

Which Patients with Mild Acute Pancreatitis Require Prolonged Hospitalization?

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OBJECTIVES: In our experience, a subset of mild acute pancreatitis (AP) patients, as defined by the Revised Atlanta Classification, has longer than expected hospitalization. Our aims are to report the prevalence of patients with mild AP who have a prolonged length of stay (LOS), evaluate the etiology, thoroughly phenotype, and finally compare this subset to those with expected LOS. **METHODS:** Patients admitted with AP from 2003 to 2015 were prospectively enrolled into this cohort study. LOS ≥ 8 days was considered as prolonged LOS. Data on demographics, clinical and laboratory variables, management, and outcomes was both prospectively and retrospectively collected. Continuous variables were compared using the nonparametric *t*-test (Wilcoxon's test) and categorical variables using the Pearson's χ^2 test.

RESULTS: Among 231 enrolled mild AP patients, 46 (20%) had a prolonged LOS (≥ 8 days). The main determinants of prolonged LOS included ongoing pancreatitis-related symptoms ($n = 31$, 67.4%) and performance of cholecystectomy ($n = 11$, 23.9%). When compared to patients with expected LOS (< 8 days, $n = 185$), patients with prolonged LOS due to ongoing symptoms ($n = 31$) were more likely to have systemic inflammatory response syndrome at 48 h from admission (37% vs. 13.4%, $P < 0.001$), a prolonged fasting period (6.6 vs. 2.8 days, $P < 0.001$), and need for nutritional support (30% vs. 1.6%, $P < 0.001$).

CONCLUSIONS: About 20% of patients with mild AP have a longer than expected hospital stay, mostly attributed to ongoing pancreatitis-related symptoms. An early decision (at 72 h) for enteral nutrition support in these patients needs to be explored so as to shorten hospitalization and reduce cost of care.

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INTRODUCTION

Acute pancreatitis (AP) is the third most common 'principal' hospital discharge diagnosis for gastrointestinal (GI), liver, and pancreatic disease with ~275,000 patient discharges, following GI hemorrhage and cholecystitis.¹ The direct health-care costs associated with AP exceed 2.6 billion dollars annually,¹ with two-thirds of the cost being attributable to hospitalizations.² The mean hospital length of stay (LOS) for AP-related hospitalizations is 4.7 days, which has improved over the past few decades from 5.8 days in 2003 and 6.4 days in 1997.¹ This has likely been a result of a better understanding of the pathophysiology of AP, earlier recognition and improved management of its complications, and increased awareness for the need for health-care cost reduction.

The natural progression and associated morbidity in AP is directly related to the severity of the disease.^{3–5} The Revised Atlanta Classification (RAC) classifies AP severity into three categories; mild, moderately severe, and severe AP. This is based on the presence and duration of organ failure (OF), and local and systemic complications.⁶ Fortunately, the majority of

patients develop mild AP with a brief and uncomplicated hospital course.^{7,8} Moderately severe and severe AP has been associated with increased morbidity and mortality, and thus longer hospital stays with higher costs of care.^{3,4,7,8}

In our institutional experience, a significant portion of mild AP patients remain hospitalized for longer than the expected 4–5 days. There is a paucity of data evaluating the causes and management of this subset of mild AP patients—who require a longer hospitalization. A few prior studies have shown that the presence of comorbidities, longer duration of fasting period, oral refeeding intolerance, need for abdominal cross-sectional imaging, endoscopic retrograde cholangiopancreatography (ERCP) during hospitalization, and low volume of fluid resuscitation within 24 h of presentation are related to increase LOS in mild AP patients. However, these studies have been heterogeneous and mainly used the original Atlanta classification for defining disease severity.^{9–11} An improved understanding of these patients would enable interventions aiming at reducing LOS. This could lead to significant cost savings, particularly for a disease with an

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increasing incidence and because mild disease comprises the majority of patients^{7,12–14}

The primary aim of this study was to report the prevalence of patients with mild AP who required a longer than expected LOS, evaluate the etiologies of prolonged LOS, and thoroughly phenotype this subgroup. Our secondary aim was to compare the demographics, clinical and laboratory variables, in-hospital management, and outcomes between the mild AP patients with prolonged and expected LOS. Last, we propose a management algorithm for such patients aiming to reduce LOS.

