In this context, another population-based study confirmed an association between cardiovascular diseases and AP; especially ischemic heart disease and arterial hypertension were reported to be related to increase the risk of AP [73] and longitudinal studies detected that a history of AP was accompanied with an increased risk of acute atherosclerotic cardiovascular disease and acute coronary syndrome [74]. Among the multiple organ system dysfunctions in severe AP, cardiovascular manifestations are frequently comprising abnormalities of cardiac rhythm, contractility, and vasomotor tone of peripheral vessels [72]. Pathogenic key factors/drivers of cardiac manifestation consist of AP related hypovolemia as well as metabolic disturbances (e.g., hyperkalemia, hypomagnesemia, and hypophosphatemia) resulting in hypotension, tachycardia, and signs of systemic inflammatory response syndrome [72]. Besides the AP related cardiovascular deviations, other organ systems such as the lung, kidneys and the coagulation system are also involved. Thus, it is no surprise that our analysis revealed that shock, sepsis, pneumonia, pulmonary embolism, acute kidney failure, the need of surgical intervention, and bleeding complications requiring transfusion of blood constituents are common in severe AP: These complications are strong and independent risk factors for ICU admission with a more than 10-fold increased risk in AP patients in our study; complications like these are typical indications for optimized management on an ICU setting.

In addition, our study results revealed that nutritional status of the patients is important for patients' risk to be admitted on an ICU, but also for survival of patients with pancreatitis, who had to be admitted to an ICU. In accordance with literature [75], we identified that obese patients are afflicted by an increased necessity to be admitted to an ICU. Importantly, the survival of the patients with pancreatitis on an ICU was significantly affected by the nutritional status of the patients. Although obesity is an established risk factor for the development of several diseases [76–81] and is related to increased incidence of acute pancreatitis and aggravated acute pancreatitis severity [44,75], the survival curve of the patients with acute pancreatitis of our epidemiological study indicated for an obesity paradox of these patients with lowest case fatality and MACCE rates in mild obesity. Several studies published in the past decades underlined that obese patients with cardiovascular diseases [82–85], such as coronary artery disease (CAD) [83,85–87], heart failure (HF) [83,88], pulmonary embolism [89], peripheral artery disease [90] and atrial fibrillation [91], as well as end stage renal disease [92] and chronic obstructive pulmonary disease (COPD) [93] have a better prognosis compared to their leaner counterparts, which is called "obesity paradox" [94]. A possible explanation for the survival benefit of obese patients with pancreatitis is that obesity may protect against malnutrition and energy wastage during acute pancreatic infection. Obesity as a nutritional reserve is exceptionally important in old patients and in those with a high comorbidity burden [95]. Another explanatory approach focuses on the hypothesis that having a normal weight is uncommon in older patients of Western populations and may reflect the presence of serious known or unknown comorbid conditions as compared to their obese counterparts for whom this is not the case [96–98]. Therefore, when following this hypothesis, the protective effects that have been attributed to overweight and moderate obesity may not exist, and the effects of unmeasured confounding factors such as cancer or undiagnosed comorbidities may significantly influence outcomes in normal-weight individuals [89,90,95–98]. Furthermore, it was argued that obesity classification by body mass index (BMI) might not adequately reflect obesity [99–102]. Certainly, BMI is not able to discriminate between an excess in body fat and an increase in lean body mass and thus might not be the most accurate tool for defining obesity [99–101], but studies using body fat measurements are generally in widely accordance with those using BMI in their confirmation of an obesity paradox [86,87,103,104].

Despite the optimized management and progress in treatments in the last decades [62], patients with severe AP who have to be treated on ICU revealed still a 10-fold increased case-fatality in comparison to those AP patients who are not burdened by a severe course and are not admitted to an ICU. In Germany, the in-hospital case fatality of AP patients treated on an ICU was with 13.7 % similar to studies of the United Kingdom (16 %) [105], but distinctly lower than published data of earlier studies of the United States (25 %) [106], Serbia (53.6 %) [107] and Pakistan (82 %) [108].

