

Retrospective Cohort Study

Association between acute peripancreatic fluid collections and early readmission in acute pancreatitis: A propensity-matched analysis

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Abstract

BACKGROUND

Patients with acute pancreatitis (AP) frequently experience hospital readmissions, posing a significant burden to healthcare systems. Acute peripancreatic fluid collection (APFC) may negatively impact the clinical course of AP. It could worsen symptoms and potentially lead to additional complications. However, clinical evidence regarding the specific association between APFC and early readmission in AP remains scarce. Understanding the link between APFC and readmission may help improve clinical care for AP patients and reduce healthcare costs.

AIM

To evaluate the association between APFC and 30-day readmission in patients with AP.

METHODS

This retrospective cohort study is based on the Nationwide Readmission Database for 2016-2019. Patients with a primary diagnosis of AP were identified. Participants were categorized into those with and without APFC. A 1:1 propensity score matching for age, gender, and Elixhauser comorbidities was performed. The primary outcome was early readmission rates. Secondary outcomes included the incidence of inpatient complications and healthcare utilization. Unadjusted analyses used Mann-Whitney *U* and χ^2 tests, while Cox regression models assessed 30-day readmission risks and reported them as adjusted hazard ratios (aHR). Kaplan-Meier curves and log-rank tests verified readmission risks.

RESULTS

A total of 673059 patients with the principal diagnosis of AP were included. Of these, 5.1% had APFC on initial admission. After propensity score matching, each cohort consisted of 33914 patients. Those with APFC showed a higher incidence of inpatient complications, including septic shock (3.1% *vs* 1.3%, $P < 0.001$), portal venous thrombosis (4.4% *vs* 0.8%, $P < 0.001$), and mechanical ventilation (1.8% *vs* 0.9%, $P < 0.001$). The length of stay (LOS) was longer for APFC patients [4 (3-7) *vs* 3 (2-5) days, $P < 0.001$], as were hospital charges (\$29451 *vs* \$24418, $P < 0.001$). For 30-day readmissions, APFC patients had a higher rate (15.7% *vs* 6.5%, $P < 0.001$) and a longer median readmission LOS (4 *vs* 3 days, $P < 0.001$). The APFC group also had higher readmission charges (\$28282 *vs* \$22865, $P < 0.001$). The presence of APFC increased the risk of readmission twofold (aHR 2.52, 95% confidence interval: 2.40-2.65, $P < 0.001$). The independent risk factors for 30-day readmission included female gender, Elixhauser Comorbidity Index ≥ 3 , chronic pulmonary diseases, chronic renal disease, protein-calorie malnutrition, substance use disorder, depression, portal and splenic venous thrombosis, and certain endoscopic procedures.

CONCLUSION

Developing APFC during index hospitalization for AP is linked to higher readmission rates, more inpatient complications, longer LOS, and increased healthcare costs. Knowing predictors of readmission can help target high-risk patients, reducing healthcare burdens.

Key Words: Acute pancreatitis; Acute peripancreatic fluid collections; Readmission predictors; Inpatient complications; Healthcare utilization and costs

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Core Tip: The specific association between acute peripancreatic fluid collection (APFC) and early readmission in patients with acute pancreatitis (AP) has not been well characterized. Using a propensity-matched cohort from the Nationwide Readmission Database, this is the first study to reveal that AP patients with APFC have a significantly higher risk of 30-day readmission compared to those without APFC. Patients with APFC also have a higher incidence of inpatient complications, longer hospital stays, and higher healthcare expenditures. Our findings underscore the need for targeted interventions and close monitoring of AP patients with APFC to reduce readmissions and healthcare costs.

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INTRODUCTION

Acute pancreatitis (AP) is an unpredictable and potentially lethal gastrointestinal disease[1]. The annual worldwide incidence of AP is 33.74 cases per 100000 person-years, and it is more than twice as high in some regions[2,3]. The epidemiological trends in AP are showing improvements, but the overall morbidity and mortality still remain high with an aging population[4,5]. It accounts for substantial healthcare utilization and expenditures in the United States, with hospitalization costs of over \$30000 per person[6,7]. Hospital readmission is responsible for a considerable AP-related healthcare burden. In a recent nationwide study, Peery *et al*[8] revealed that 40036 patients had an early readmission documented out of 259284 index AP hospitalizations. In a narrative literature review, Bogan *et al*[9] described the overall AP-related readmission rate as ranging from 7% to 34%. Therefore, it is crucial to reduce readmission rates in AP[9]. It requires an adequate understanding of the risk factors associated with rehospitalization[9]. Previous research has identified a number of important risk factors, including recurrent AP, discharge to nonhome facilities, a higher Charlson Comorbidity Index, a longer hospital stay, smoldering symptoms, and/or local pancreatic complications[9-12]. Pertinently, early readmission can often be due to smoldering symptoms and the progression of local complications of AP[13]. These two factors are responsible for up to 38% of all readmissions in AP cases[9]. Therefore, it is imperative to investigate the specific effect of various AP-related local complications on readmission.