METHODS

Patients, who were admitted or transferred to the University of Pittsburgh Medical Center (UPMC) with AP from 2003 to 2015, were prospectively enrolled into the Severity of Acute Pancreatitis Study/Pancreatitis-associated Risk Of Organ Failure (SAPS/PROOF) studies. The SAPS/PROOF protocol has been approved by the Institutional Review Board at the University of Pittsburgh (IRB ID: PRO08010374).^{15–17} Patients above 18 years of age, who met the diagnostic criteria for AP and signed the informed consent, were enrolled in the studies. Diagnosis of AP was based on the presence of at least two of the following three criteria: (1) abdominal pain consistent with AP; (2) serum amylase and/or lipase level greater than three times the upper limit of normal; and/or (3) characteristic findings on abdominal imaging. AP patients with underlying chronic pancreatitis and/or pancreaticobiliary malignancy were excluded. For transferred patients, data from the initial center were retrieved and reviewed.

Following publication of the RAC in 2013, two experienced abdominal radiologists retrospectively reviewed all contrast-enhanced abdominal imaging studies (computed tomography (CT) and magnetic resonance imaging (MRI)) for the enrolled patients. The radiologists were blinded to the actual clinical outcomes of these patients. Local complications including acute peripancreatic fluid collections and pancreatic or peripancreatic necrosis based on the RAC were recorded. The confidence level in correctly diagnosing necrosis was recorded using a three-point scale (1 = poorly confident or unsure; 2 = moderately confident; 3 = strongly confident). Cases initially classified as “poorly

confident” were reviewed to reach a final consensus; any inter/intraobserver variation among the two radiologists was not assessed. All patients were reclassified by the investigators with respect to the severity of AP based on the RAC definitions. Investigators were not blinded to the clinical course of the patients. For the purpose of this study, only patients with mild AP were included.

Total LOS was defined as the number of days of hospitalization from admission to discharge. For transferred patients the LOS at the outside hospital was added to the LOS at our institution. LOS ≥ 8 days was considered to be a prolonged LOS. LOS stay < 8 days was considered an expected LOS. Eight days was used as the cutoff between prolonged and expected LOS based on the sum of the median LOS for mild AP patients (5 days) plus one interquartile range (3 days).

Data on demographics, clinical and laboratory variables, imaging studies, management, and outcomes were prospectively collected as per the study protocol, with some exceptions as mentioned ahead. Clinical and laboratory variables included systemic inflammatory response syndrome (SIRS) score and lipase levels. SIRS score was calculated on admission, at 48 and 72 h. SIRS calculations were based on the most extreme values of vital signs and laboratory studies. Similarly, available lipase levels were recorded on admission, at 48 and 72 h. Lipase level ratio (lipase level divided by the upper limit of normal for the reference lab) was calculated for all available lipase levels. The upper limit of normal varied between institutions and in different time periods; these cutoff changes were incorporated for the lipase level ratio calculations.

Data regarding nutritional management, use of pain medications, amount of intravenous fluid resuscitation within the first 24 h of admission, etiology of prolonged LOS, and need for readmission within 3 months from discharge were extracted after careful retrospective review of the medical records. Through the later part of SAPS/PROOF studies (2011 onwards), intravenous fluid resuscitation and nutritional management was prospectively recorded, and enrolled patients were contacted at 3 months and 1 year after discharge for follow-up information regarding readmissions.

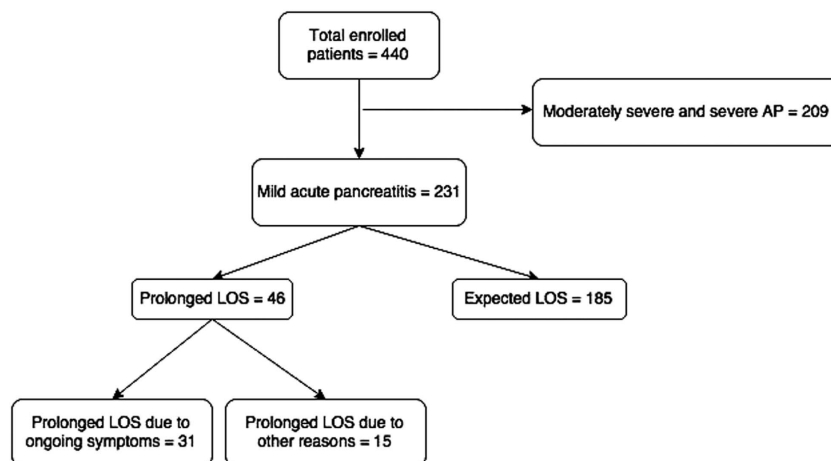


Figure 1 Enrolled patients (pancreatitis severity based on Revised Atlanta Classification).