Since ICU is both a very important cornerstone in the treatment of severe AP and on the same time a critical bottleneck in treatment capacities of the hospitals, early determination of severity and accurate risk stratification for an optimized management and more aggressive treatment approaches in severe AP are continually updated in guidelines and adopted in most clinical practices [6,20,29,30]. Although these advancements resulted in a further decrease of overall mortality rate [19,20], the mortality is still high in severe AP with 21–40 % in the United States and the European Union [109]. Fortunately, our study showed a lower in-hospital case-fatality rate of patients with severe AP admitted to ICU in Germany. Nevertheless, the risk stratification process in severe AP should be rendered more precisely and patients‘ comorbidity burden is an important, but underestimated possibility to specify and predict patients‘ risk for severe AP and (multiple) organ system dysfunctions [17,19,41,56,57,64,72].

5. Limitations

There are several limitations of our present study that should be considered: I) the study results are based on ICD and OPS codes of hospitalized patients, which are prone for under-reporting or under-coding. II) We were only able to provide data for the in-hospital stay, no follow-up data were present and available. III) Patients were not stratified to other important prognosis influencing factors like classification of AP severity, etiology, (persistent) organ failure or (infected) necrosis. IV) Due to the structure of the German nationwide inpatient statistics, we were not able to analyse laboratory markers or ultrasound examinations. V) Finally, we could not distinguish the included patient-cases of our study regarding first admission or recurrent admission of the same patient.

6. Conclusions

Approximately 10 % of the hospitalized AP patients had to be admitted on ICU. Besides AP complications, male sex, obesity, diabetes mellitus, heart failure and atrial fibrillation/flutter were associated with ICU admission. Necessity for ICU admission was afflicted by approximately 10-fold increased case-fatality.

Author contributions

KK, VS and LH designed the study. KK and LH performed the study and analysed the data. VS and KK wrote the manuscript. All authors revised the manuscript and approved the final version of the manuscript.

Ethical aspects and study oversight

Since the present study did not contain direct access by us as the investigators to data of individual patients, but in contrast only to aggregate results provided by the RDC, approval by an ethics committee and informed consent were not required, in compliance with German law.

Data availability statement

All ICD and OPS codes used in this study are publicly available online. The data used in this study are aggregated results provided by the Federal Statistical Office of Germany (Statistisches Bundesamt, DEStatis), which were analysed on patient-level data at the RDC (source: RDC of the Federal Statistical Office and the Statistical Offices of the federal states, DRG Statistics 2005–2019, and own calculations).

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Conflicts of interest

VS, VHS, OH, CL, CB, MM und KK reported no conflicts of interests. LH received lecture/consultant fees from MSD, Boston Scientific, INARI Medical and Johnson&Johnson, outside the submitted work.

