

Hospital frailty risk score predicts worse outcomes in patients with chronic pancreatitis

Aalam Sohal^{a*}, Hunza Chaudhry^{b*}, Isha Kohli^c, Gagan Gupta^d, Piyush Singla^d, Raghav Sharma^e, Dino Dukovic^f, Devang Prajapati^g

Liver Institute Northwest, Seattle, WA; University of California, San Francisco, Fresno, CA, USA; Icahn School of Medicine, Mount Sinai, New York, NY, USA, USA; Dayanand Medical College and Hospital, Punjab, India; Punjab Institute of Medical Sciences, Punjab, India; Ross University School of Medicine, Bridgetown, Barbados

Abstract

Background Chronic pancreatitis (CP) is a pathological fibroinflammatory response to persistent inflammation or stress to the pancreas. The effect of frailty on outcomes in patients with CP has not been previously examined. In this study, we examined the effect of frailty on outcomes in hospitalized patients with CP.

Methods Records of patients with a primary or secondary discharge diagnosis of CP (ICD10-CM codes K86.0, K86.1) between January 2016 and December 2019 were obtained from the National Inpatient Sample database. Data were collected on patient demographics, hospital characteristics, comorbidities, and etiology of CP. The relationship between frailty and outcomes, including mortality, intensive care unit (ICU) admission, sepsis, shock, length of stay (LOS), and total hospitalization charges (THC), were analyzed using multivariate analysis.

Results 722,160 patients were included in the analysis. Patients with a high hospital frailty risk score had a higher mortality risk (adjusted odds ratio [aOR] 12.57, 95% confidence interval [CI] 10.42-15.16; $P < 0.001$) compared to patients with low frailty scores. Patients with high frailty scores also had a higher risk of sepsis (aOR 5.75, 95%CI 4.97-6.66; $P < 0.001$), shock (aOR- 26.25, 95%CI-22.83-30.19; $P < 0.001$), ICU admission (aOR 25.86, 95% CI-22.58-29.62; $P < 0.001$), and acute kidney injury (aOR 24.4, 95%CI 22.39-26.66; $P < 0.001$). They also had a longer LOS (7.04 days, 95%CI 6.57-7.52; $P < 0.001$) and higher THC (\$72,200, 95%CI 65,904.52-78,496.66; $P < 0.001$).

Conclusions Frail patients, as determined by their hospital frailty risk score, are at high risk of worse outcomes. This data suggests opportunities for physicians to risk-stratify patients and predict outcomes.

Keywords Chronic pancreatitis, frailty, national inpatient sample

Ann Gastroenterol 2023; 36 (1): 73-80

^aLiver Institute Northwest, Seattle, WA (Aalam Sohal); ^bDepartment of Internal Medicine, University of California, San Francisco, Fresno, CA, USA (Hunza Chaudhry); ^cDepartment of Public Health, Icahn School of Medicine, Mount Sinai, New York, NY, USA (Isha Kohli); ^dDayanand Medical College and Hospital, Punjab, India (Gagan Gupta, Piyush Singla); ^ePunjab Institute of Medical Sciences, Punjab, India (Raghav Sharma); ^fRoss University School of Medicine, Bridgetown, Barbados (Dino Dukovic); ^gDepartment of Gastroenterology and Hepatology, University of California, San Francisco, Fresno, CA, USA (Devang Prajapati)
^{*}Both authors contributed equally to the manuscript

Conflict of Interest: None

Correspondence to: Hunza Chaudhry, MD, 155 N. Fresno St., Fresno, CA 93701, USA e-mail: hunza.chaudhry@ucsf.edu

Received 11 July 2022; accepted 3 November 2022; published online 29 November 2022

DOI: <https://doi.org/10.20524/aog.2022.0765>

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms

Introduction

Chronic pancreatitis (CP) is a pathological fibroinflammatory response to persistent inflammation or stress to the pancreas. This pathological response can result in glandular fibrosis, atrophy, calcifications, blockage, or distortions of the pancreatic duct. As a result, patients can develop chronic abdominal pain, malnutrition, diabetes mellitus, and exocrine pancreatic insufficiency and have an increased risk of pancreatic ductal adenocarcinoma [1,2]. CP is an uncommon adult-onset condition with a prevalence of less than 50 per 100,000 adults in the United States (US) and a slight male predominance [3]. Mortality in patients with CP is higher than in the general population. Ten-year survival after the diagnosis has been estimated to be 70-90% [4]. Multiple scores, such as ABC, Manchester, MANNHEIM, and CPI, have been studied to stratify the severity of CP. However, the validity of the scores is inconclusive [5-8]. Thus, a clinical classification and scoring system identifying patients at risk would be beneficial to prognosticate patients.

