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ORIGINAL ARTICLE

Extra-pancreatic complications, especially hemodialysis predict mortality and length of stay, in ICU patients admitted with acute pancreatitis

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Abstract

Background and aims: Patients in the intensive care unit (ICU) with acute pancreatitis (AP) are at risk for extra-pancreatic complications given their severe illness and prolonged length of stay. We sought to determine the rate of extra-pancreatic complications and its effect on length of stay (LOS) and mortality in ICU patients with AP.
Methods: We performed a retrospective cohort study of ICU patients admitted to a tertiary-care center with a diagnosis of AP. A total of 287 ICU patients had a discharge diagnosis of AP, of which 163 met inclusion criteria. We calculated incidence rates of extra-pancreatic complications and performed a univariate and multi-variable analysis to determine predictors of LOS and mortality.
Results: There were a total of 158 extra-pancreatic complications (0.97 extra-pancreatic complications per patient). Ninety-five patients had at least one extra-pancreatic complication, whereas 68 patients had no extra-pancreatic complications. Patients with extra-pancreatic complications had a significantly longer LOS (14.7 vs 8.8 days, $p < 0.01$) when controlling for local pancreatic complications. Patients with non-infectious extra-pancreatic complications had a higher rate of mortality (24.0% vs 16.2%, $p = 0.04$). Patients requiring dialysis was an independent predictor for LOS and mortality (incidence risk ratio [IRR] 1.73, 95% confidence interval [CI]: 1.263–2.378 and IRR 1.50, 95% CI 1.623–6.843, $p < 0.01$) on multi-variable analysis. Coronary events were also a predictor for mortality ($p = 0.05$). Other extra-pancreatic complications were not significant.
Conclusions: Extra-pancreatic complications occur frequently in ICU patients with AP and impact LOS. Patients with non-infectious extra-pancreatic complications have a higher mortality rate. After controlling for local pancreatic complications, patients requiring dialysis remained an independent predictor for LOS and mortality.

Key words: Severe acute pancreatitis; extra-pancreatic complications; intensive care unit; length of stay; in-hospital mortality; infections

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INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory condition presenting with severe, persistent epigastric pain with nausea and vomiting [1]. It is the leading discharge diagnosis of all gastrointestinal disorders [2]. The majority of patients with AP have a mild, self-limiting course without organ failure or pancreatic complications (i.e. necrosis or fluid collections). However, approximately 15–25% of patients have severe AP requiring close monitoring in the intensive care unit (ICU), given its relatively high morbidity and mortality [3, 4]. The mortality from severe AP is approximately 30%, but may be as high as 47% in patients with persistent multi-organ system dysfunction and/or infected necrosis [5–8]. Additionally, the presence of extra-pancreatic complications contributes to morbidity and mortality [9, 10].

Broadly, extra-pancreatic complications can be divided into infectious events and non-infectious events. Infectious extra-pancreatic complications have been previously reported in patients hospitalized with AP but not specifically in patients admitted to ICUs [9, 10]. Moreover, non-infectious extra-pancreatic complications have not been explored in this population.

A systematic review reported the incidence of infectious extra-pancreatic complications as 32% [9]. Further, in 2008, one population-based study explored the impact of hospital-acquired infections on outcomes for all patients diagnosed with AP. The authors found a significantly longer length of stay (LOS) and high mortality in patients with hospital-acquired infections [10]. Several studies have documented the impact of non-infectious complications on LOS, hospital costs and mortality in hospitalized patients of other similarly morbid conditions [11–15].

Patients admitted to the ICU with AP are particularly at risk for extra-pancreatic complications given their severe illness and extended LOS. However, little is known about the impact of infectious and non-infectious extra-pancreatic complications in patients with AP admitted to the ICU. Hence, we conducted a review of all patients admitted to the ICU for AP that aimed to determine the rate of extra-pancreatic complications and their effect on LOS and mortality. Additionally, we sought to determine independent predictors for LOS and mortality.