Acute peripancreatic fluid collection (APFC) is a homogeneous collection with fluid density that can form within or around the pancreas following acute interstitial edematous pancreatitis[14]. The revised Atlanta classification defines it as an early local complication that develops within four weeks with no associated peripancreatic necrosis[14]. A retrospective cohort study from Saudi Arabia revealed an APFC incidence of 48.3% in patients presenting with AP[15]. A prospective multicenter study from Korea also revealed an incidence of 42.7%[16]. It is known that significant morbidity may arise from APFC due to hemorrhage, biliary obstruction, gastric outlet obstruction, and secondary infection[17]. However, there is a paucity of population-based research investigating the relationship between APFC and 30-day readmission rates and inpatient outcomes in AP. In recent years, a number of endoscopic interventions have been introduced for pancreatic fluid collections with acceptable safety and efficacy[18-21]. Therefore, clinical evidence regarding APFC-related readmission rates and predictors may help in improving patient outcomes.

To our knowledge, this is the first cohort study conducted in the United States with the aim of evaluating 30-day readmission rates and predictors linked to APFC in patients with AP using a multicenter database. These predictors may help to identify high-risk patients, provide an opportunity to improve the quality of care and discharge planning, reduce morbidity, and save valuable hospital resources by reducing readmissions in AP. Our findings regarding APFC-related readmission risk may also help in refining the selection criteria for a timely treatment for peripancreatic fluid collections.

MATERIALS AND METHODS

Design and data source

We utilized data from the publicly available Nationwide Readmission Database (NRD) from 2016 to 2019[22]. NRD was developed by the Agency for Healthcare Research and Quality (AHRQ) as part of the Healthcare Cost and Utilization Project (HCUP)[22]. The database includes samples from 22 state inpatient registries, accounting for approximately 50% of the population and hospitalizations in the United States[22]. Complete information about sample procedures and NRD design can be accessed at: <https://www.hcup-us.ahrq.gov/nrdoverview.jsp>. NRD 2016 and above uses the International Classification of Diseases, Tenth Revision (ICD-10) codes to identify diagnoses and procedures. It also contains several hospital-specific variables and predefined comorbid conditions (Elixhauser comorbidities)[23]. The NRD uses unique identification numbers to follow the same patient through multiple hospital stays within the same state. However, it does not track patients across different states or over the transition to a new year. In line with previous research, individuals who had been discharged in December were not included in our analysis because their readmissions might have occurred in January of the subsequent year[24]. This retrospective cohort study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[25].

Study population

The ICD-10 codes were used to identify index admissions with a primary diagnosis of AP (I10_DX1) (Supplementary Table 1). These admissions were further classified into: (1) Patients with a secondary diagnosis of APFC on index admission; and (2) those without a secondary diagnosis of APFC on index admission using the ICD-10 code "K86.3" (I10_DX2-40). According to the revised Atlanta classification, a pancreatic pseudocyst takes at least four weeks to form[14]. Therefore, collections developed during index hospitalization should be reported as APFC. Hence, this code is thought to be more indicative of APFC than pancreatic pseudocyst. Participants were excluded if their age was < 18 years or they had concomitant comorbid conditions such as malignant neoplasm, lymphoma, end-stage renal disease, solid organ malignancies, paraplegia, or paresis. These were considered high-risk conditions that could confound the analysis. Patients were also excluded if they had elective or same-day readmissions. The final weighted analytical cohort had a total of 673059 and 67828 patients before and after propensity score matching, respectively.

Outcome measures

The major outcomes of interest included 30-day readmission rates, the incidence of inpatient complications, length of stay (LOS), hospital charges, and factors influencing readmission among AP patients with APFC compared to those without APFC.

Statistical analysis

Propensity score matching was used to create matched cohorts, which reduced the influence of comorbid imbalances between comparative cohorts. Each case was ascribed a propensity score based on a multivariable logistic regression model that considered the baseline demographics of the patient, any Elixhauser comorbidities, and the characteristics of the institution. We then utilized a 1:1 matching algorithm by general caliper matching (without replacement) using a caliper width equal to 0.2 of the standard deviation of the propensity score[26]. In unadjusted analyses, continuous variables were reported as medians with an interquartile range (IQR) and were compared using Mann-Whitney *U* tests. Categorical variables were presented as frequencies with percentages and were compared using χ^2 tests. The discharge weights provided by the HCUP were used to obtain national estimates. All *P* values were two-sided. A univariate Cox regression model was initially used for readmission risk to report hazard ratios (HR) with a 95% confidence interval (CI) in the matched cohort. A multivariate model was then prepared for final predictors, including variables with *P* < 0.20 from univariate analysis, and results were reported as adjusted hazard ratios (aHR). The Kaplan-Meier curve was generated to display the overall risk of readmission between cases and controls, and significance was assessed using the log-rank test. The Statistical Software for Data Science (STATA) (StataCorp LLC, College Station, TX, United States), version 16.0, was used for statistical analysis. The 'pmsampsize' command in STATA was utilized to calculate the minimum sample size to assess a risk ratio of at least 50% (HR 1.5) between cases and controls for readmission. This computation indicated that a minimum sample size of 800 in each arm was sufficient.

Ethical considerations

The NRD uses de-identification and anonymization strategies to protect the privacy of patients. The present study did not require institutional review board oversight as it contains de-identified, publicly available observations that cannot be connected to or identified with any specific person. The patient consent for participation and publication of these data was also waived. According to the HCUP Data Use Agreement, any individual table cell counts of ≤ 10 have been masked to ensure privacy and compliance.

RESULTS

Patient characteristics

Clinical characteristics of patients with a primary diagnosis of AP stratified by APFC on index admission are outlined (Table 1). In the unmatched cohort of 673059 patients, 5.1% had a secondary diagnosis of APFC. The propensity-matched cohort included 33914 in each arm with a satisfactory balance of comorbidities. In the matched cohort, the median (IQR) index LOS was longer among patients with APFC compared to those without APFC [4 (3-7) vs 3 (2-5) days, *P* < 0.001]. The median (IQR) index hospitalization cost was higher in the APFC cohort than the non-APFC cohort [\$29451 (\$17292-\$56774) vs \$24418 (\$14865-\$42640), *P* < 0.001]. The Elixhauser comorbidities of index AP hospitalizations before and after matching were also stratified by APFC (Table 2).