References

[1] Ahmed NS, Forbes N, Stukalin I, Singh S, Shaheen AA, Ma C, et al. Population-based trends in healthcare utilization and national healthcare spending on pancreatitis in North America. Gastroenterology 2021;161:1698–1701 e5.
[2] Gapp J, Hall AG, Walters RW, Jahann D, Kassim T, Reddymasu S. Trends and outcomes of hospitalizations related to acute pancreatitis: epidemiology from 2001 to 2014 in the United States. Pancreas 2019;48:548–54.
[3] Roberts SE, Morrison-Rees S, John A, Williams JG, Brown TH, Samuel DG. The incidence and aetiology of acute pancreatitis across Europe. Pancreatology 2017;17:155–65.
[4] Iannuzzi JP, King JA, Leong JH, Quan J, Windsor JW, Tanyingoh D, et al. Global incidence of acute pancreatitis is increasing over time: a systematic review and meta-analysis. Gastroenterology 2022;162:122–34.
[5] Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. Gastroenterology 2019;156:254–272 e11.
[6] Beyer G, Hoffmeister A, Michl P, Gress TM, Huber W, Algul H, et al., Collaborators. Z Gastroenterol 2022;60:419–521 [Not Available].
[7] Phillip V, Huber W, Hagemes F, Lorenz S, Matheis U, Preinfalk S, et al. Incidence of acute pancreatitis does not increase during oktoberfest, but is higher than previously described in Germany. Clin Gastroenterol Hepatol 2011;9:995–1000 e3.
[8] Lankisch PG, Weber-Dany B, Hebel K, Maisonneuve P, Lowenfels AB. The harmless acute pancreatitis score: a clinical algorithm for rapid initial stratification of nonsevere disease. Clin Gastroenterol Hepatol 2009;7: 702–5. quiz 607.
[9] Ye X, Lu G, Huai J, Ding J. Impact of smoking on the risk of pancreatitis: a systematic review and meta-analysis. PLoS One 2015;10:e0124075.
[10] Sun X, Huang X, Zhao R, Chen B, Xie Q. Meta-analysis: tobacco smoking may enhance the risk of acute pancreatitis. Pancreatology 2015;15:286–94.
[11] Yuhara H, Ogawa M, Kawaguchi Y, Igarashi M, Mine T. Smoking and risk for acute pancreatitis: a systematic review and meta-analysis. Pancreas 2014;43:1201–7.
[12] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[13] Dellinger EP, Forsmark CE, Layer P, Levy P, Maravi-Poma E, Petrov MS, et al., Pancreatitis Across Nations Clinical R and Education A. Determinant-based classification of acute pancreatitis severity: an international multidisciplinary consultation. Ann Surg 2012;256:875–80.
[14] Sternby H, Bolado F, Canaval-Zuleta HJ, Marra-Lopez C, Hernando-Alonso AI, Del-Val-Antonana A, et al. Determinants of severity in acute pancreatitis: a nation-wide multicenter prospective cohort study. Ann Surg 2019;270: 348–55.
[15] Leppaniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg 2019;14:27. 2019.
[16] Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, American Gastroenterological Association Institute Clinical Guidelines C. American gastroenterological association institute guideline on initial management of acute pancreatitis. Gastroenterology 2018;154:1096–101.
[17] Werge M, Novovic S, Schmidt PN, Gluud LL. Infection increases mortality in necrotizing pancreatitis: a systematic review and meta-analysis. Pancreatology 2016;16:698–707.
[18] Working party of the British society of G, Association of Surgeons of Great B, Ireland, Pancreatic Society of Great B, Ireland, Association of Upper GISoGB and Ireland. UK guidelines for the management of acute pancreatitis. Gut 2005;54(Suppl 3):iii1–9.
[19] Forsmark CE, Vege SS, Wilcox CM. Acute pancreatitis. N Engl J Med 2016;375:1972–81.
[20] Metri A, Bush N, Singh VK. Predicting the severity of acute pancreatitis: current approaches and future directions. Surg Open Sci 2024;19:109–17.
[21] Keller K, Sivanathan V, Farmakis IT, Schmitt VH, Espinola-Klein C, Schmidt FP, et al. Incidence and impact of venous thromboembolism in hospitalized patients with acute pancreatitis. Dig Liver Dis 2024;56(12):2085–94.
[22] Sun HW, Dai SJ, Kong HR, Fan JX, Yang FY, Dai JQ, et al. Accurate prediction of acute pancreatitis severity based on genome-wide cell free DNA methylation profiles. Clin Epigenet 2021;13:223.