PATIENTS AND METHODS

Study population and study design

We performed a retrospective review of patients with a discharge diagnosis of AP (ICD-9 code: 577.1) who were admitted to the ICU at Beth Israel Deaconess Medical Center in Boston, Massachusetts, between 1 January 2008 and 1 October 2015. AP was diagnosed in patients who presented with at least two of the three following findings: (i) classic abdominal pain, (ii) lipase greater than three times the upper limit of normal and (iii) imaging findings suggestive of AP [16]. Diagnosis of AP in intubated or non-verbal patients was made using the latter two criteria. Patients who did not meet these criteria were excluded. Additional exclusion criteria included patients with a history of chronic pancreatitis, previous pancreatic surgery, concurrent pancreatic, biliary, duodenal or ampulla carcinoma, patients with a prior history of severe or necrotizing pancreatitis and patients admitted to an outside hospital for greater than 2 days. Lastly, patients who developed AP while admitted to the hospital for another reason were excluded.

Patients were admitted to the ICU if they met criteria for severe AP (i.e. end-organ failure and/or local pancreatic complications) or if they required vasopressor support, respiratory support by invasive and non-invasive mechanical ventilation, insulin drips for diabetic ketoacidosis, frequent medication administration (i.e. for alcohol withdrawal), airway monitoring for altered consciousness or close monitoring as deemed necessary by the admitting clinician. While admitted to the ICU, patients received standard institutional-based care, including stress-ulcer prophylaxis, deep-venous thrombosis prophylaxis and, when needed, urinary catheter and venous catheter care. Local pancreatic complications were defined as sterile intra-abdominal collections (i.e. necrosis or fluid collections) or infectious collections (i.e. abscesses).

Data collection and extra-pancreatic complications

Institutional-board review approval was obtained prior to initiating the study in compliance with institutional ethical standards. Demographic, laboratory, microbiologic, radiographic (i.e. number of imaging tests), procedural (i.e. dialysis, intubation and endoscopy) and LOS data were collected. Additionally, in-hospital death and presence of local pancreatic complication were recorded. A bedside index for severity in acute pancreatitis (BISAP) score and Charlson comorbidity index (CCI) was calculated for patients from admission data [17, 18]. The BISAP score was calculated using the blood urea nitrogen, mental status, presence of systemic inflammatory response syndrome, age greater than 60 and presence of pleural effusions on admission. The CCI was calculated retrospectively by reviewing the patient's medical history as noted on the admission note. Presence of infectious and non-infectious extra-pancreatic complications was noted. Definitions of extra-pancreatic complications are summarized in Table 1.

Main outcomes and statistical analysis

Our primary outcome was in-hospital mortality and our secondary outcomes were total and ICU LOS. Qualitative data are expressed as absolute numbers and percentages, and quantitative data are expressed as median and range. We compared total hospital and ICU LOS, and mortality between the groups for statistical significance using *t*-test of proportions. We then repeated analysis to control for local pancreatic complications. We hypothesized that patients with in-hospital extra-pancreatic complications would have a higher mortality rate, which, based on one prior study, was 17%. To detect a difference in 17%, assuming an error of 5%, we calculated our sample size to be 168. Univariate analysis of patients without local pancreatic complications for LOS and mortality was completed using a *t*-test of proportions. Furthermore, multi-variable analysis of the significant findings from univariate analysis was done using a negative binomial model for LOS and using logistical regression for mortality. Lastly, we completed a Fisher T-test to determine whether there was a significant association between BISAP scores, CCI scores and the number of extra-pancreatic complications.

RESULTS

Study population and patient characteristics

Two hundred eighty-seven ICU patients were identified with a discharge diagnosis of AP during the study period, of which 163 met inclusion criteria for this study (Figure 1). The majority of patients were male (98/163, 60.1%) and Caucasian (116/163, 71.7%) with a mean age of 58 years. The most common etiology