Statistical analysis. Continuous data were presented as means with standard deviations (s.d.) and categorical data as frequencies. Continuous variables were compared using the nonparametric *t*-test (Wilcoxon's test) and categorical variables using the Pearson's chi-squared test. *P* values <0.05 were considered significant. Multivariate logistic regression analysis was performed using the significant variables in the univariate analysis. Multiple comparison adjustment was not performed. Analyses were performed using IBM-SPSS 19 (IBM corp, Armonk, NY).

RESULTS

A total of 440 patients with AP were enrolled in this cohort between 2003 and 2015. Two hundred and thirty-one patients (52.5%) were classified as having mild AP based on the RAC. Among those, 46 (19.9%) patients required a prolonged LOS (LOS \geq 8 days) and 185 (80.1%) stayed in the hospital for <8 days (expected LOS; **Figure 1**).

Etiology of prolonged LOS and mean LOS. Ongoing pancreatitis-related symptoms (ongoing symptoms) including persistent upper abdominal pain and/or intolerance to oral refeeding (pain, nausea, and/or vomiting on initiating diet) was the primary reason for prolonged LOS in 31 (67.4%) of these 46 patients (**Table 1**). Cholecystectomy during the same admission was the primary reason for prolonged LOS in 11 (23.9%) patients. Only one patient had a prolonged LOS attributed to an ERCP procedure. **Table 1** reports all other less frequent causes of prolonged LOS. Statistical comparison of demographics and clinical data was performed between mild AP patients with prolonged LOS due to ongoing symptoms ($n=31$) and mild AP patients with expected LOS ($n=185$). We excluded patients with other causes of prolonged LOS to focus on ongoing pancreatitis-related symptoms and prevent making our comparison groups heterogeneous, which could lead to potential confounding. The mean LOS for patients with prolonged LOS due to ongoing symptoms was significantly higher than those with expected LOS (11 vs. 4.5 days; $P<0.001$; **Table 2**). **Figure 2** shows the distribution of number of patients discharged on a particular day of hospitalization.

Demographic and other baseline characteristics. There were no significant differences in age, sex, body mass index (BMI), comorbidities, etiology of AP, sentinel AP, smoking history, and alcohol consumption between mild AP with prolonged LOS due to ongoing symptoms and expected LOS

Table 1 Etiologies of prolonged LOS

Etiology of prolonged LOS	<i>n</i> = 46
Ongoing pancreatitis-related symptoms (pain, oral refeeding intolerance) (%)	31 (67.4)
Cholecystectomy during the same hospitalization (%)	11 (23.9)
Others (%)	4 (8.7)
Liver transplant-related morbidity	1
Suspected duodenal microperforation during ERCP	1
Alcohol withdrawal	1
Post cholecystectomy collection and fever	1

ERCP, endoscopic retrograde cholangiopancreatography; LOS, length of stay.

(**Table 3**). The proportion of transferred patients was significantly higher among patients with ongoing symptoms and prolonged LOS (61.3%) compared to patients with expected LOS (30.8%, $P=0.001$).

SIRS, lipase ratios, and imaging studies. No significant difference was found in the presence of SIRS on admission (19.3% vs. 21.3%) between the two groups. However, at 48 h from admission, presence of SIRS was significantly higher in patients with prolonged LOS due to ongoing symptoms compared to those with expected LOS (37% vs. 13.4% respectively, $P<0.001$). There was a trend, which did not reach statistical significance, for SIRS score \geq 2 at 72 h following admission between the two groups (18.2% vs. 7.6%, $P=0.11$; **Table 2**). At 72 h from admission, the mean SIRS score of patients with prolonged LOS due to ongoing symptoms was significantly higher compared to patients with expected LOS (0.91 vs 0.45, $P=0.013$). Mean lipase elevation ratios between the two groups were not significantly different upon admission (31.1 vs. 51.8, $P=0.27$), at 48 h (9.4 vs. 7.7, $P=0.26$), or at 72 h from admission (4.3 vs. 3.6, $P=0.50$). The trend of lipase levels at 48 and 72 h from admission compared to levels at admission also showed no significant difference when evaluated for an upward or downward trend. The proportion of patients with an elevated lipase to greater than 3 times the upper limit of normal was also similar in both the groups at 48 (54.2% vs. 46.7%, $P=0.49$) and 72 h from admission (33.3% vs. 25.6%, $P=0.44$; **Table 2**).