Frailty has been defined as a decline in the function of organ systems and is associated with worse outcomes when patients are exposed to stressors [9]. Multiple studies have assessed frailty as a marker for adverse health outcomes and found it to have good predictive value [10]. In a study by Wei *et al* of patients with CP undergoing pancreatic surgery, frailty was an indicator of post-surgical complications [11]. Multiple frailty measurement tools have been developed to identify patients at risk. Some commonly used measurement tools include the FRAIL scale (questionnaire) and the CSHA clinical frailty scale [12,13]. Gilbert *et al* created a hospital frailty risk score (HFRS) using electronic health records. This score was developed using ICD-10 codes of diseases overrepresented in frail patients. Each ICD-10 code was awarded specific values in proportion to how strongly it predicted frailty and represented a suitable surrogate marker of frailty in national databases [14]. This score has been studied in patients undergoing spinal surgery, percutaneous coronary interventions, cardiac arrest and endoscopy for gastrointestinal bleeding [15-18]. In the studies mentioned above, HFRS predicted poor clinical outcomes.

Until now, no studies have assessed the effect of frailty based on HFRS score on outcomes in patients with CP. To understand the effect of frailty in patients with CP, we assessed whether HFRS could determine the outcomes in patients with CP. We hypothesize that frailty will strongly indicate worse outcomes and higher resource utilization.

Materials and methods

Data source

The National Inpatient Sample (NIS), maintained by the Healthcare Cost and Utilization Project (HCUP) of the Agency

for Healthcare Research and Quality, is the largest database of inpatient hospital stays in the United States [19]. NIS collects data from a 20% stratified sample of United States hospitals in 37 states and has been reliably used to estimate disease burden and outcomes. Each hospitalization is de-identified and maintained in the NIS as a unique entry with one primary discharge diagnosis and up to 39 secondary diagnoses during that hospitalization, depending on the year of data collection. Each entry records patient demographics, including age, sex, race, insurance status, primary and secondary procedures (up to 25), hospitalization outcome, total charges, and length of stay (LOS). Internal Review Board approval was not required, as NIS is a publicly available de-identified database.

Study population

Diagnosis codes from the International Classification of Diseases 10th Version, Clinical Modification (ICD-10 CM), were used to identify patients (age >18 years) hospitalized with CP between 2016 and 2019. Cases with missing mortality data, sex, or demographics were excluded. In total, 722,160 cases met the inclusion criteria. This information is presented in Fig. 1.

Definition of frailty

Gilbert *et al* developed HFRS using 109 ICD-10 codes [14]. These ICD-10 codes were noted to be overrepresented in frail patients. Each ICD-10 code was awarded a specific value proportional to how strongly it predicted frailty. In their analysis, HFRS >5 was used to classify patients as frail. Scores between 5-15 were classified as patients with medium frailty, while a score greater than 15 was classified as high frailty. We used a similar approach to classify our patients.

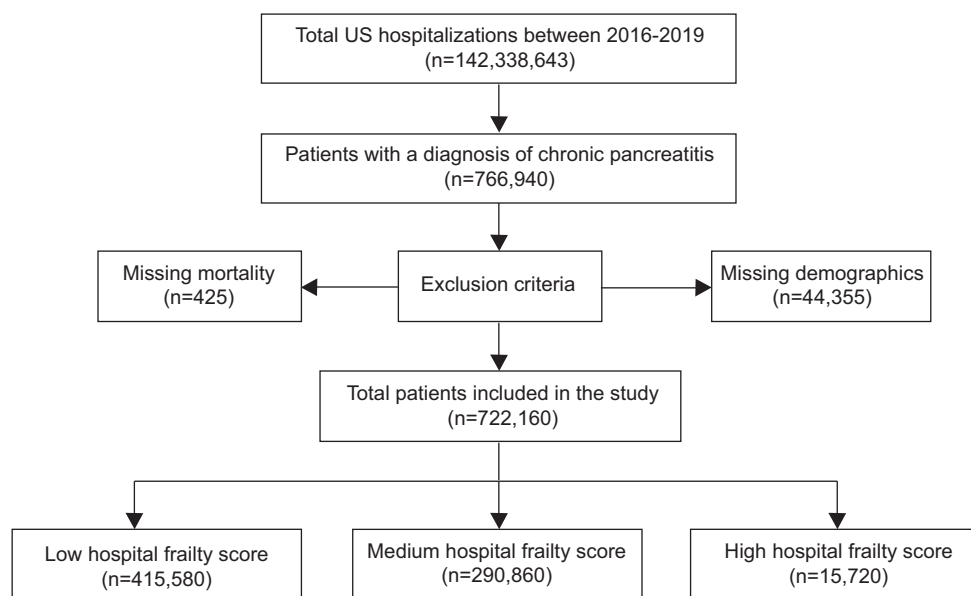


Figure 1 Flowchart of case selection for patients with chronic pancreatitis

Study outcomes and variables

The primary outcome assessed was the impact of HFRS on inpatient mortality comparing low, medium, and high HFRS. Secondary outcomes studied included shock, acute kidney injury (AKI), sepsis, and intensive care unit (ICU) admissions. We also compared the mean LOS and total hospitalization charges between HFRS as surrogate markers for healthcare cost utilization. Hospital charges were defined as the dollar amount a hospital charges for services before negotiating discounts with insurance companies.