Table 1. Definitions of extra-pancreatic complications

Event	Definition
Ventilator-associated pneumonia	Positive culture data from a respiratory sample collected from an endotracheal tube
Hospital-acquired pneumonia	Positive culture data from an expectorated or induced respiratory sample collected in a patient hospitalized for greater than 48 h
Aspiration pneumonia	Positive culture data from a respiratory sample after a documented aspiration event in a patient hospitalized for greater than 48 h
Catheter-associated urinary-tract infection	Positive urinary culture data in patient with an indwelling urinary catheter or in patient with a recent history of an indwelling urinary catheter (i.e. within 48 h)
Central or peripheral line-associated blood-stream infection	Positive blood culture data in patient with a peripheral or central blood (arterial or venous) catheter or a recent history of a peripheral or central blood catheter (i.e. within 48 h) in greater than one culture bottle
Non-line-associated blood-stream infection	Positive blood culture data in greater than one culture bottle in a patient hospitalized for greater than 48 h
Clostridium difficile-associated diarrhea	Toxin assay or PCR-positive stool assay for *Clostridium difficile* in a patient hospitalized for at least 48 h
Cardiac arrest	Loss of pulse either resulting in death or requiring cardiopulmonary resuscitation in patient hospitalized for at least 48 h
Fall with injury	A fall resulting in bodily harm (i.e. fracture) in patient hospitalized for at least 48 h
Gastrointestinal bleed	Gastrointestinal bleeding in any part of the gastrointestinal tract during ICU stay, with endoscopic evidence or based on clinical note in discharge summary
Acute coronary syndrome	An ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction documented by cardiology consultation note
Initiation of hemodialysis	Patient with a new requirement for renal replacement therapy while admitted
Delirium	Acute confusional state marked by gross inattentiveness and waxing and waning changes in mental status in the absence of an underlying primary central nervous event

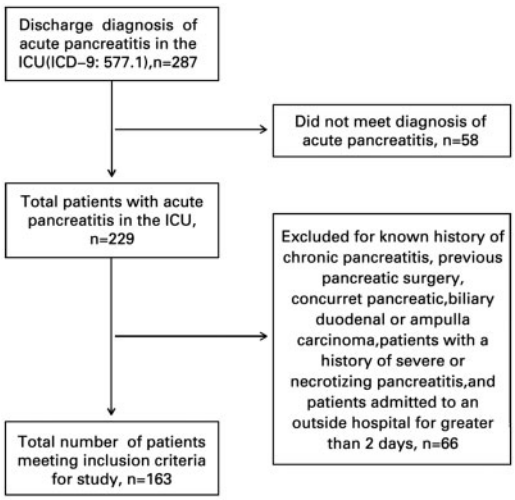

Figure 1. Patient-eligibility flowchart.

was gallstone-related disease (57/163, 35.0%). Patient characteristics are outlined in Table 2.

Extra-pancreatic complications

One hundred fifty-eight extra-pancreatic complications (0.97 events/patient) occurred during the study period. Ninety-five patients (58.3%, 95/163) had at least one extra-pancreatic complication, whereas 68 patients (41.7%, 68/163) had no any extra-pancreatic complications. There were an equal number of infectious and non-infectious complications (79 events each). The most common infectious extra-pancreatic complications in this cohort were catheter-associated urinary-tract infection and hospital-acquired pneumonia (both 17/79, 21.5%). Together, respiratory infections (hospital-acquired pneumonia, ventilator-associated pneumonia and aspiration pneumonia) composed the largest component of the infectious extra-pancreatic complications (34/79, 43.0%). Delirium was the most common non-infectious extra-pancreatic complication in the ICU (32/79, 40.5%). Figure 2 illustrates the distribution of extra-pancreatic complications.

Patients with extra-pancreatic complications had significantly longer ICU and total LOS than those without extra-pancreatic complications (9.8 vs 4.1 days, $p < 0.01$ and 18.0 vs 12.0 days, $p < 0.01$, respectively). The overall mortality rate was 11.7% (19/163). There was no significant difference in mortality between those with extra-pancreatic complications and those without extra-pancreatic complications (14.8% vs 7.4%, $p = 0.15$). Moreover, there was significantly more imaging performed ($p < 0.01$) in patients with extra-pancreatic complications. There were no statistically significant differences in age, gender, CCI, BISAP, etiology of AP or other admission laboratory values between the two groups (Table 2).

Patients with local pancreatic complications

There were 60 patients with local pancreatic complications in the study period (36.8%, 60/163). Patients with local pancreatic complications had longer total LOS than those without local pancreatic complications (21.3 vs 12.1 days, $p < 0.01$) as well as longer ICU LOS (11.1 vs 5.2 days, $p < 0.01$). There were no differences in mortality ($p = 0.13$) or number of events ($p = 0.89$); however, there were more imaging studies in the patients with pancreatic complications ($p < 0.01$; Table 3).