The number of patients that underwent a contrast-enhanced imaging during the hospitalization was significantly higher, as expected, in the prolonged LOS due to ongoing symptoms group (77.4% vs. 43.2%, $P=0.001$). Of importance, all imaging in these patients showed no local complications. Among the patients with CT scans, 61.5% underwent a scan within 48 h of presentation and 38.5% had an imaging performed later in the hospital course.

Fluid resuscitation. The volume of intravenous fluid resuscitation during the first 24 h of hospitalization was similar in both groups (3.5 vs. 3.2 L, $P=0.43$), even when considering only direct admissions to our institution (3.6 vs. 3.3 L, $P=0.45$).

Pain medications. Evaluation of the chronic use of narcotic pain medications before admission showed no statistically significant difference between the two groups (17.9% vs. 15.4%, $P=0.74$). Similarly, the proportion of patients discharged on narcotics was also similar in both the groups (54.8% vs. 47.6%, $P=0.77$; **Table 2**).

Fasting and nutrition. The mean duration of fasting during hospitalization was 6.6 and 2.8 days from admission in patients with prolonged LOS due to ongoing symptoms and expected LOS, respectively, which was statistically significant ($P<0.001$). In patients with prolonged LOS due to ongoing symptoms, oral refeeding was tolerated as an initial route of nutrition in 21 (70%) patients, while 9 (30%) patients received nutritional support. Among these nine patients, seven patients received enteral, and two received total parenteral nutrition. A significantly higher portion of mild AP patients with expected LOS tolerated oral refeeding as the initial route of

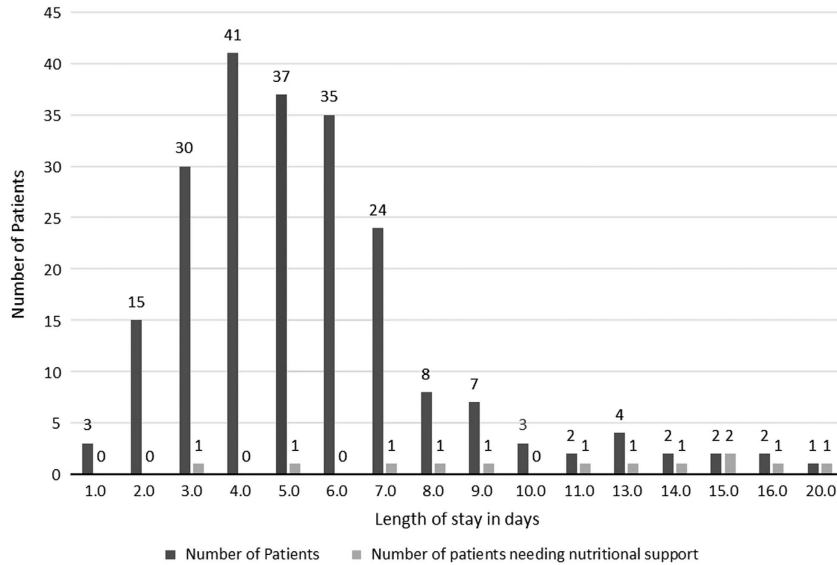


Figure 2 Length of stay plotted against number of patients.

nutrition (181/184; 98.4%) with only three patients requiring enteral feeding. **Figure 2** shows the hospital day of discharge of patients requiring any form of nutritional support.

Follow-up. There was no difference in readmission rates related to pancreatitis or associated abdominal symptoms at 3 months from discharge between the two groups (18.5% vs. 14.1%; $P=0.61$). For the enrolled patients, the response rate to post 3-month hospital discharge contact was 65%.

Analysis of patients who underwent cholecystectomy during same admission. Among the 46 patients with prolonged LOS, 11 (23.9%) had cholecystectomy during the same admission, which was the cause of increased LOS. The mean LOS of these patients was 9.3 days and day 7 of hospitalization was the mean day of cholecystectomy. Mean postoperative stay before discharge was 2.8 days. Out of these 11 patients, three patients were feeling well on day 4 and underwent the procedure on day 5. Three patients underwent preoperative cardiac work up which delayed cholecystectomy. Treatment for possible pneumonia, persistent abdominal pain symptoms, and wait time for attenuation of the anti-platelet effect of clopidogrel were the causes of delayed cholecystectomy in three other patients. In the remaining two patients, cholecystectomy was delayed due to logistic issues in scheduling.