Our primary exposure variable was the patient's HFRS. Other variables included age (divided into 3 groups: <44 years, 45-64 years, and >65 years), sex, race, primary insurance, median income, hospital characteristics such as region, bed size, and rural/urban location, pre-specified by HCUP. Data were also collected on the patients diagnosed with alcohol-related CP. To assess comorbidities, the Charlson Comorbidity Index was used. This is a well-validated index based on ICD-10 codes and intended for use on large quantities of administrative data to predict mortality and hospital resource use [20].

Statistical analysis

Hospital-level discharge weights provided by NIS were used to generate national estimates. Categorical variables were compared using the chi-square test, whereas an independent sample *t*-test was used for continuous variables. Univariate logistic regression was performed to study the effect of HFRS on categorical and continuous outcomes. It was followed by multivariate logistic regression analysis, adjusting for patient demographics, hospital characteristics, Charlson comorbidities, and CP secondary to alcohol dependence who met the cutoff on univariate analysis ($P < 0.1$). A complete list of ICD-10 codes is presented in Supplementary Table 1. The unadjusted and adjusted odds ratios were calculated with a 95% confidence interval (CI). A type I error of < 0.05 was considered statistically significant. Data analysis was performed using STATA 17.0 (Texas).

Results

Patient demographics

A total of 722,160 patients were included in the study; 57.55% of the population had low frailty scores, 40.28% medium frailty scores, and 2.17% high frailty scores. There were 32,865 patients with a primary diagnosis of CP while the remaining patients had a secondary diagnosis of CP. Females accounted for 43.94% of the study population. Most patients were in the 45 to 65-year-old age group (49.36%) and the majority were White (64.89%), followed by African American patients (22.14%). The majority of patients were from the South

(40.51%). A complete list of patient demographics, stratified by HFRS, is presented in Table 1.

Etiology and comorbidities of CP

Patients with a high frailty score had a higher incidence of acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, hemiplegia or paraplegia, and renal disease compared to patients with medium and low frailty scores. A lower proportion of patients with alcohol-related CP were noted in the high-frailty score group. A complete list of comorbidities stratified by frailty score is present in Table 2.

Outcomes

Mortality

The total number of deaths in the study population was 12,795 (1.77%). Mortality was 1790 (0.43%) in patients with low frailty scores, 9675 (3.33%) in patients with medium frailty scores, and 1330 (8.46%) in patients with high frailty scores. Compared to patients with low frailty scores, patients with medium and high frailty scores had a higher mortality risk (adjusted odds ratio [aOR] 5.65, 95%CI 5-6.37; $P < 0.001$, and aOR 12.57, 95%CI 10.42-15.16; $P < 0.001$, respectively). The results of the multivariate analysis for categorical and continuous outcomes, stratified by frailty score, are presented in Tables 3 and 4, and Fig. 2.

Sepsis

A total of 22,890 (3.17%) patients developed sepsis. The incidence of sepsis in patients with low frailty scores was 7840 (1.89%). There were 13,660 (4.70%) patients with medium frailty and 1390 (8.84%) patients with high frailty scores. Compared to patients with low frailty scores, patients with medium and high frailty scores had a higher risk of sepsis (aOR 2.64, 95%CI 2.46-2.84, $P < 0.001$, and aOR 5.75, 95%CI 4.97-6.66; $P < 0.001$, respectively) on multivariate analysis.

Shock

A total of 24,910 (3.45%) patients developed shock. There were 3265 (0.79%) patients with low frailty scores, 18,810 (6.47%) patients with medium frailty scores, and 2835 (18.03%) patients with high frailty scores. Compared to patients with low frailty scores, patients with medium and high frailty scores had a higher risk of shock (aOR 7.75, 95%CI 7.08-8.49; $P < 0.001$, and aOR 26.25, 95%CI 22.83-30.19; $P < 0.001$, respectively) on multivariate analysis.