After excluding patients with local pancreatic complications, 57 of the 103 patients had a total of 99 extra-pancreatic complications (1.73 events/patient), of which 56 were infectious extra-pancreatic complications and 43 were non-infectious extra-pancreatic complications. Patients with extra-pancreatic complications had longer total and ICU LOS (14.7 vs 8.8 days, $p < 0.01$ and 7.1 vs 2.9 days,

Table 2. Patient characteristics

Patient characteristic	No extra-pancreatic complications ($n = 68$)	At least one extra-pancreatic complication ($n = 95$)	p-value
Mean age (SD)	58.0 (16.3)	57.9 (18.5)	0.98
Male gender, *n* (%)	38 (55.8)	60 (63.1)	0.35
Prior history of acute pancreatitis, *n* (%)	19 (27.9)	22 (23.2)	0.49
History of congestive heart failure, *n* (%)	7 (10.3)	11 (11.6)	0.80
History of myocardial infarction, *n* (%)	7 (10.3)	10 (10.5)	0.96
History of chronic kidney disease, *n* (%)	6 (8.8)	10 (10.5)	0.72
Diabetes with end-organ damage, *n* (%)	3 (4.4)	5 (5.3)	0.92
Mild liver disease, *n* (%)	7 (10.3)	8 (8.4)	0.29
Moderate to severe liver disease, *n* (%)	1 (1.5)	4 (4.2)	0.32
Mean CCI (SD)	1.28 (1.40)	1.41 (1.69)	0.60
Mean age-adjusted CCI (SD)	2.78 (2.38)	2.96 (2.65)	0.66
Mean BISAP (SD)	1.97 (1.17)	2.10 (1.21)	0.51
Presence of local pancreatic complication (fluid collection or necrosis), *n* (%)	22 (32.4)	38 (40.0)	0.32
Mean ICU length of stay (SD)	4.1 (5.7)	9.8 (15.2)	**<0.01**
Mean total length of stay (SD)	12.0 (9.4)	18.0 (14.7)	**<0.01**
Mean admission blood urea nitrogen (mg/dL)	23.7	29.9	0.08
Mean admission white blood cell count (1000/μL)	15.2	13.6	0.12
Mean admission lipase (IU/L)	2108	1583	0.33
Mean admission hematocrit (%)	38.5	37.4	0.40
Mean admission lactate (mmol/L)	2.3	2.7	0.36
Mean admission albumin (g/dL)	3.6	3.3	0.06
Medical ICU admission, *n* (%)	65 (95.6)	62 (65.3)	0.48
Mortality rate, *n* (%)	5 (7.4)	14 (14.7)	0.15
Mean number of images	6.06	13.36	**<0.01**

SD, standard deviation; CCI, Charlson comorbidity index; BISAP, bedside index of severity in acute pancreatitis; ICU, intensive care unit.

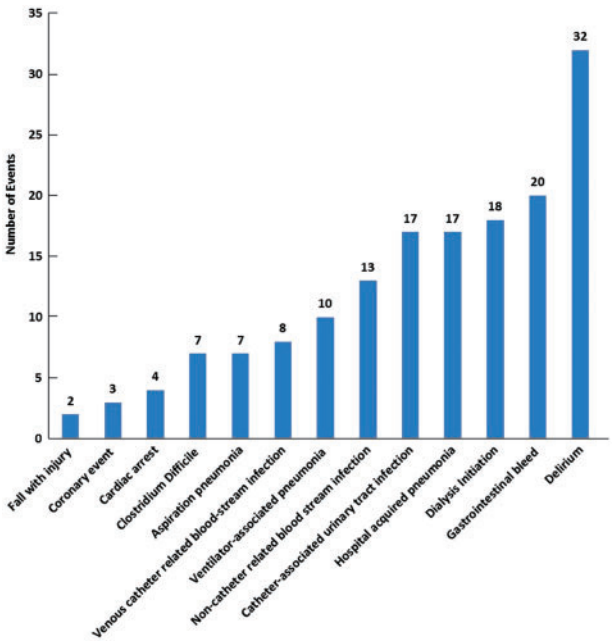

Figure 2. Histogram of extra-pancreatic complications.

$p = 0.03$). The mortality rate in this group was 8.7% (9/103) and there was no difference in mortality rates between those with extra-pancreatic complications and without extra-pancreatic complications (12.3% vs 4.3%, $p = 0.16$). Lastly, there were significantly more imaging studies in patients with extra-pancreatic complications than without (10.9 vs 4.80 images/patient, $p = 0.03$).