Multivariate analysis. A multivariate logistic regression analysis was performed by including the variables that were significant in the univariate analysis. Only three variables were placed in the analysis at a single time due to the small sample size ($n=31$ in prolonged LOS group) and this was rotated through six variables. Six variables (SIRS at 48 h, mean SIRS at 72 h, outside hospital transfers, number of patients who underwent contrast-enhanced imaging, fasting days, and need for nutritional support) were chosen as the others were either not independent covariates to the prolonged LOS or were not mutually exclusive to other covariates. Except for mean SIRS at 72 h, the other five variables

remained significant after multivariate logistic regression analysis (**Tables 2 and 3**).

DISCUSSION

In this prospective AP cohort, we focused on a unique subset of AP patients who required a prolonged hospitalization of more than 1 week despite being categorized as having mild disease by the RAC. Nearly 20% of all mild AP patients fit into this category. Furthermore, two-thirds (67.4%) of these patients had prolonged LOS due to ongoing pancreatitis-related symptoms, which include persistent pain and/or oral refeeding intolerance. These patients were more likely to be transferred from community hospitals and had ongoing SIRS at 48 h from admission, compared to patients with mild AP and expected LOS. Thirty percent of these patients were treated with enteral or parenteral nutritional support during their hospitalization.

Abdominal pain is the major symptom of pancreatic injury in AP and SIRS indirectly reflects the magnitude of inflammatory response to pancreatic injury. In our cohort, patients with prolonged LOS due to ongoing symptoms showed higher prevalence of SIRS at 48 and 72 h of admission. In addition, the mean duration of fasting was much higher for prolonged LOS group compared to expected LOS group (6.6 vs. 2.2 days). These findings suggest that patients with prolonged LOS have a more robust and/or prolonged underlying systemic inflammatory response lasting for at least 48 to 72 h following admission. This inflammatory response eventually subsides and does not result in local complications or OF, and thus continues to satisfy the RAC criteria for mild AP. Thus, along with significant pain, SIRS at 48 to 72 h may be used as an indicator to predict prolonged LOS in mild AP.

With respect to factors resulting in prolonged hospitalization in mild AP patients, a recent retrospective study from Spain including 232 mild AP patients showed that a Charlson comorbidity index ≥ 2 , fasting period >3 days, intolerance to oral refeeding, need for abdominal imaging (CT or MRI), performance of ERCP, and admission to a GI department are

Table 2 Clinical and laboratory variables, in-hospital management, and outcomes for mild AP

Variables	Prolonged LOS due to ongoing symptoms (n = 31)	Expected LOS (n = 185)	P value
Total LOS, mean (s.d.)	11 (3.1)	4.5 (1.5)	<0.001 ^a
LOS at outside hospital, mean (s.d.)	3.3 (3.9)	0.8 (1.1)	<0.001 ^a
<i>SIRS admission</i>	n = 29	n = 183	
Mean (s.d.)	0.93 (0.96)	0.84 (0.87)	0.69
Score ≥ 2 (%)	6 (19.3)	39 (21.3)	0.23
<i>SIRS at 48 h</i>	n = 27	n = 172	
Mean (s.d.)	1.15 (1.16)	0.56 (0.56)	0.007 ^a
Score ≥ 2 (%)	10 (37)	23 (13.4)	<0.001 ^{a, b}
<i>SIRS at 72 h</i>	n = 22	n = 132	
Mean (s.d.)	0.91 (0.92)	0.45 (0.65)	0.013 ^a
Score ≥ 2 (%)	4 (18.2)	10 (7.6)	0.11
<i>Lipase at admission</i>	n = 22	n = 165	
Lipase ratio at admission, mean (s.d.)	31.1 (37.6)	51.8 (80.6)	0.27
Lipase > 3x normal at admission (%)	20 (90.9)	147 (89.1)	0.79
<i>Lipase at 48 h</i>	n = 24	n = 150	
Lipase ratio at 48 h, mean (s.d.)	9.4 (21.6)	7.7 (13.7)	0.26
Lipase > 3x normal at 48 h (%)	13 (54.2)	70 (46.7)	0.49
Lipase trending upward at 48 h (%)	3/21 (14.3)	12/137 (8.8)	0.42
<i>Lipase at 72 h</i>	n = 24	n = 117	
Lipase ratio at 72 h, mean (s.d.)	4.3 (8.9)	3.6 (8.9)	0.50
Lipase > 3x normal at 72 h	8 (33.3)	30 (25.6)	0.44
Lipase trending upward at 72 h (%)	1/22 (4.5)	1/113 (0.9)	0.19
Number of patients who underwent contrast-enhanced imaging during hospitalization (%)	24 (77.4)	80 (43.2)	0.001 ^{a, b}
<i>Fluid resuscitation data</i>	n = 25	n = 143	
Total fluid resuscitation in liters within first 24 h of admission, mean (s.d.)	3.48 (1.33)	3.2 (1.1)	0.43
Total fluid resuscitation in liters within first 24 h of admission for direct admissions, mean (s.d.)	3.56 (1.29)	3.29 (1)	0.45
<i>Narcotic use</i>			
Before admission (%)	5 (17.9)	28 (15.4)	0.74
On discharge (%)	17 (54.8)	88 (47.6)	0.77
<i>Nutrition</i>	n = 30	n = 184	
Fasting in days from admission, mean (s.d.)	6.6 (3.1)	2.8 (1.7)	<0.001 ^{a, b}
Successful oral feeding as first route of nutrition (%)	21/30 (70)	181/184 (98.4)	<0.001 ^a
Need for enteral or parenteral nutritional support (%)	9/30 (30)	3/184 (1.6)	<0.001 ^{a, b}
<i>Readmission data</i>	n = 27	n = 142	
Number of patients with readmission within 3 months of discharge (%)	5/27 (18.5)	20/142 (14.1)	0.61