[23] Beyer G, Hoffmeister A, Lorenz P, Lynen P, Lerch MM, Mayerle J. Clinical practice guideline-acute and chronic pancreatitis. Dtsch Arztebl Int 2022;119:495–501.
[24] Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, et al. Acute pancreatitis. Lancet 2020;396:726–34.
[25] Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut 2008;57:1698–703.
[26] Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991;100:1619–36.
[27] Knudsen JS, Heide-Jorgensen U, Mortensen FV, Sorensen HT, Ehrenstein V. Acute pancreatitis: 31-year trends in incidence and mortality - a Danish population-based cohort study. Pancreatology 2020;20:1332–9.
[28] Gurusamy KS, Debray TPA, Rompianesi G. Prognostic models for predicting the severity and mortality in people with acute pancreatitis. Cochrane Database Syst Rev 2018:1–15.
[29] 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;119:419–37.
[30] Garg PK, Singh VP. Organ failure due to systemic injury in acute pancreatitis. Gastroenterology 2019;156:2008–23.
[31] Keller K, Farmakis IT, Valerio L, Koelmel S, Wild J, Barco S, et al. Predisposing factors for admission to intensive care units of patients with COVID-19 infection—Results of the German nationwide inpatient sample. Front Public Health 2023;11:1113793. 1-12.
[32] Keller K, Sagoschen I, Schmitt VH, Sivanathan V, Espinola-Klein C, Lavie CJ, et al. Obesity and its impact on adverse In-Hospital outcomes in hospitalized patients with COVID-19. Front Endocrinol 2022;13:876028.
[33] Keller K, Hobohm L, Ebner M, Kresoja KP, Munzel T, Konstantinides SV, et al. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. Eur Heart J 2020;41:522–9.
[34] (WHO) WHO. Obesity and overweight. 2021. p. 2023.
[35] Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al., Group ESCSD. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2019.
[36] Perkins GD, Handley AJ, Koster RW, Castren M, Smyth MA, Olasveengen T, et al. Adult basic life s and automated external defibrillation section C. European Resuscitation Council Guidelines for Resuscitation 2015: section 2. Adult basic life support and automated external defibrillation. Resuscitation 2015;95:81–99.
[37] Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al., Group ESCSD. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J 2023;44:3720–826.
[38] Keller K, Hobohm L, Ostad MA, Gobel S, Lankeit M, Konstantinides S, et al. Temporal trends and predictors of inhospital death in patients hospitalised for heart failure in Germany. Eur J Prev Cardiol 2021;28:990–7.
[39] Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:175–84.
[40] Devani K, Charilaou P, Radadiya D, Brahmbhatt B, Young M, Reddy C. Acute pancreatitis: trends in outcomes and the role of acute kidney injury in mortality- A propensity-matched analysis. Pancreatology 2018;18:870–7.
[41] Loosen SH, Essing T, Jordens M, Koch A, Tacke F, Knoefel WT, et al. Current epidemiological trends and in-hospital mortality of acute pancreatitis in Germany: a systematic analysis of standardized hospital discharge data between 2008 and 2017. Z Gastroenterol 2022;60:310–9.
[42] Trikudanathan G, Yazici C, Evans Phillips A, Forsmark CE. Diagnosis and management of Acute pancreatitis. Gastroenterology 2024 Dec;56(12):2085–209.
[43] Lee PJ, Papachristou GI. New insights into acute pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:479–96.
[44] Khatua B, El-Kurdi B, Singh VP. Obesity and pancreatitis. Curr Opin Gastroenterol 2017;33:374–82.
[45] Camilleri M, Malhi H, Acosta A. Gastrointestinal complications of obesity. Gastroenterology 2017;152:1656–70.
[46] Schienkiewitz A, Kuhnert R, Blume M, Mensink G. Übergewicht und Adipositas bei Erwachsenen in Deutschland – Ergebnisse der Studie GEDA 2019/2020-EHIS. J Health Monit 2022;7:23–31.
[47] Crosignani A, Spina S, Marrazzo F, Cimbanassi S, Malbrain M, Van Regenmortel N, et al. Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review. Ann Intensive Care 2022;12:98.
[48] Ali H, Moond V, Vikash F, Dahiya DS, Gangwani MK, Sohail AH, et al. Risk score to predict inpatient mortality of acute pancreatitis patients admitted to the intensive care unit. Pancreatology 2024;24:1213–8.
[49] Stewart CF, Adeniran EA, Yadav D, Gorelick FS, Liddle RA, Wu B, et al. Early hypophosphatemia as a prognostic marker in acute pancreatitis. Pancreas 2024;53:e611–6.
[50] Wen S, Zhang Y, Zhao G, Tu Z, Zhang K, Cui Y. Association of admission serum triglyceride levels with intensive care unit hospitalization rates in acute pancreatitis patients: a retrospective study. Medicine (Baltim) 2024;103:e38265.
[51] Ammer-Herrmenau C, Antweiler KL, Asendorf T, Beyer G, Buchholz SM, Cameron S, et al. Gut microbiota predicts severity and reveals novel metabolic signatures in acute pancreatitis. Gut 2024;73:485–95.
[52] Keller K, Schmitt VH, Hahad O, Espinola-Klein C, Munzel T, Lurz P, et al. Categorization of patients with pulmonary embolism by charlson comorbidity index. Am J Med 2024 Aug;137(8):727–35.