Univariate analysis

Patients with infectious extra-pancreatic complications had longer total LOS (14.6 vs 10.6 days, $p = 0.05$). Specifically, patients with hospital-acquired pneumonia had a significantly longer total LOS (23.1 vs 14.6 days, $p = 0.01$). Further, patients with non-venous catheter-related blood-stream infections had significantly longer ICU LOS (11.3 vs 4.5 days, $p = 0.04$). No other infectious extra-pancreatic complications had significantly longer ICU or total LOS. Moreover, mortality was not affected by any infectious extra-pancreatic complication (Table 4).

Patients with non-infectious extra-pancreatic complications had significantly longer total and ICU LOS (16.7 vs 9.5 days, $p < 0.01$ and 8.4 vs 3.4 days, $p = 0.01$, respectively) and had significantly more in-hospital deaths than those without non-infectious extra-pancreatic complications (24.0% vs 16.2%, $p = 0.04$). Specifically, total and ICU LOS was longer in patients with delirium (19.0 vs 15.2 days, $p < 0.01$ and 10.1 vs 4.1 days, $p = 0.01$, respectively), gastrointestinal bleeding (17.7 vs 11.5 days, $p = 0.04$ and 11.2 vs 4.6 days, $p = 0.04$, respectively) and patients requiring dialysis (24.1 vs 11.1 days, $p < 0.01$ and 16.6 vs 4.2 days, $p < 0.01$, respectively). Lastly, mortality rates were significantly higher in patients with coronary events (33.3% vs 8.0%, $p = 0.04$) and in patients requiring dialysis (25.0% vs 9.4%, $p = 0.04$).

Multi-variable analysis

On multi-variable analysis, patients' requiring dialysis was an independent predictor for total and ICU LOS (IRR 1.73, 95% CI: 1.263–2.378, $p < 0.01$ and IRR 3.20, 95% CI: 1.878–5.463, $p < 0.01$), whereas other variables were not (all $p > 0.05$, Table 5). Similarly, patients' requiring dialysis was an independent predictor for in-hospital mortality (IRR 1.50, 95% CI 1.623–6.843,

Table 3. Patients with local pancreatic complications

	Pancreatic complications ($n = 60$)	No pancreatic complications ($n = 103$)	p-value
Mean total length of stay, days (SD)	21.3 (14.8)	12.1 (10.7)	**<0.01**
Mean ICU length of stay, days (SD)	11.1 (15.5)	5.2 (9.8)	**<0.01**
Mortality, *n* (%)	10 (16.7)	9 (8.7)	0.13
Mean number of events	0.97	0.96	0.89
Mean number of images	15	8	**<0.01**

SD, standard deviation; ICU, intensive care unit.

Table 4. *P*-values from univariate analysis of patients with and without extra-pancreatic complications for total and intensive care unit length of stay and mortality

Event	Total length of stay	ICU length of stay	Mortality
Hospital-acquired pneumonia	**0.01**	**0.07**	0.96
Aspiration pneumonia	0.26	0.40	0.53
Ventilator acquired pneumonia	0.81	0.80	0.40
Catheter-associated urinary-tract infection	0.24	0.95	0.82
Line-associated blood-stream infection	0.34	0.28	0.48
Non-line-associated blood-stream infection	0.16	**0.04**	0.88
All blood-stream infections	0.42	0.21	0.82
Clostridium difficile-associated diarrhea	0.59	0.30	0.53
Delirium	**<0.01**	**0.01**	0.23
Fall with injury	0.94	0.91	0.66
Coronary event	0.78	0.88	**0.04**
Gastrointestinal bleeding	**0.04**	**0.04**	0.88
Cardiac arrest	0.49	0.36	0.53
Dialysis initiation	**<0.01**	**<0.01**	**0.04**
Any infectious complication	**0.05**	0.30	0.77
Any non-infectious complication	**<0.01**	**0.01**	**0.04**

$p < 0.01$), along with coronary events (IRR 14.61, 95% CI: 1.008–24.534, $p = 0.05$).

Association between severity scores and extra-pancreatic complications

There was a significant association between having extra-pancreatic complications events and higher BISAP score using an a priori cut-off score of 3 ($p = 0.02$). On post-hoc analysis, we adjusted the cut-off to 2 and 4 and there was a significant association at 4 ($p = 0.05$), although the association was no longer significant when the cut-off was reduced to 2 ($p > 0.05$).