Clinical outcomes in index hospitalizations

In the matched cohort, there was a higher incidence of septic shock (3.1% vs 1.3%, *P* < 0.001), mechanical ventilation (1.8% vs 0.9%, *P* < 0.001), portal venous thrombosis (4.4% vs 0.8%, *P* < 0.001), splenic venous thrombosis (2.4% vs 0.5%, *P* < 0.001), intensive care unit (ICU) level care (1.5% vs 0.8%, *P* < 0.001), vasopressor use (0.4% vs 0.2%, *P* < 0.001), diarrhea (3.2% vs 2.6%, *P* < 0.001), and jaundice (3.0% vs 1.4%, *P* < 0.001) in patients with APFC compared to those without APFC (Table 3). Participants in both cohorts also showed a higher predilection for a number of endoscopic diagnostic and therapeutic procedures.

Acute peripancreatic fluid collections and early readmission

After propensity score matching, 30-day readmissions were higher among AP patients with APFC than non-APFC (15.7% vs 6.5%, *P* < 0.001). For patients who had an APFC on readmission, the median readmission LOS was longer than patients without an APFC [4 (IQR 3-7) vs 3 (IQR 2-5) days, *P* < 0.001]. The median readmission costs were also higher among patients who had APFCs on readmission compared to the non-APFC cohort [\$28282 (\$17012-\$50543) vs \$22865 (\$14131-\$39627), *P* < 0.001]. A plethora of causes were found to be responsible for hospital readmissions in both cohorts (Figure 1). Notably, 3.5% of patients who did not have APFC at their index admission were readmitted due to a new pseudocyst/APFC diagnosis. The presence of an APFC increased the risk of readmission twofold [aHR 2.52 (95%CI: 2.40-2.65), *P* < 0.001] (Figure 2).

Clinical predictors of early readmission

A complete univariate and multivariate analysis was conducted to find independent predictors of 30-day readmission after discharge with a primary diagnosis of AP with APFC (Supplementary Table 2). A number of variables were found to increase the risk of readmission, including female gender [aHR 0.93 (95%CI: 0.89-0.98) *P* = 0.01], Elixhauser Comorbidity Index ≥ 3 [aHR 1.55 (95%CI: 1.34-1.8), *P* < 0.001], chronic pulmonary diseases [aHR 1.15 (95%CI: 1.08-1.22), *P* < 0.001], chronic renal disease (ESRD not included) [aHR 1.17 (95%CI: 1.07-1.41), *P* = 0.01], protein-calorie malnutrition [aHR 1.19 (95%CI: 1.12-1.26), *P* < 0.001], alcohol abuse [aHR 1.17 (95%CI: 1.11-1.23), *P* < 0.001], substance abuse [aHR 1.11 (95%CI: 1.03-1.2), *P* = 0.005], depression [aHR 1.11 (95%CI: 1.04-1.18), *P* = 0.045], portal venous thrombosis [aHR 1.65 (95%CI: 1.47-1.85), *P* < 0.001], and splenic venous thrombosis [aHR 1.57 (95%CI: 1.34-1.84), *P* < 0.001]. Several procedures

Table 1 Clinical characteristics of patients with primary diagnosis of acute pancreatitis, stratified by acute peripancreatic fluid collections on index admission, *n* (%)