Table 1 Patient demographics, stratified by frailty score

Variables	Low frailty score N (%)	Medium frailty score N (%)	High frailty score N (%)	P-value
Age categories				<0.001
18-44	142,955 (34.4)	64,140 (22.05)	1345 (8.56)	
45-65	203,970 (49.08)	145,745 (50.11)	6730 (42.81)	
>65	68,655 (16.52)	80,975 (27.84)	7645 (48.63)	
Sex				<0.001
Male	241,010 (57.99)	156,015 (53.64)	7830 (49.81)	
Female	174,570 (42.01)	134,845 (46.36)	7890 (50.19)	
Race				<0.001
White	273,595 (65.83)	184,790 (63.53)	10,235 (65.11)	
African American	85,480 (20.57)	70,590 (24.27)	3845 (24.46)	
Hispanic	38,160 (9.18)	22,880 (78.66)	890 (56.62)	
Asian/Pacific islander	5630 (1.36)	4225 (1.45)	350 (2.23)	
Native American	3150 (0.76)	2530 (0.87)	100 (0.64)	
Other	9565 (2.3)	5845 (2.01)	300 (1.91)	
Insurance status				<0.001
Medicare	135,495 (32.6)	137,275 (47.2)	9905 (63.01)	
Medicaid	124,940 (30.06)	79,130 (27.21)	3250 (20.67)	
Private	104,210 (25.08)	49,830 (17.13)	1860 (11.83)	
Uninsured	34,100 (8.21)	15,130 (5.2)	375 (2.39)	
Income quartile				<0.001
Lowest quartile	145,295 (34.96)	107,085 (36.82)	5415 (34.45)	
Second quartile	111,355 (26.8)	75,045 (25.8)	4030 (26.37)	
Third quartile	92,800 (22.33)	63,220 (21.74)	3445 (21.91)	
Highest quartile	66,130 (15.91)	45,510 (15.65)	2830 (18)	
Region				<0.001
Northeast	78,440 (18.87)	48,125 (16.55)	2160 (13.74)	
Midwest	98,470 (23.69)	71,990 (24.75)	5035 (32.03)	
South	169,495 (40.79)	117,450 (40.38)	5620 (35.75)	
West	69,175 (16.65)	53,295 (18.32)	2905 (18.48)	
Hospital location				<0.001
Rural	35,395 (8.52)	20,575 (7.07)	885 (5.63)	
Urban	380,185 (91.48)	270,285 (92.93)	14,835 (94.37)	
Teaching status				<0.001
Non-teaching hospitals	121,595 (29.26)	76,840 (26.42)	3880 (24.68)	
Teaching hospitals	293,985 (70.74)	214,020 (73.58)	11,840 (75.32)	
Hospital size				<0.001
Small	86,080 (20.71)	57,510 (19.77)	3015 (19.18)	
Medium	118,265 (28.46)	81,550 (28.04)	4680 (29.77)	
Large	211,235 (50.83)	151,800 (52.19)	8025 (51.05)	
Charlson comorbidity index				<0.001
0	126,990 (30.56)	38,380 (13.2)	785 (4.99)	
1	121,200 (29.16)	60,360 (20.75)	1835 (25.4)	
2	70,620 (16.99)	52,955 (18.21)	2320 (17.43)	
3 or more	96,770 (23.29)	139,165 (47.85)	10,780 (68.58)	

AKI

A total of 129,825 (17.98%) patients developed AKI. There were 22,190 (5.34%) patients with low frailty scores, 97,965 (33.70%) patients with medium frailty scores, and 9,670 (61.51%) patients with high frailty scores. Compared to patients with low frailty scores, patients with medium and high frailty scores had a higher risk of AKI on multivariate analysis

(aOR 7.27, 95%CI 6.99-7.55; $P < 0.001$, and aOR 24.43, 95%CI 22.39-26.66; $P < 0.001$, respectively).

ICU admission

A total of 27,460 (3.8%) patients required ICU admission. There were 3915 (0.94%) patients with low frailty scores, 20,355 (6.70%) patients with medium frailty scores, and

Table 2 Comorbidities stratified by frailty score

Variables	Low frailty score N (%)	Medium frailty score N (%)	High frailty score N (%)	P-value
Etiology				
Alcohol-related chronic pancreatitis	89,405 (21.51)	57,435 (19.75)	2245 (14.28)	<0.001
Comorbidities				
Acute myocardial infarction	22,925 (5.52)	23,865 (8.21)	1625 (10.34)	<0.001
Congestive heart failure	34,460 (8.29)	53,420 (18.37)	3940 (25.06)	<0.001
Peripheral vascular disease	20,375 (4.9)	23,395 (8.04)	1595 (10.15)	<0.001
Cerebrovascular disease	4445 (1.07)	15,870 (5.46)	3700 (23.54)	<0.001
Dementia	2665 (0.64)	11,775 (4.05)	3385 (21.53)	<0.001
COPD	91,490 (22.02)	86,805 (29.84)	5000 (31.81)	<0.001
Rheumatoid disease	10,920 (26.28)	10,380 (3.57)	595 (3.79)	<0.001
Peptic ulcer disease	12,335 (2.97)	12,565 (84.32)	740 (4.71)	<0.001
Mild liver disease	69,170 (16.64)	56,275 (19.35)	2530 (16.09)	<0.001
Uncomplicated diabetes	101,895 (24.52)	61,935 (21.29)	2645 (16.83)	<0.001
Complicated diabetes	48,150 (11.59)	68,560 (23.57)	4910 (31.23)	<0.001
Hemiplegia/paraplegia	870 (0.21)	3535 (1.22)	1300 (8.27)	<0.001
Renal disease	33,290 (8.01)	82,565 (28.39)	7015 (44.62)	<0.001
Cancer without metastasis	12,650 (30.44)	11,795 (40.55)	680 (4.33)	<0.001
Moderate/severe liver disease	21,655 (5.21)	24,825 (8.54)	1380 (8.78)	<0.001
Metastatic cancer	6235 (1.5)	6130 (2.11)	325 (2.07)	<0.001
AIDS	2600 (0.63)	2775 (0.95)	145 (0.92)	<0.001