A significant association did not exist for either the CCI or the age-adjusted CCI when an a priori cut-off set at 3 ($p = 0.44$). On post-hoc analysis, the cut-off was adjusted to 2, 4, 5 and 6, and there remained no significant associations ($p > 0.05$).

DISCUSSION

Only a minority of patients with AP require ICU level of care; however, mortality may be as high as 30%. While it is known that the severity of AP predicts mortality, the impact of in-hospital extra-pancreatic complications, however, is not well studied. In this study, we sought to determine the rate of extra-pancreatic complications in patients admitted to the ICU with AP and to identify predictors for LOS and mortality.

Our study demonstrates the significant impact that extra-pancreatic complications have on outcomes in ICU patients with AP. We report an extra-pancreatic complications event rate of nearly one event per patient and, when controlling for patients with local pancreatic complications, an event rate of greater than one event per patient. Moreover, these events prolong both ICU and total LOS, and increase in-hospital mortality especially in patients with non-infectious extra-pancreatic complications. Above all, even after controlling for patients with local pancreatic complications, patients requiring dialysis remained the strongest predictor of total and ICU LOS as well as in-hospital mortality.

To date, infectious extra-pancreatic complications have been reported in patients hospitalized with AP, but not specifically in patients admitted to the ICU. In a systematic review, Brown *et al.* compiled 1700 patients admitted for AP from 19 studies and reported an incidence rate of 32%, with the most common infections being respiratory infections, blood-stream infection and urinary-tract infections [9]. Similarly, our study found that respiratory infections, blood-stream infection and urinary-tract infections were the most common infectious extra-pancreatic complications in patients admitted with AP to the ICU. We, however, reported a higher incidence (48.5%) of infectious extra-pancreatic complications which likely reflects our sicker ICU-only cohort. Further, Wu *et al.* conducted a population-based assessment to determine the rate of hospital-acquired infections using a large national database. The authors showed that patients with infectious extra-pancreatic complications had longer LOS [10], which was corroborated in our study.

Of the non-infectious extra-pancreatic complications, gastrointestinal bleeding has been previously reported in patients hospitalized for AP with an incidence ranging from 3.7 to 17.8% and with a significantly higher mortality rate [14, 19–21]. Our

Table 5. Multi-variable analysis for predictors of length of stay and mortality

Event	Incidence risk ratio	*p*-value	95% confidence interval
Total length of stay			
Hospital-acquired pneumonia	1.36	0.10	0.944–1.951
Dialysis	1.73	**<0.01**	1.263–2.378
Gastrointestinal bleeding	1.32	0.09	0.957–1.815
Delirium	1.26	0.09	0.962–1.651
ICU length of stay			
Hospital-acquired pneumonia	1.50	0.18	0.825–2.713
Non-line blood-stream infection	1.41	0.21	0.768–3.139
Dialysis	3.20	**<0.01**	1.878–5.463
Gastrointestinal bleeding	1.56	0.11	0.898–2.705
Delirium	1.53	0.06	0.979–2.392
Mortality			
Coronary event	14.61	**0.05**	1.008–24.534
Dialysis	1.50	**<0.01**	1.623–6.843

study found an incidence of 12.2% but no significant difference in mortality. Our institution regularly practices stress-ulcer prophylaxis whereas previous studies did not mention use of prophylaxis. While it is unclear what effect this practice had on the incidence of gastrointestinal bleeding in our study, at least one study has demonstrated the efficiency of the use of a proton pump inhibitor on the prevention of stress ulcers in patients with AP [22]. Our study also found that patients who suffered from gastrointestinal bleeding had longer total and ICU LOS, which is in keeping the largest population-based study [21].

Our study is the first to report other non-infectious complications in ICU patients with AP. One such complication is delirium, which is an acute confusional state with waxing and waning changes in mental status precipitated by an underlying acute condition [12]. The incidence of delirium in hospitalized patients has been estimated at 30%. ICU-related conditions including sepsis, diabetic keto-acidosis and heart-failure delirium range between 16 and 89% [12–13, 23–25]. These studies have also demonstrated longer hospitalization and higher mortality rates [23]. In our study, the incidence of delirium was 19.6% (32/163) and our patients had significantly longer LOS, in keeping with these studies that explored similarly morbid conditions.