Patient characteristics	Before matching			After matching		
	No acute peripancreatic fluid collections	Acute peripancreatic fluid collections	<i>P</i> value	No acute peripancreatic fluid collections	Acute peripancreatic fluid collections	<i>P</i> value
Total patients	638801	34258		33914	33914	
Age in years at admission, median (IQR)	52.0 (39.0, 63.0)	49.0 (38.0, 59.0)	< 0.001	51.0 (39.0, 61.0)	49.0 (38.0, 58.0)	< 0.001
Age groups (yr)			< 0.001			< 0.001
18-33	108146 (16.9)	5663 (16.5)		5716 (16.9)	5641 (16.6)	
34-49	181354 (28.4)	12056 (35.2)		10353 (30.5)	11962 (35.3)	
50-64	200484 (31.4)	11619 (33.9)		11169 (32.9)	11490 (33.9)	
65-79	107936 (16.9)	4118 (12.0)		4895 (14.4)	4033 (11.9)	
≥ 80	40881 (6.4)	802 (2.3)		1781 (5.3)	788 (2.3)	
Length of stay (days), median (IQR)	3.0 (2.0, 5.0)	4.0 (3.0, 7.0)	< 0.001	3.0 (2.0, 5.0)	4.0 (3.0, 7.0)	< 0.001
Total charges (USD), median (IQR)	24238.0 (14623.0, 42043.0)	29616.5 (17365.0, 57476.0)	< 0.001	24418.5 (14865.0, 42640.5)	29451.0 (17292.0, 56774.0)	< 0.001
30-day readmission	37949 (5.9)	5363 (15.7)		2215 (6.5)	5326 (15.7)	< 0.001
Elixhauser Comorbidity Index score			< 0.001			0.093
0	49536 (7.8)	1366 (4.0)		1430 (4.2)	1366 (4.0)	
1	97030 (15.2)	3875 (11.3)		3994 (11.8)	3875 (11.4)	
2	131055 (20.5)	6353 (18.5)		6472 (19.1)	6353 (18.7)	
≥ 3	361180 (56.5)	22664 (66.2)		22018 (64.9)	22320 (65.8)	
Primary payer			< 0.001			< 0.001
Medicare	195352 (32.1)	7702 (23.8)		9348 (29.1)	7572 (23.6)	
Medicaid	140070 (23.0)	9413 (29.1)		8332 (25.9)	9340 (29.2)	
Private	213873 (35.1)	11274 (34.8)		10763 (33.5)	11163 (34.8)	
Other	60026 (9.9)	3980 (12.3)		3697 (11.5)	3958 (12.4)	
Median household income national quartile for patient ZIP code			< 0.001			0.005
1 st (0-25 th)	203221 (32.2)	11120 (32.9)		11169 (33.3)	11002 (32.8)	
2 nd (26 th -50 th)	177998 (28.2)	9619 (28.4)		9373 (28.0)	9535 (28.5)	
3 rd (51 st -75 th)	148894 (23.6)	8093 (23.9)		7756 (23.2)	8020 (23.9)	
4 th (76 th -100 th)	100757 (16.0)	5018 (14.8)		5199 (15.5)	4955 (14.8)	
Disposition of patient (uniform)			< 0.001			< 0.001
Routine	561425 (87.9)	28082 (82.0)		29204 (86.1)	27894 (82.3)	
Transfer to short-term hospital	4817 (0.8)	753 (2.2)		275 (0.8)	742 (2.2)	
Transfer other: SNF, ICF, another type of facility	17446 (2.7)	1392 (4.1)		1074 (3.2)	1320 (3.9)	
Home health care	27211 (4.3)	2600 (7.6)		1600 (4.7)	2540 (7.5)	

Against medical advice	25350 (4.0)	1209 (3.5)		1582 (4.7)	1207 (3.6)	
Died during hospitalization	2386 (0.4)	209 (0.6)	< 0.001	169 (0.5)	198 (0.6)	0.12

SNF: Skilled nursing facility; ICF: Intermediate care facility; IQR: Interquartile range.

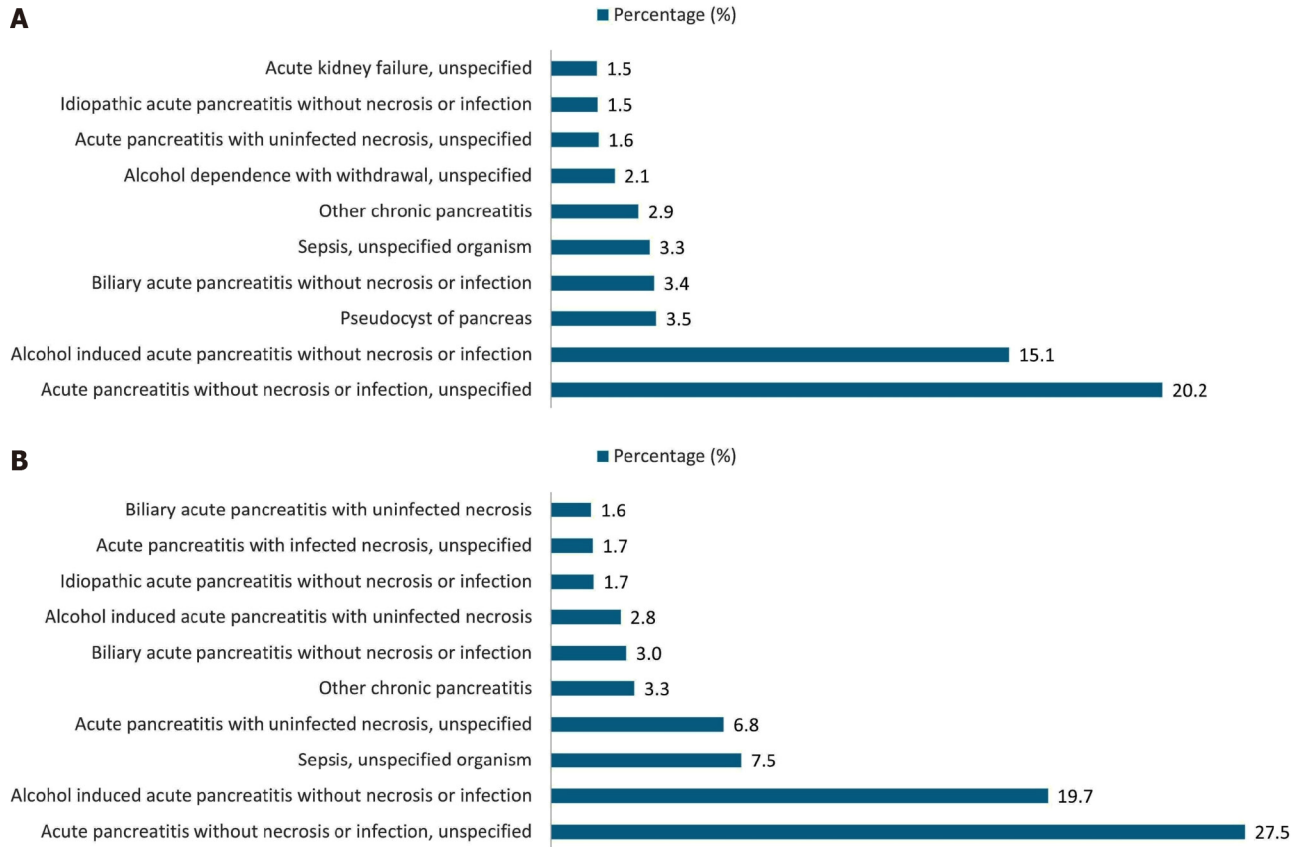


Figure 1 Absolute rates of cause-specific 30-day readmission stratified by acute peripancreatic fluid collections on index admission in the matched cohort. A: No acute peripancreatic fluid collection; B: Acute peripancreatic fluid collection.