[53] Hobohm L, Sagoschen I, Barco S, Schmidtmann I, Espinola-Klein C, Konstantinides S, et al. Trends and risk factors of In-Hospital mortality of patients with COVID-19 in Germany: results of a large nationwide inpatient sample. Viruses 2022;14.
[54] Keller K, Schmitt VH, Sagoschen I, Munzel T, Espinola-Klein C, Hobohm L. CRB-65 for risk stratification and prediction of prognosis in pulmonary embolism. J Clin Med 2023;12.
[55] Keller K, Wollner J, Schmitt VH, Ostad MA, Sagoschen I, Munzel T, et al. Risk factors for pulmonary embolism in patients with paralysis and deep venous thrombosis. J Clin Med 2021;10.
[56] Murata A, Matsuda S, Mayumi T, Yokoe M, Kuwabara K, Ichimiya Y, et al. Effect of hospital volume on clinical outcome in patients with acute pancreatitis, based on a national administrative database. Pancreas 2011;40:1018–23.
[57] Singla A, Simons J, Li Y, Csikesz NG, Ng SC, Tseng JF, et al. Admission volume determines outcome for patients with acute pancreatitis. Gastroenterology 2009;137:1995–2001.
[58] Teng TZJ, Tan JKT, Baey S, Gunasekaran SK, Junnarkar SP, Low JK, et al. Sequential organ failure assessment score is superior to other prognostic indices in acute pancreatitis. World J Crit Care Med 2021;10:355–68.
[59] Ali H, Inayat F, Dhillon R, Patel P, Afzal A, Wilkinson C, et al. Predicting the risk of early intensive care unit admission for patients hospitalized with acute pancreatitis using supervised machine learning. Proc (Bayl Univ Med Cent) 2024;37:437–47.
[60] Zhu J, Wu L, Wang Y, Fang M, Liu Q, Zhang X. Predictive value of the Ranson and BISAP scoring systems for the severity and prognosis of acute pancreatitis: a systematic review and meta-analysis. PLoS One 2024;19:e0302046.
[61] de-Madaria E, Buxbaum JL. Advances in the management of acute pancreatitis. Nat Rev Gastroenterol Hepatol 2023;20:691–2.
[62] Neoptolemos JP, Raraty M, Finch M, Sutton R. Acute pancreatitis: the substantial human and financial costs. Gut 1998;42:886–91.
[63] Yu L, Zhou X, Li Y, Liu M. Establishment and evaluation of early in-hospital death prediction model for patients with acute pancreatitis in intensive care unitc. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2023;35:865–9.
[64] Yasuda H, Horibe M, Sanui M, Sasaki M, Suzuki N, Sawano H, et al. Etiology and mortality in severe acute pancreatitis: a multicenter study in Japan. Pancreatology 2020;20:307–17.
[65] Marta K, Lazarescu AM, Farkas N, Matrai P, Cazacu I, Ottoffy M, et al. Aging and comorbidities in acute pancreatitis I: a meta-analysis and systematic review based on 194,702 patients. Front Physiol 2019;10:328.
[66] Fan ST, Choi TK, Lai CS, Wong J. Influence of age on the mortality from acute pancreatitis. Br J Surg 1988;75:463–6.
[67] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245–51.
[68] Patel K, Li F, Luthra A, Hinton A, Lara L, Groce R, et al. Acute biliary pancreatitis is associated with adverse outcomes in the elderly: a propensity score-matched analysis. J Clin Gastroenterol 2019;53:e291–7.
[69] Szakacs Z, Gede N, Pecsi D, Izbeki F, Papp M, Kovacs G, et al. Aging and comorbidities in acute pancreatitis II.: a cohort-analysis of 1203 prospectively collected cases. Front Physiol 2018;9:1776.
[70] Miko A, Farkas N, Garami A, Szabo I, Vincze A, Veres G, et al. Preexisting diabetes elevates risk of local and systemic complications in acute pancreatitis: systematic review and meta-analysis. Pancreas 2018;47:917–23.
[71] Zechner D, Spitzner M, Bobrowski A, Knapp N, Kuhla A, Vollmar B. Diabetes aggravates acute pancreatitis and inhibits pancreas regeneration in mice. Diabetologia 2012;55:1526–34.
[72] Yegneswaran B, Kostis JB, Pitchumoni CS. Cardiovascular manifestations of acute pancreatitis. J Crit Care 2011;26:225 e11–8.
[73] Bexelius TS, Ljung R, Mattsson F, Lagergren J. Cardiovascular disease and risk of acute pancreatitis in a population-based study. Pancreas 2013;42:1011–5.
[74] Chen B, Moin A, Virk HUH, Jneid H, Virani SS, Krittanawong C. Association of cardiovascular disease and pancreatitis: what came first, the chicken or the egg? J Clin Med 2023;12.
[75] Krishna SG, Hinton A, Oza V, Hart PA, Swei E, El-Dika S, et al. Morbid obesity is associated with adverse clinical outcomes in acute pancreatitis: a propensity-matched study. Am J Gastroenterol 2015;110:1608–19.
[76] Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366:1640–9.
[77] Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics–2010 update: a report from the American heart association. Circulation 2010;121:e46–215.
[78] Suk SH, Sacco RL, Boden-Albala B, Cheun JF, Pittman JG, Elkind MS, et al. Abdominal obesity and risk of ischemic stroke: the Northern Manhattan stroke study. Stroke; a journal of cerebral circulation 2003;34:1586–92.
[79] Stein PD, Beemath A, Olson RE. Obesity as a risk factor in venous thromboembolism. Am J Med 2005;118:978–80.
[80] Yang G, De Staercke C, Hooper WC. The effects of obesity on venous thromboembolism: a review. Open J Prev Med 2012;2:499–509.
[81] Borch KH, Braekkan SK, Mathiesen EB, Njolstad I, Wilsgaard T, Stormer J, et al. Abdominal obesity is essential for the risk of venous thromboembolism in the