AP, acute pancreatitis; LOS, length of stay; SIRS, systemic inflammatory response syndrome.

^aSignificant P value on univariate analysis.

^bSignificant on multivariate analysis.

independently associated with a prolonged LOS.⁹ However, 35% of the 66 patients who underwent abdominal imaging in their cohort had peripancreatic collections, and thus should have been classified as moderately severe based on RAC. Therefore, the findings of this study are limited by patient heterogeneity as it is well known that patients with moderately severe AP have increased morbidity and LOS compared to those with mild AP. Our analysis did not show any difference in the Charlson comorbidity index between prolonged and expected LOS groups. Patients with persistent symptoms are likely to undergo cross-sectional imaging to assess for local complications, which was seen in our cohort as well. Additionally, performance of

ERCP had an impact on the LOS in only a single patient in our study. This is in contrast to cholecystectomy, which significantly affected the LOS. Cholecystectomy during the same hospitalization is the standard of care for gallstone-induced mild AP, unless medically contraindicated.^{18,19}

Currently, there are no guidelines for optimal timing of oral refeeding in patients with mild AP. In routine clinical practice, refeeding is initiated when symptoms of pain, nausea, and vomiting have resolved or are adequately controlled without requiring significant doses of pain medications. Previous studies have shown that patients with pain relapse following oral refeeding have a longer LOS.^{20–23} Factors related to refeeding

Table 3 Baseline characteristics of patients with mild AP

	Prolonged LOS due to ongoing symptoms (n = 31)	Expected LOS (n = 185)	P value
Age, mean (s.d.)	47.7 (17.3)	49.5 (19.5)	0.63
Sex, male (%)	11 (35.5)	79 (42.7)	0.45
BMI, mean (s.d.)	28.8 (7.1)	28.8 (7.4)	0.96
Charlson Score (%)	0 = 19 (61.3) 1 = 6 (19.4) ≥ 2 = 6 (19.4)	0 = 106 (57.3) 1 = 34 (18.4) ≥ 2 = 45 (24.3)	0.63
Outside hospital transfers (%)	19 (61.3)	57 (30.8)	0.001 ^{a, b}
<i>Etiology</i>			0.21
Gallstones (%)	8 (25.8)	81 (43.8)	
Alcohol (%)	3 (9.7)	15 (8.1)	
Idiopathic (%)	6 (19.4)	34 (18.4)	
Hypertriglyceridemia (%)	1 (3.2)	7 (3.8)	
Post ERCP (%)	6 (19.4)	32 (17.3)	
Other (%)	7 (22.6)	16 (8.6)	
<i>First vs. recurrent episodes</i>			0.55
First episode (%)	21 (67.7)	115 (62.2)	
Recurrent episode (%)	10 (32.3)	70 (37.8)	
Current smoker (%)	11 (35.5)	48 (25.9)	0.27
Any alcohol in past 6 months (%)	11 (35.5)	80 (43.2)	0.41

AP, acute pancreatitis; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography; LOS, length of stay.