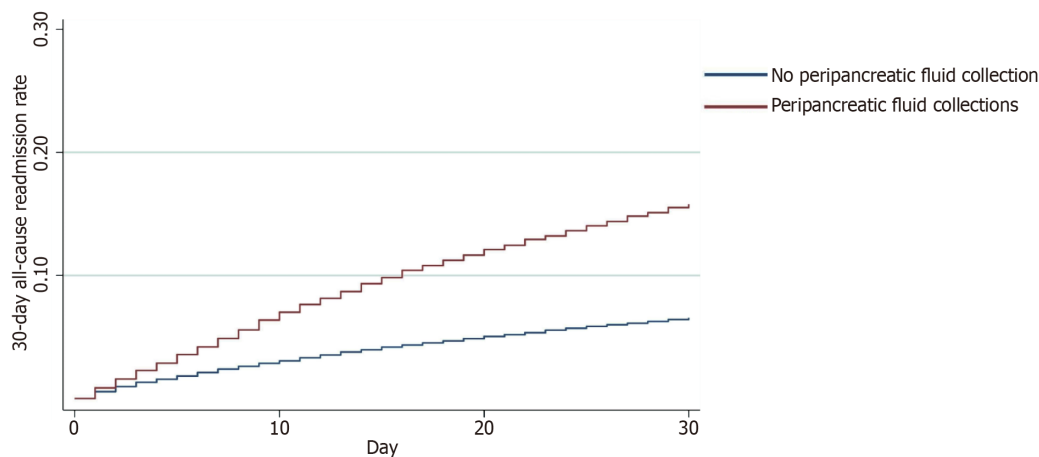


Figure 2 The 30-day readmission risk based on acute peripancreatic fluid collections present on readmission in patients with a primary diagnosis of acute pancreatitis in the matched cohort (log rank $P < 0.01$).

Table 2 Distribution of the Elixhauser comorbidities in patients with acute pancreatitis as a primary diagnosis during index hospitalizations, both before and after matching, stratified by acute peripancreatic fluid collections, *n* (%)

Factors	Before matching		P value	After matching		P value
	No acute peripancreatic fluid collections	Acute peripancreatic fluid collections		No acute peripancreatic fluid collections	Acute peripancreatic fluid collections	
Total patients	638801	34258		33914	33914	
Congestive heart failure	41809 (6.5)	1922 (5.6)	< 0.001	1804 (5.3)	1804 (5.3)	1.00
Cardiac arrhythmias	71251 (11.2)	3992 (11.7)	0.004	3745 (11.0)	3909 (11.5)	0.047
Valvular disease	13556 (2.1)	505 (1.5)	< 0.001	439 (1.3)	439 (1.3)	1.00
Pulmonary circulation	7130 (1.1)	482 (1.4)	< 0.001	380 (1.1)	380 (1.1)	1.00
Peripheral vascular disease	22966 (3.6)	1354 (4.0)	< 0.001	1248 (3.7)	1248 (3.7)	1.00
Uncomplicated hypertension	293986 (46.0)	16996 (49.6)	< 0.001	16804 (49.5)	16804 (49.5)	1.00
Chronic pulmonary diseases	99431 (15.6)	5533 (16.2)	0.004	5264 (15.5)	5440 (16.0)	0.064
Uncomplicated diabetes	90054 (14.1)	4365 (12.7)	< 0.001	4261 (12.6)	4261 (12.6)	1.00
Complicated diabetes	91044 (14.3)	4178 (12.2)	< 0.001	4049 (11.9)	4049 (11.9)	1.00
Hypothyroidism	58431 (9.1)	2132 (6.2)	< 0.001	2028 (6.0)	2028 (6.0)	1.00
Chronic renal disease	55947 (8.8)	2114 (6.2)	< 0.001	2458 (7.2)	2063 (6.1)	0.088
Liver disease	130401 (20.4)	8674 (25.3)	< 0.001	8303 (24.5)	8554 (25.2)	0.096
PUD excluding bleeding	10343 (1.6)	634 (1.9)	< 0.001	582 (1.7)	582 (1.7)	1.00
HIV/AIDS	2063 (0.3)	128 (0.4)	0.11	115 (0.3)	115 (0.3)	1.00
Rheumatoid arthritis/CVD	13799 (2.2)	569 (1.7)	< 0.001	504 (1.5)	504 (1.5)	1.00
Coagulopathy	42399 (6.6)	2778 (8.1)	< 0.001	2667 (7.9)	2667 (7.9)	1.00
Obesity	118599 (18.6)	4066 (11.9)	< 0.001	3946 (11.6)	3946 (11.6)	1.00
Weight loss	34338 (5.4)	6255 (18.3)	< 0.001	6053 (17.8)	6053 (17.8)	1.00
Fluid and electrolyte disorder	251252 (39.3)	16382 (47.8)	< 0.001	16174 (47.7)	16174 (47.7)	1.00
Blood loss anemia	1984 (0.3)	211 (0.6)	< 0.001	119 (0.4)	206 (0.6)	< 0.001
Iron-deficiency anemia	23358 (3.7)	2539 (7.4)	< 0.001	1557 (4.6)	2512 (7.4)	< 0.001
Alcohol abuse	198085 (31.0)	17070 (49.8)	< 0.001	16908 (49.9)	16908 (49.9)	1.00
Substance abuse	57163 (8.9)	4181 (12.2)	< 0.001	4074 (12.0)	4074 (12.0)	1.00
Tobacco use disorder	96674 (15.1)	4761 (13.9)	< 0.001	4616 (13.6)	4689 (13.8)	0.42
Smoking history	4722 (0.7)	276 (0.8)	0.16	199 (0.6)	274 (0.8)	< 0.001
Psychoses	7357 (1.2)	471 (1.4)	< 0.001	418 (1.2)	469 (1.4)	0.085
Depression	93044 (14.6)	5899 (17.2)	< 0.001	5445 (16.1)	5804 (17.1)	< 0.001
Complicated hypertension	72236 (11.3)	2941 (8.6)	< 0.001	3136 (9.2)	2836 (8.4)	< 0.001