Table 3 Results of categorical and continuous variables stratified by frailty score

Categorical variables	Low frailty score N (%)	Medium frailty score N (%)	High frailty score N (%)	P-value
Mortality	1790 (0.43%)	9675 (3.33%)	1330 (8.46)	<0.001
Sepsis	7840 (1.89%)	13,660 (4.70%)	1390 (8.84%)	<0.001
Shock	3265 (0.79%)	18,810 (6.47%)	2835 (18.03%)	<0.001
AKI	22,190 (5.34%)	97,965 (33.70%)	9670 (61.51%)	<0.001
ICU admission	3915 (0.94%)	20,355 (6.70%)	3190 (20.29%)	<0.001
Continuous variables				
LOS	4.28 (± 0.02)	6.96 (± 0.04)	11.88 (± 0.24)	<0.001
Total charges	40,401.28 (± 346.93)	71,770.49 (± 767.86)	120,715.3 (± 3143.84)	<0.001

AKI, acute kidney injury; ICU, intensive care unit; LOS, length of hospital stay

3190 (20.29%) patients with high frailty scores who required ICU admission. Compared to patients with low frailty scores, patients with medium and high frailty scores had a higher risk of ICU admission on multivariate analysis (aOR 7.21, 95%CI 6.58-7.89; $P < 0.001$, and aOR 25.86, 95%CI 22.58-29.62; $P < 0.001$, respectively).

LOS

The mean LOS in patients with low frailty scores was 4.28 days (± 0.02). It was 6.96 days (± 0.04) in patients with medium frailty score and 11.88 days (± 0.24) in patients with high frailty score. Compared to patients with low frailty scores, patients with medium and high frailty scores had a greater LOS on multivariate analysis (+2.39 days, 95%CI 2.31-2.47; $P < 0.001$, and 7.04 days, 95%CI- 6.57-7.52; $P < 0.001$, respectively).

Total hospitalization charges

The mean total hospitalization charges were \$40,401.28 in patients with low frailty scores, \$71,770.49 in patients with medium frailty scores and \$120,715.3 in patients with high frailty scores. Compared to patients with low frailty scores, patients with medium and high frailty scores had higher total charges on multivariate analysis (\$26,605.99, 95%CI 25,577.77-28,234.2; $P < 0.001$, and \$72,200.59, 95%CI 65,904.52-78,496.66; $P < 0.001$, respectively).

Discussion

Frailty has become an increasingly important topic in today's healthcare system. It is a robust predictor of outcomes in various

Table 4 Adjusted odds ratio/coefficient for categorical and continuous outcomes for patients with chronic pancreatitis

Outcomes	Adjusted odds ratio	95%CI	P-value
In-hospital mortality			
Low frailty score	Reference		
Medium frailty score	5.65	5.00-6.37	<0.001
High frailty score	12.57	10.42-15.16	<0.001
Sepsis			
Low frailty score	Reference		
Medium frailty score	2.64	2.46-2.84	<0.001
High frailty score	5.75	4.97-6.66	<0.001
Shock			
Low frailty score	Reference		
Medium frailty score	7.75	7.08-8.49	<0.001
High frailty score	26.25	22.83-30.19	<0.001
AKI			
Low frailty score	Reference		
Medium frailty score	7.27	6.99-7.55	<0.001
High frailty score	24.43	22.39-26.66	<0.001
ICU			
Low frailty score	Reference		
Medium frailty score	7.21	6.58-7.89	<0.001
High frailty score	25.86	22.58-29.62	<0.001
	Adjusted coefficient	95%CI	P-value
LOS			
Low frailty score	Reference		
Medium frailty score	2.39 days	2.31-2.47	<0.001
High frailty score	7.04 days	6.57-7.52	<0.001
Total hospitalization charges			
Low frailty score	Reference		
Medium frailty score	\$26,605.99	25,577.77-28,234.2	<0.001
High frailty score	\$72,200.59	65,904.52-78,496.66	<0.001

CI, confidence interval; AKI, acute kidney injury; ICU, intensive care unit; LOS, length of hospital stay

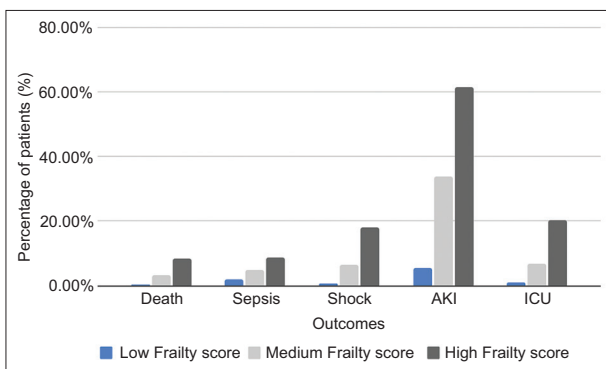


Figure 2 Distribution of categorical outcomes, stratified by frailty score
AKI, acute kidney injury; ICU, intensive care unit

medical conditions. HFRS, a novel administrative measure to identify patients at risk for frailty, can predict long-term survival and other clinical outcomes. No studies to date have evaluated the impact of frailty on CP. Using a nationally representative cohort of 722,160 patients with CP, we found that high HFRS predicted higher in-hospital mortality and resource utilization.