Hospitalized patients are also at risk for falling [26]. Specifically, patients with delirium, patients with ischemic strokes, those in geriatric units and those with cancer are at higher risk for falls, with some studies quoting a 10% risk of fall [11, 26, 27]. In contrast, there was a relatively low rate of falls (1.2%, 2 falls in 158 complications) in our patient population in spite of receiving narcotics and other sedatives, perhaps due to the relatively lower rate of delirium (19.6%) and younger patient population.

Acute coronary syndrome was a rare event in our cohort (1.8%, 3/163), which is in keeping with several published case reports [28–31]. The incidence is lower than in similarly morbid conditions such as sepsis, where the incidence has been reported as 4.1% [32, 33]. The mortality rate in our study for patients with acute coronary syndrome was significantly higher and was an independent predictor for mortality in our cohort, similarly to patients with sepsis [30]. Along with acute coronary syndrome, cardiac arrest is another important complication that rarely occurred in our study (2.5%, 4/163) as reported in other studies [34, 35]. The overall incidence of in-hospital cardiac arrest has been quoted as 1.6 arrests per 1000 admissions, which is lower than in our cohort of ICU patients and is explained by our sicker population. Further studies are needed to explore the relationship between cardiac complications and AP.

Transient or persistent acute renal failure is a marker for severity in patients diagnosed with AP [1, 3–5, 36]. Patients whose renal function does not improve and those who develop severe hypervolemia, uremia or electrolyte disturbances may require urgent therapy via hemodialysis. The incidence of ICU patients with AP requiring urgent hemodialysis is not well reported. Studies reported a rate of 3% in all patients admitted for AP as well as in other critically ill patients [37, 38]. In our cohort, the incidence rate was 8.7%, likely due to a sicker ICU population. Importantly, our study demonstrates that renal failure is an independent predictor for LOS and mortality, even after controlling for the presence of local pancreatic complications. These findings further emphasize the critical impact that renal failure has on outcomes in patients with AP.

Several studies have demonstrated that comorbid conditions impact outcomes in patients with AP, including organ failure and mortality [38–40]. BISAP scores of greater than 3 have a mortality rate ranging between 5 and 22%, whereas scores less than 2 have lower mortality [17, 40]. Furthermore, a BISAP score of 3 had 99.1% specificity for severe AP in one study [41]. A CCI score of greater than 3 also had a higher rate of mortality [42]. However, little is known about the correlation between BISAP and CCI and rates of extra-pancreatic complications. Using this information, we set a cut-off of 3 to determine whether there is an association between BISAP and extra-pancreatic complications as well as CCI and extra-pancreatic complications. In our study, BISAP score had a significant association in predicting extra-pancreatic complications, whereas comorbidity scores did not.

Naturally, in our study, patients with local pancreatic complications had longer hospital and ICU LOS and thus confound LOS measurements in patients with extra-pancreatic complications. However, after excluding these patients, LOS remained significantly longer in patients with extra-pancreatic complications, suggesting that these complications independently prolong hospitalization.

Because of the retrospective nature of our study and its inherit limitations, more studies are needed to understand the impact that these extra-pancreatic complications have on mortality and LOS. Further, as CCI scores were calculated retrospectively, there may have been significant bias in its calculation. Thus, it is unclear what impact comorbidity has on extra-pancreatic complications. In our study, we report that there was not a statistically significant difference in our primary outcome, highlighting that our study was underpowered. Thus, larger studies are necessary to further investigate what impact in-hospital complications have on mortality in patients with AP. While admission to the ICU had clear criteria, discharge criteria from the ICU were not clearly delineated and were left to the clinician, which confounds our LOS analysis. Moreover, in an effort to reduce in-hospital complications, there may have been institutional practice changes to improve care. It is unclear what effect, if any, these had on our study, as we did not account for them. Lastly, we did not collect data on whether patients with pancreatic fluid collections required endoscopic, surgical or percutaneous drainage, which could confound our results. Studies that further clarify the impact of these fluid collections on in-hospital complications are needed.

In summary, both infectious and non-infectious extra-pancreatic complications occur frequently in patients with AP who are admitted to the ICU and impact LOS when present. After

controlling for local pancreatic complications, patients with renal failure requiring dialysis remained the strongest predictor for LOS and mortality.

Conflict of interest statement: none declared.

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