PUD: Peptic ulcer disease; HIV: Human immunodeficiency virus; AIDS: Acquired immunodeficiency syndrome; CVD: Collagen vascular disorder.

were also identified as predictors, including endoscopic retrograde cholangiography (no intervention) [aHR 0.66 (95% CI: 0.52-0.85), $P = 0.001$], endoscopic dilation of the ampulla and biliary duct [aHR 0.65 (95% CI: 0.47-0.9), $P = 0.01$], and endoscopic removal of stone(s) from the biliary tract [aHR 0.69 (95% CI: 0.54-0.89), $P = 0.005$].

DISCUSSION

This population-based study shows that patients diagnosed with an APFC during their initial AP hospitalization have a higher 30-day readmission risk. Patients with APFC also have a higher incidence of inpatient complications, a longer LOS, and higher healthcare costs than those without APFC. A number of readmission predictors were identified to help stratify high-risk AP patients with APFC, which may aid in reducing healthcare burden.

Hospital readmission for AP has been extensively researched[9,27,28]. However, the specific association between APFC and early readmission has not been investigated. Our study revealed a significantly higher 30-day readmission risk among AP patients with APFC compared to those without APFC (aHR 2.52, $P < 0.001$). While there is a paucity of evidence on gender-specific outcomes of AP, readmission has often been associated with male gender[11,13,29]. However, a prospective study also identified female gender as a significant predictor of AP readmission (odds ratio 2.57, 95% CI: 1.13-5.81, $P = 0.024$)[30]. Our analysis also revealed female gender as a risk factor for 30-day readmission in AP patients with APFC. Consistent with previous research, an Elixhauser Comorbidity Index score of ≥ 3 was another independent predictor of 30-day readmission in our APFC cohort[9,29]. A retrospective study from the United States revealed chronic pulmonary disease as a readmission predictor after biliary AP (aHR 1.22, $P < 0.001$)[31]. Previous studies demonstrated that protein-energy malnutrition and chronic kidney disease may also predict readmission in patients with AP[27,32]. Similarly, early systemic anticoagulation in severe AP cases may help in reducing venous thrombosis, which may also help in decreasing readmission risk[33]. In our analysis, chronic pulmonary diseases, protein-calorie malnutrition, chronic kidney disease, and portal and splenic venous thrombosis were also identified as predictors of readmission. Therefore, it is important for clinicians to screen AP patients with APFC for these comorbidities to evaluate the readmission risk.

Alcohol-associated AP was the second most common etiology for 30-day readmissions in our study. It was also associated with worse outcomes in both the APFC and the non-APFC cohorts. Alcohol abuse has been linked in the past to increased rates of AP readmissions. In two retrospective studies from the United States, 30-day readmission rates for alcohol-related AP ranged from 12% to 70%[34,35]. Furthermore, alcoholic etiology is also independently associated with organ failure and pancreatic necrosis in index AP events[36]. Pertinently, Sorrento *et al*[37] conducted a retrospective study showing AP patients who received alcohol cessation counseling were half as likely to be readmitted after 30 days compared to those who did not get therapy (odds ratio 0.52, $P = 0.046$). Similarly, a post-hoc data analysis showed that 79% of patients with alcohol-related AP who received brief psychological intervention reported abstinence and no 30-day readmission for recurrent AP[38]. Moreover, the brief intervention effectively decreased gamma-glutamyl transferase levels, correlating this reduction with alcohol abstinence[38]. Notably, depression was also one of the predictors of AP readmission in our APFC cohort. Therefore, psychiatric evaluation and therapy may help to decrease readmissions in AP patients with APFC suspected to have depression or substance use disorder.

Hospital readmissions are a significant problem in the context of healthcare policy and reform[39,40]. The rates of readmission may indicate the quality of care offered by hospitals, which may be independent of patient-level factors[41]. As up to 50% of readmissions are potentially preventable, a decreased complexity of inpatient care may help improve the early readmission rate[42-44]. Our study revealed that the presence of APFC increases the risk of readmission up to twofold. In a retrospective study from the United States, AP patients with 30-day readmissions had a 4.5 times higher one-year mortality risk than those who were not readmitted (HR 4.5, 95% CI: 2.2-9.1)[45]. Therefore, the concurrent occurrence of APFC and any of the aforementioned predictors in index AP hospitalizations merits effective prognostication and clinical vigilance. AP patients with APFC may also require tailored clinical management[46]. Approximately 50% of APFCs produce minimal to no symptoms and undergo spontaneous resolution with supportive medical care[47]. However, persistent symptoms and APFC-related complications necessitate invasive treatments, including percutaneous, surgical, or endoscopic drainage procedures[48].