Although initial studies have validated HFRS in patients aged 75 years or older, several publications have demonstrated the predictive value of HFRS in patients as young as 18 years of age [21-25]. In our study, about 8.56% of the patients aged 18-44 had high HFRS, while the prevalence of frailty in patients aged 45-65 was 42.81%. Prior literature has questioned distinguishing age-related frailty from disease-related frailty [26]. Angioni *et al* suggested that further studies should target the underlying biological cascades responsible for these different frailty classifications. This differentiation is warranted, as patients with frailty-related diagnoses, even in the younger age group, can have worse outcomes. In our study, HFRS was associated with higher mortality risk and worse outcomes, even after adjustment for age.

In our analysis, patients with medium and high HFRS had a 5.65 and 12.57 times higher mortality risk, respectively, than patients with low HFRS. Frailty has been identified as a predictor of mortality in patients admitted to acute care wards [27-30]. Social, psychological, lifestyle, and cognitive domains have been identified as mediators of the frailty-mortality association [31]. A study by Breij *et al* contradicted

these findings and reported that these factors did not play a role in the association between frailty and mortality. In our research, even after adjusting for social factors such as insurance status and the income quartile, HFRS was independently associated with a higher mortality risk.

Patients with higher HFRS had a higher incidence of surrogate markers of severity, such as AKI, sepsis, shock and ICU admission. The risk of developing AKI in patients with a high HFRS was 24 times higher than in the low HFRS group. Previous studies have revealed that frail patients are susceptible to dehydration [32]. A study by Hooper *et al* that included 188 elderly residents in long-term care reported that dehydration was higher in these patients and was associated with greater mortality. Electrolyte abnormalities secondary to dehydration might also have contributed to worse outcomes. Additionally, frail patients are prone to decubitus ulcers, urinary tract infections and aspiration pneumonia [33-35]. These factors might contribute to increased rates of sepsis and shock in the high HFRS group and, as a result, higher rates of ICU admission.

This nationwide analysis demonstrates Charlson comorbidities are more prevalent in patients with a high HFRS. About 68.5% of patients with high frailty scores had 3 or more comorbidities. This finding could be due to the similar comorbidities in both scoring systems. The shared comorbidities in both scores are hemiplegia, stroke and peptic ulcer disease (only duodenal ulcer used in HFRS). In our study, even after adjusting for the Charlson comorbidity index and individual Charlson comorbidities, patients in the high HFRS group were at 12.57 times higher risk of death than those in the low HFRS group.

Our study highlights higher resource utilization in patients with medium and high HFRS scores. Patients with medium and high HFRS incurred costs of \$31,369.21 and \$80,314.2 more than those with low frailty scores, after adjustment for confounding variables. The differences in cost could be attributed to the greater LOS in patients with medium and high HFRS. Another factor contributing to the higher cost could be the disposition of these patients. Frail patients are at higher risk of being discharged to skilled nursing facilities and rehabilitation centers than non-frail patients [36-38]. Disposition to skilled nursing facilities requires care coordination among providers, social workers and the post-acute care facilities, which may contribute to the higher costs seen in these patients.

We acknowledge the following limitations of our study. Our study relies on a large national database and is subject to observational data limitations. Information regarding dietary compliance and pharmaceutical therapies is not included in NIS. These are important confounders and can affect patient outcomes. Since the data only contains information on acute hospitalization episodes, we cannot follow the patient longitudinally and track readmissions. As a result, outcome measures such as long-term survival cannot be studied. Owing to the nature of the database, it is difficult to ascertain whether CP was in remission or not. The major strength of this study is the large study population size, from several hospitals across the country, which excludes selection bias. Furthermore, since

HFRS is based on ICD-10 coding, it can be incorporated into electronic health records. This would be beneficial for providers, as it will be a useful tool for risk-stratifying patients. Our findings should be validated in a prospective cohort study that captures more granular clinical data and assesses long-term outcomes.

Our study further expands on the effects of frailty on outcomes in CP. Our principle finding is that frailty is associated with higher in-hospital mortality and resource utilization. Physicians should be aware of this association and identify at-risk patients early to prevent the high morbidity and mortality observed in these patients.