metabolic syndrome: the Tromso study. J Thromb Haemostasis : JTH 2009;7: 739–45.

[82] Wang S, Ren J. Obesity paradox in aging: from prevalence to pathophysiology. Prog Cardiovasc Dis 2018;61:182–9.

[83] Lavie C, Laddu D, Arena R, Ortega FB, Alpert MA, Kushner RF. Healthy weight and obesity prevention. J Am Coll Cardiol 2018;72:1506–31.

[84] Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, et al. An overview and update on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis 2018;61:142–50.

[85] Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009;53: 1925–32.

[86] Lavie CJ, De Schutter A, Patel D, Artham SM, Milani RV. Body composition and coronary heart disease mortality–an obesity or a lean paradox? Mayo Clin Proc 2011;86:857–64.

[87] Lavie CJ, De Schutter A, Patel DA, Romero-Corral A, Artham SM, Milani RV. Body composition and survival in stable coronary heart disease: impact of lean mass index and body fat in the "obesity paradox". J Am Coll Cardiol 2012;60:1374–80.

[88] Horwich TB, Fonarow GC, Clark AL. Obesity and the obesity paradox in heart failure. Prog Cardiovasc Dis 2018;61:151–6.

[89] Keller K, Hobohm L, Munzel T, Ostad MA, Espinola-Klein C, Lavie CJ, et al. Survival benefit of Obese patients with pulmonary embolism. Mayo Clin Proc 2019;94:1960–73.

[90] Keller K, Hobohm L, Geyer M, Munzel T, Lavie CJ, Ostad MA, et al. Obesity paradox in peripheral artery disease. Clin Nutr 2019;38:2269–76.