^aSignificant P value on univariate analysis.

^bSignificant on multivariate analysis.

intolerance include a higher Balthazar's CT score on admission, higher mean lipase level before refeeding, duration of pain before admission, and the total duration of pain before refeeding. The above studies, however, were limited by heterogeneous patient populations; one study included patients with pancreatic necrosis and another classified mild AP based on the outdated original Atlanta classification.^{20,21} In our cohort, in which the updated RAC was used, the mean lipase levels on admission, 48 and 72 h, as well as the trend of lipase level at 48 and 72 h were not found to be significantly different between the mild AP prolonged LOS and expected LOS groups. Two small randomized controlled trials have shown that in patients with mild and moderate AP, early nasoenteral tube feeding reduces the incidence of refeeding intolerance and can also potentially decrease LOS, compared with a strategy of initially keeping patients nil per oral until the treating team decides to initiate oral refeeding.^{22,24} Moreover, oral refeeding intolerance has been shown to significantly impair the in-hospital quality of life. Whereas an early nasogastric tube feeding strategy does not impact quality of life negatively, compared with the nil per oral strategy, and results in shorter duration of abdominal pain, decreased need for opiates as well as reduces the incidence of oral refeeding intolerance.^{24–26} Such an approach with early nasogastric or naso-jejunal feeding was not followed in our cohort.

Fluid resuscitation is a critical component of early management in patients with AP. Early and adequate intravenous fluid resuscitation is a well-established means of decreasing morbidity and mortality. However, recent reports have suggested that overaggressive resuscitation could result in worse clinical outcomes.^{10,11,27–32} The rationale for adequate intravenous fluid resuscitation is to replete the macrovascular volume loss, prevent hypoperfusion, and end organ dysfunction, as well as maintain the microcirculation of the pancreas, which in turn may decrease local inflammation, cell death, and pancreatic necrosis.^{4,33}

A recent retrospective study showed that patients with mild AP at admission (based on original Atlanta classification) who received greater than one-third of the total 72-h fluid resuscitation volume within the first 24 h of presentation had significantly lower SIRS, ICU admission rate, OF at 72 h, and LOS when compared with those who did not (mean 7 vs. 11 days, $P=0.001$).¹⁰ In a recent prospective study, the use of a clinical decision support tool in changing clinician behavior in accordance with recent advances in AP management was evaluated.³⁴ The intervention included a web-based point-of-care instrument with an intuitive algorithm containing early management recommendations for AP, which included early goal-directed fluid resuscitation in all.³² In the implementation group, early risk stratification and goal-directed resuscitation was achieved more frequently and led to a significant overall mean reduction in LOS of 2.1 days, with a reduction of 0.9 days in patients with mild AP.³⁴ Another recent study in post-ERCP pancreatitis patients concluded that greater intravenous volume infusion within the first 24 h was associated with reduced LOS.¹¹ In our cohort, the amount of intravenous fluids received within the first 24 h of admission exceeded 3 L and was similar between the prolonged LOS due to ongoing symptoms and expected LOS groups.

Our study results may help guide the management of mild AP patients. We propose that mild AP patients who experience persistent severe upper abdominal pain requiring narcotics or develop recurrence of significant pain, nausea, or vomiting after a trial of oral diet should be initiated on nasoenteric feedings as early as 72 h from admission (**Figure 3**). Positive SIRS at 48–72 h may be an additional helpful tool for clinical decision making in such patients. Nasoenteral feeding can provide adequate nutrition, pancreatic rest (with nasojejunal feeding), and may reduce duration of abdominal pain, the need for narcotics, improve in-hospital quality of life, and potentially decrease the LOS. When symptoms persist despite enteral feeding, patients