Summary Box

What is already known:

- Chronic pancreatitis is a very common disease and is costly for the United States healthcare system
- The impact of frailty is poorly documented
- No prior studies have investigated the effect of frailty on outcomes in chronic pancreatitis

What the new findings are:

- Frailty was associated with greater mortality and healthcare utilization in patients with chronic pancreatitis
- Patients with medium and high frailty scores had higher rates of sepsis, shock, acute kidney injury and intensive care unit admission compared to patients with low frailty scores
- Patients with medium and high frailty scores had greater resource utilization, evidenced by a longer stay and higher total hospitalization charges compared to patients with low frailty scores
- Physicians should identify the patients with frailty on admission and should monitor them closely to prevent worse outcomes

References

1. Madro A. Malnutrition in chronic pancreatitis: causes, assessment methods, and therapeutic management. *Can J Gastroenterol Hepatol* 2020;**2020**:8875487.
2. Wang T, Camilleri M, Lebwohl B. Yamada's Atlas of Gastroenterology (6th ed.). Wiley Online Library, 2022.
3. Hart PA, Conwell DL. Chronic pancreatitis: managing a difficult disease. *Am J Gastroenterol* 2020;**115**:49-55.
4. Seicean A, Tantău M, Grigorescu M, Mocan T, Seicean R, Pop T. Mortality risk factors in chronic pancreatitis. *J Gastrointest Liver Dis* 2006;**15**:21-26.
5. Ramesh H. Proposal for a new grading system for chronic pancreatitis: the ABC system. *J Clin Gastroenterol* 2002;**35**:67-70.
6. Bagul A, Siriwardena AK. Evaluation of the Manchester classification system for chronic pancreatitis. *JOP* 2006;**7**:390-396.
7. Schneider A, Löhr JM, Singer MV. The M-ANNHEIM classification

- of chronic pancreatitis: introduction of a unifying classification system based on a review of previous classifications of the disease. *J Gastroenterol* 2007;**42**:101-119.
8. Orlikov GA, Pliavinia IA, Pokrotnieks II, Seleznev IV. [Ultrasonographic assessment of chronic pancreatitis severity. Pancreatic index]. *Ter Arkh* 2007;**79**:48-51.
 9. Proietti M, Cesari M. Frailty: what is it? *Adv Exp Med Biol* 2020;**1216**:1-7.
 10. Walston J, Buta B, Xue QL. Frailty screening and interventions: considerations for clinical practice. *Clin Geriatr Med* 2018;**34**:25-38.
 11. Nakano Y, Hirata Y, Shimogawara T, et al. Frailty is a useful predictive marker of postoperative complications after pancreaticoduodenectomy. *World J Surg Oncol* 2020;**18**:194.
 12. Gleason LJ, Benton EA, Alvarez-Nebreda ML, Weaver MJ, Harris MB, Javedan H. FRAIL questionnaire screening tool and short-term outcomes in geriatric fracture patients. *J Am Med Dir Assoc* 2017;**18**:1082-1086.
 13. Basic D, Shanley C. Frailty in an older inpatient population: using the clinical frailty scale to predict patient outcomes. *J Aging Health* 2015;**27**:670-685.
 14. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet* 2018;**391**:1775-1782.
 15. Veronesi F, Borsari V, Martini L, et al. The impact of frailty on spine surgery: systematic review on 10 years clinical studies. *Aging Dis* 2021;**12**:625-645.
 16. Abugroun A, Daoud H, Hallak O, Abdel-Rahman ME, Klein LW. Frailty predicts adverse outcomes in older patients undergoing transcatheter aortic valve replacement (TAVR): from the National Inpatient Sample. *Cardiovasc Revasc Med* 2022;**34**:56-60.
 17. Ibitoye SE, Rawlinson S, Cavanagh A, Phillips V, Shipway DJH. Frailty status predicts futility of cardiopulmonary resuscitation in older adults. *Age Ageing* 2021;**50**:147-152.
 18. Acosta CJ, Goldberg D, Amin S. Evaluating the impact of frailty on periprocedural adverse events and mortality among patients with GI bleeding. *Gastrointest Endosc* 2021;**94**:517-525.
 19. Healthcare Cost and Utilization Project (HCUP). Content last reviewed October 2022. Agency for Healthcare Research and Quality, Rockville, MD. Available from: <https://www.ahrq.gov/data/hcup/index.html> [Accessed 14 November 2022].
 20. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol* 2004;**57**:1288-1294.
 21. Kwok CS, Achenbach S, Curzen N, et al. Relation of frailty to outcomes in percutaneous coronary intervention. *Cardiovasc Revasc Med* 2020;**21**:811-818.
 22. Hannah TC, Neifert SN, Caridi JM, et al. Utility of the hospital frailty risk score for predicting adverse outcomes in degenerative spine surgery cohorts. *Neurosurgery* 2020;**87**:1223-1230.
 23. Smith RJ, Reid DA, Santamaria JD. Frailty is associated with reduced prospect of discharge home after in-hospital cardiac arrest. *Intern Med J* 2019;**49**:978-985.
 24. Kochar B, Cai W, Cagan A, Ananthakrishnan AN. Pretreatment frailty is independently associated with increased risk of infections after immunosuppression in patients with inflammatory bowel diseases. *Gastroenterology* 2020;**158**:2104-2111.
 25. Kochar B, Cai W, Cagan A, Ananthakrishnan AN. Frailty is independently associated with mortality in 11 001 patients with inflammatory bowel diseases. *Aliment Pharmacol Ther* 2020;**52**:311-318.
 26. Angioni D, Macaron T, Takeda C, et al. Can we distinguish age-related frailty from frailty related to diseases? data from the MAPT study. *J Nutr Health Aging* 2020;**24**:1144-1151.
 27. Hao Q, Zhou L, Dong B, Yang M, Dong B, Weil Y. The role of frailty in predicting mortality and readmission in older adults in acute care wards: a prospective study. *Sci Rep* 2019;**9**:1207.
 28. De Smet R, Mellaerts B, Vandewinckele H, et al. Frailty and mortality in hospitalized older adults with COVID-19: retrospective observational study. *J Am Med Dir Assoc* 2020;**21**:928-932.
 29. Zhang XM, Jiao J, Cao J, et al. Frailty as a predictor of mortality among patients with COVID-19: a systematic review and meta-analysis. *BMC Geriatr* 2021;**21**:186.
 30. Benraad CEM, Haaksma ML, Karlietis MHJ, et al. Frailty as a predictor of mortality in older adults within 5 years of psychiatric admission. *Int J Geriatr Psychiatry* 2020;**35**:617-625.
 31. de Breijl S, Rijnhart JJM, Schuster NA, Rietman ML, Peters MJL, Hoogendijk EO. Explaining the association between frailty and mortality in older adults: The mediating role of lifestyle, social, psychological, cognitive, and physical factors. *Prev Med Rep* 2021;**24**:101589.
 32. McCrow J, Morton M, Travers C, Harvey K, Eeles E. Associations between dehydration, cognitive impairment, and frailty in older hospitalized patients: an exploratory study. *J Gerontol Nurs* 2016;**42**:19-27.
 33. Barry M, Nugent L. Pressure ulcer prevention in frail older people. *Nurs Stand* 2015;**30**:50-58.
 34. Chao CT, Lee SY, Wang J, Chien KL, Huang JW. Frailty increases the risk for developing urinary tract infection among 79,887 patients with diabetic mellitus and chronic kidney disease. *BMC Geriatr* 2021;**21**:349.
 35. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. *J Am Med Dir Assoc* 2011;**12**:344-354.
 36. Ramdass SK, Brennan MJ, Starr R, et al. The association of frailty with discharge disposition for hospitalized community dwelling elderly patients. *J Hosp Med* 2018;**13**:182-184.
 37. Joseph B, Pandit V, Rhee P, et al. Predicting hospital discharge disposition in geriatric trauma patients: is frailty the answer? *J Trauma Acute Care Surg* 2014;**76**:196-200.
 38. Pearl JA, Patil D, Filson CP, et al. Patient frailty and discharge disposition following radical cystectomy. *Clin Genitourin Cancer* 2017;**15**:e615-e621.