[91] Lavie CJ, Pandey A, Lau DH, Alpert MA, Sanders P. Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis: effects of weight loss and exercise. J Am Coll Cardiol 2017;70:2022–35.

[92] Naderi N, Kleine CE, Park C, Hsiung JT, Soohoo M, Tantisattamo E, et al. Obesity paradox in advanced kidney disease: from bedside to the bench. Prog Cardiovasc Dis 2018;61:168–81.

[93] Chittal P, Babu AS, Lavie CJ. Obesity paradox: does fat alter outcomes in chronic obstructive pulmonary disease? COPD J Chronic Obstr Pulm Dis 2015;12:14–8.

[94] Lavie CJ, McAuley PA, Church TS, Milani RV, Blair SN. Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. J Am Coll Cardiol 2014;63:1345–54.

[95] Bucholz EM, Beckman AL, Krumholz HA, Krumholz HM, Dr. Bucholz was affiliated with the Yale School of M and Yale School of Public Health during the time that the work was c. Excess weight and life expectancy after acute myocardial infarction: the obesity paradox reexamined. Am Heart J 2016;172:173–81.

[96] Das SR, Alexander KP, Chen AY, Powell-Wiley TM, Diercks DB, Peterson ED, et al. Impact of body weight and extreme obesity on the presentation, treatment, and in-hospital outcomes of 50,149 patients with ST-Segment elevation myocardial infarction results from the NCDR (National Cardiovascular Data Registry). J Am Coll Cardiol 2011;58:2642–50.

[97] McAuley PA, Beavers KM. Contribution of cardiorespiratory fitness to the obesity paradox. Prog Cardiovasc Dis 2014;56:434–40.

[98] Keller K, Munzel T, Ostad MA. Gender-specific differences in mortality and obesity paradox of patients with myocardial infarction aged 70 years and older. Nutrition 2018 Feb;46:124–30.

[99] De Schutter A, Lavie CJ, Milani RV. The impact of obesity on risk factors and prevalence and prognosis of coronary heart disease-the obesity paradox. Prog Cardiovasc Dis 2014;56:401–8.

[100] Romero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006;368:666–78.

[101] Uretsky S, Messerli FH, Bangalore S, Champion A, Cooper-Dehoff RM, Zhou Q, et al. Obesity paradox in patients with hypertension and coronary artery disease. Am J Med 2007;120:863–70.

[102] Lavie CJ, De Schutter A, Milani RV. Body composition and the obesity paradox in coronary heart disease: can heavier really be healthier? Heart 2015;101:1610–1.

[103] Lavie CJ, Milani RV, Artham SM, Patel DA, Ventura HO. The obesity paradox, weight loss, and coronary disease. Am J Med 2009;122:1106–14.

[104] De Schutter A, Lavie CJ, Kachur S, Patel DA, Milani RV. Body composition and mortality in a large cohort with preserved ejection fraction: untangling the obesity paradox. Mayo Clin Proc 2014;89:1072–9.

[105] Pavlidis P, Crichton S, Lemmich Smith J, Morrison D, Atkinson S, Wyncoll D, et al. Improved outcome of severe acute pancreatitis in the intensive care unit. Crit Care Res Pract 2013;2013:897107.

[106] Soran A, Chelluri L, Lee KK, Tisherman SA. Outcome and quality of life of patients with acute pancreatitis requiring intensive care. J Surg Res 2000;91:89–94.

[107] Bumbasirevic V, Radenkovic D, Jankovic Z, Karamarkovic A, Jovanovic B, Milic N, et al. Severe acute pancreatitis: overall and early versus late mortality in intensive care units. Pancreas 2009;38:122–5.

[108] Shafiq F, Khan MF, Asghar MA, Shamim F, Sohaib M. Outcome of patients with acute pancreatitis requiring intensive care admission: a retrospective study from a tertiary care center of Pakistan. Pak J Med Sci 2018;34:1082–7.

[109] Sarri G, Guo Y, Iheanacho I, Puelles J. Moderately severe and severe acute pancreatitis : a systematic review of the outcomes in the USA and European Union-5. BMJ Open Gastroenterol 2019;6:e000248.