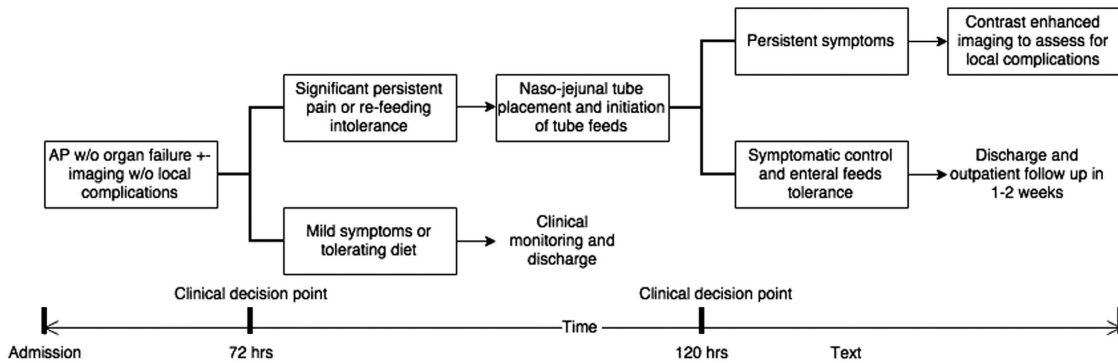


Figure 3 Management algorithm for patients with mild acute pancreatitis.

should then undergo a contrast-enhanced imaging around day 5 to assess for local pancreatic complications. Once nutritional goals and symptom control is achieved, these patients can be discharged home and followed up early in the outpatient setting within 1–2 weeks. We believe such patients may only require a brief duration of pancreatic rest in contrast to moderately severe and severe AP. The relatively brief period of enteral feedings may also result in a lower incidence of feeding tube malfunction, i.e., dislodgement, clogging, and patient discomfort.

In clinical practice, the decision to recommend enteral feeding in mild AP patients is frequently deferred in a hope that symptoms will resolve in the near future by virtue of it being mild AP. Based on our analysis, the mean fasting duration in the prolonged LOS group was 6.6 days with a mean LOS of 11 days, which partially reflects this delay in decision making. With a large number of AP admissions in the United States (275,000) annually, the majority of which develop mild disease, there is a window of opportunity to significantly reduce hospital stay and health costs. A properly designed RCT is needed to test the above-proposed decision-making pathway.

The main strengths of our study include the prospective nature of enrollment, the thorough phenotyping, and categorization of severity based on the RAC definition. To our knowledge, this is the first study to focus on patients with mild AP by RAC who remain hospitalized for a longer period than expected. We also propose a decision-making algorithm for management of such patients. One of the limitations of this study is that the cohort was captured at a tertiary-care referral center with 35% of the analyzed patients transferred from outside facilities potentially resulting in patient selection bias. In addition, a large portion of patients in the prolonged LOS cohort were transfers compared to expected LOS cohort, and delays in initiation of enteral feeding were likely related to prolonged conservative management in this group, as well as potential delay in management from hospital transfer itself. Furthermore, serial lipase levels and contrast-enhanced imaging were ordered based on the discretion of treating physicians and were not available in all patients. Finally, part of the data on fluid resuscitation, nutritional support, and 3-month follow-up were captured in a retrospective manner.

In summary, within the mild AP category, there is a distinct subset of patients (~20%), which requires longer than expected hospitalization. These patients do not differ from the rest of AP patients with mild disease with respect to demographics, comorbidities, etiology, laboratory variables, or fluid resuscitation. In the majority of these patients, the LOS is

prolonged due to ongoing symptoms of persistent abdominal pain and oral refeeding intolerance. Such patients could be identified as soon as 72 h from admission and may benefit from initiation of nasoenteral tube feeding at this point aiming for adequate symptom control, providing enteral nutrition, improving patient quality of life with the potential for significant cost savings by reducing LOS.

CONFLICT OF INTEREST

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Specific author contributions: H.S., A.G., and G.I.P. were involved in the study concept/design, data acquisition, statistical analysis and interpretation, and drafting the manuscript. R.M. and E.K. were involved data acquisition and reviewing the manuscript. G.I.P., D.Y., A.S., and D.C.W. were involved in critical revision of manuscript and important intellectual content. All authors approved the final draft submitted.

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Cost of care for acute pancreatitis is related to the length of hospital stay.
- ✓ Mild acute pancreatitis involves a brief hospitalization.
- ✓ Oral feeding is usually started when abdominal pain, nausea, and vomiting have resolved.

WHAT IS NEW HERE

- ✓ A subset of mild acute pancreatitis patients (20%) requires prolonged hospitalization (8 days or more).
- ✓ Ongoing pancreatitis-related symptoms are the most common cause for increased LOS.
- ✓ An early enteral feeding strategy may reduce costs and LOS in such patients.

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