We also observed a higher rate of inpatient complications among AP patients with APFC compared to those without APFC. These included ICU admission, progression to septic shock, vasopressor use, mechanical ventilation, and portal and splenic venous thrombosis. In two retrospective studies from China, the systemic immune-inflammation index (SII) was considered a severity predictor and a marker of serious complications like acute kidney injury (AKI) in patients with severe AP[49,50]. In a retrospective study from Turkey, Solakoglu *et al*[51] revealed that the presence of APFC in AP patients was associated with higher values of SII and C-reactive protein. Therefore, the higher rate of inpatient complications may be explained by possible higher levels of SII in the APFC cohort compared to the non-APFC cohort. Sepsis, vasopressor use, and mechanical ventilation in AP patients may also predict other major complications, such as early AKI [52]. A prospective trial from Korea also underscored the clinical importance of close observation for late complications in patients with an early radiological identification of an APFC, especially in moderately severe and severe AP patients[53]. Therefore, APFC detection supplements the need for careful surveillance in moderate and severe AP.

In our study, AP patients with APFC showed higher odds of progression to septic shock compared to those without APFC. A prospective multicenter study from Germany showed colonization of peripancreatic fluid collections in 59% of cultures of the collections[54]. Notably, this study had no clear demarcation of the type of peripancreatic collections (50% of the patients were hospitalized for < 1 month), the positive cultures could have been related to pancreatic seeding of extrapancreatic infections, and it may be a simple colonization rather than a true infection[55]. APFCs have previously

Table 3 Clinical outcomes of patients with a primary diagnosis of acute pancreatitis during index hospitalizations, stratified by acute peripancreatic fluid collections on index admission, *n* (%)

Clinical outcomes	Before matching			After matching		
	No acute peripancreatic fluid collections	Acute peripancreatic fluid collections	<i>P</i> value	No acute peripancreatic fluid collections	Acute peripancreatic fluid collections	<i>P</i> value
Total patients	638801	34258		33914	33914	
Cholangitis	3814 (0.6)	164 (0.5)	0.005	190 (0.6)	160 (0.5)	0.11
Mechanical ventilation	3309 (0.5)	669 (2.0)	< 0.001	300 (0.9)	626 (1.8)	< 0.001
Nausea	13222 (2.1)	650 (1.9)	0.029	752 (2.2)	641 (1.9)	0.003
Diarrhea	15337 (2.4)	1089 (3.2)	< 0.001	898 (2.6)	1074 (3.2)	< 0.001
Septic shock	5693 (0.9)	1110 (3.2)	< 0.001	451 (1.3)	1057 (3.1)	< 0.001
Portal venous thrombosis	4079 (0.6)	1521 (4.4)	< 0.001	265 (0.8)	1487 (4.4)	< 0.001
Splenic venous thrombosis	3194 (0.5)	818 (2.39)	< 0.001	154 (0.5)	811 (2.4)	< 0.001
ICU level admission	3118 (0.5)	529 (1.5)	< 0.001	284 (0.8)	496 (1.5)	< 0.001
Vasopressor use	772 (0.1)	138 (0.4)	< 0.001	70 (0.2)	130 (0.4)	< 0.001
Acute kidney injury	68459 (10.7)	3843 (11.2)	0.004	4038 (11.9)	3744 (11.0)	< 0.001
New RRT during admission	8545 (1.3)	434 (1.3)	0.27	386 (1.1)	421 (1.2)	0.22
Abdominal pain	3070 (0.5)	124 (0.4)	0.002	159 (0.5)	120 (0.4)	0.019
Jaundice	8149 (1.3)	1024 (3.0)	< 0.001	461 (1.4)	1013 (3.0)	< 0.001
Obstruction of bile duct	35968 (5.6)	2340 (6.8)	< 0.001	2259 (6.7)	2319 (6.8)	0.36
Endoscopic retrograde cholangiography (no intervention)	19309 (3.0)	395 (1.2)	< 0.001	740 (2.2)	390 (1.1)	< 0.001
ERCP biliary with intervention	31525 (4.9)	1150 (3.4)	< 0.001	1339 (3.9)	1134 (3.3)	< 0.001
Endoscopic dilation of ampulla and biliary duct	9456 (1.5)	253 (0.7)	< 0.001	413 (1.2)	249 (0.7)	< 0.001
Endoscopic insertion of stent (tube) into bile duct	9784 (1.5)	751 (2.2)	< 0.001	495 (1.5)	743 (2.2)	< 0.001
Endoscopic removal of stone(s) from biliary tract	19161 (3.0)	388 (1.1)	< 0.001	759 (2.2)	384 (1.1)	< 0.001
Endoscopic biopsy of bile duct	2002 (0.3)	62 (0.2)	< 0.001	99 (0.3)	62 (0.2)	0.004
ERCP pancreatic with intervention	6282 (1.0)	1107 (3.2)	< 0.001	323 (1.0)	1094 (3.2)	< 0.001
Endoscopic insertion of stent (tube) into pancreatic duct	5263 (0.8)	1005 (2.9)	< 0.001	278 (0.8)	993 (2.9)	< 0.001
Endoscopic removal of stone(s) from pancreatic duct	1045 (0.2)	152 (0.4)	< 0.001	64 (0.2)	150 (0.4)	< 0.001
Endoscopic dilation of pancreatic duct	583 (0.1)	51 (0.1)	< 0.001	28 (0.1)	50 (0.1)	0.013