Supplementary material

Supplementary Table 1 ICD-10 codes for chronic pancreatitis

Condition	ICD-10 Codes
Chronic pancreatitis	K86.1, K86.0
Alcohol-related chronic pancreatitis	K86.0
Myocardial infarction	I21.x, I22.x, I25.2
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5 - I42.9, I43.x, I50.x, P29.0
Peripheral vascular disease	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular disease	G45.x, G46.x, H34.0, I60.x - I69.x
Dementia	F00.x - F03.x, F05.1, G30.x, G31.1
Chronic pulmonary disease	I27.8, I27.9, J40.x - J47.x, J60.x - J67.x, J68.4, J70.1, J70.3
Rheumatic disease	M05.x, M06.x, M31.5, M32.x - M34.x, M35.1, M35.3, M36.0
Peptic ulcer disease	K25.x - K28.x
Mild liver disease	B18.x, K70.0 - K70.3, K70.9, K71.3 - K71.5, K71.7, K73.x, K74.x, K76.0, K76.2 - K76.4, K76.8, K76.9, Z94.4
Diabetes without chronic complication	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
Diabetes with chronic complication	E10.2 - E10.5, E10.7, E11.2 - E11.5, E11.7, E12.2 - E12.5, E12.7, E13.2 - E13.5, E13.7, E14.2 - E14.5, E14.7
Hemiplegia or paraplegia	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0 - G83.4, G83.9
Renal disease	I12.0, I13.1, N03.2 - N03.7, N05.2 - N05.7, N18.x, N19.x, N25.0, Z49.0 - Z49.2, Z94.0, Z99.2
Any malignancy	C00.x - C26.x, C30.x - C34.x, C37.x - C41.x, C43.x, C45.x - C58.x, C60.x - C76.x, C81.x - C85.x, C88.x, C90.x - C97.x
Moderate or severe liver disease	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
Metastatic solid tumour	C77.x - C80.x
AIDS/HIV	B20.x - B22.x, B24.x
Mechanical ventilation	5A1935Z, 5A1945Z, 5A1955Z
Vasopressor use	3E030XZ, 3E033XZ, 3E040XZ, 3E043XZ, 3E050XZ, 3E053XZ, 3E060XZ, 3E063XZ
ICU admission	Mechanical Ventilation+Pressor Use
Sepsis	R65.10, R65.11, R65.20
AKI	N17.0, N17.1, N17.2, N17.8, N17.9

AKI, acute kidney injury; ICU, intensive care unit