RRT: Renal replacement therapy; ERCP: Endoscopic retrograde cholangiopancreatography.

been considered low-risk entities for infections. However, our results are concerning due to the higher risk of septic shock among AP patients with APFC, possibly following infected APFCs or extrapancreatic infections. It shows the need for pertinent measures to avoid septic complications in these patients. Clinical practice guidelines from the American College of Gastroenterology, the International Association of Pancreatology (IAP), and the American Pancreatic Association (APA) require a confirmed pancreatic or extrapancreatic infection to start antibiotic treatment[56,57]. Therefore, clinicians should remain vigilant for concomitant infections in AP patients. Early diagnosis and treatment may help to avoid serious complications such as septic shock.

Inpatient complications may also occur following iatrogenic adverse events in index hospitalizations. Our data show that both cohorts underwent a variety of endoscopic diagnostic and therapeutic procedures. Moreover, published literature describes the risk of late complications weeks after the intervention, specifically for peripancreatic fluid collections[58,59]. In our analysis, several procedures were also identified as 30-day readmission predictors in AP patients with APFC, including endoscopic retrograde cholangiography (no intervention), endoscopic dilation of the ampulla and biliary duct, and endoscopic stone removal from the biliary tract. In a retrospective study from the United States, Kim *et al*[60] showed that surgical or percutaneous drainage of APFC and pancreatic pseudocysts may have a higher burden of illness and an increased local complication risk necessitating intervention compared to endoscopic drainage procedures. Therefore, it is important to opt for appropriate drainage procedures after careful patient selection[60]. Moreover, the American Society of Gastrointestinal Endoscopy recommends bacteremia risk assessment for endoscopic procedures such as drainage of peripancreatic collections[61]. Patients at risk of septic complications may receive antibiotic prophylaxis after this assessment[61]. Notably, the inpatient mortality was similar in both cohorts during index admissions (0.6% *vs* 0.5%, $P = 0.12$). However, AP patients with APFC may require targeted clinical treatment due to their higher risk of complications.

The APFC cohort showed higher hospital resource utilization compared to the non-APFC cohort in our analysis. In index hospitalizations, the LOS was longer (4 *vs* 3 days, $P < 0.001$) and costlier (\$29451 *vs* \$24418, $P < 0.001$). These trends could be attributed to the higher incidence of inpatient complications in our APFC cohort. Furthermore, these patients were more frequently discharged to short-term hospitals, skilled nursing facilities, and home health care. This trend may have also contributed to additional healthcare costs in the APFC cohort. The readmissions also revealed higher costs in the APFC cohort than the non-APFC cohort (\$28282 *vs* \$22865, $P < 0.001$). The median cost of readmissions was also higher compared to index hospitalizations. In a recent international survey, Nagy *et al*[62] revealed the efficacy of the AP discharge protocol in significantly reducing median LOS and recurrent AP-related readmission rates. Our findings could enable pancreatologists to devise novel discharge protocols that include index admission APFC and assess their impact in future research.

This retrospective cohort study has several strengths. It has a large sample size, sufficient statistical power to detect meaningful differences in outcomes, and the generalizability of the findings. Our sample population from the NRD also permits the evaluation of real-world healthcare utilization trends, including readmission rates and healthcare costs. Moreover, we used propensity-matching techniques in our analysis. In retrospective studies, these techniques can minimize confounding variables and increase the validity of the findings. Therefore, this study has pertinent implications for highlighting the clinical association between APFC and readmission risk in patients with AP. It also provides crucial insights into healthcare outcomes and utilization patterns in these patients.

Limitations

There are certain limitations to our study. One major limitation is the lack of data regarding the severity of illnesses and laboratory evaluations in the NRD. Furthermore, coding accuracy in administrative databases may vary, potentially leading to errors in identifying outcomes of interest or misclassification bias. There is also potential for selection bias in propensity score matching, which balances patient characteristics between those with and without APFC. During data extraction for our analysis, efforts were made to include only patients with an APFC diagnosis and exclude those with pancreatic necrosis (K8501, K8502, K8511, K8512, K8521, K8522, K8531, K8532, K8581, and K8582). However, there is a possibility that some misclassification may have occurred. Finally, retrospective studies cannot establish causality as they are observational and cannot account for unmeasured confounding variables.

CONCLUSION

This study reveals a correlation between the development of an APFC during index AP hospitalization and higher rates of readmission, increased inpatient complications, longer LOS, and higher healthcare costs. The readmission predictors included female gender, Elixhauser Comorbidity Index ≥ 3 , chronic pulmonary diseases, chronic renal disease, protein-calorie malnutrition, alcohol abuse, substance abuse, depression, portal and splenic venous thrombosis, and certain procedures. The readmission rate for AP patients with APFC may be reduced by vigilant surveillance of these predictors, efficient infection screening, and safe interventions. Psychological evaluation and counseling strategies can also help AP patients with psychiatric comorbidities. Our analysis may enable pancreatologists and gastroenterologists to improve patient outcomes by including APFC as a factor in AP discharge protocols.

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FOOTNOTES

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Informed consent statement: Participants were not required to give informed consent for this retrospective cohort study since the analysis of baseline characteristics used anonymized clinical data.

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