Global Health & Medicine. 2024; 6(6):394-403.
ORIGINAL ARTICLE
DOI: 10.35772/ghm.2024.01089

Prevalence of physical frailty and its associated factors among elderly patients undergoing hepatobiliary pancreatic surgery in China

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Abstract: Frailty is a geriatric syndrome characterized by a multisystem physiological decline, increased vulnerability to stressors, and adverse clinical outcomes. However, there is a knowledge gap regarding the association between frailty and its influencing factors. This study aimed to understand the current status of preoperative frailty in elderly patients with hepatobiliary pancreatic disease (HBP) and analyze debilitation-related factors. We enrolled 220 participants aged ≥ 65 years who underwent HBP surgery at two hospitals in China between December 2023 and February 2024. The physical frailty of elderly participants in communities with different characteristics was compared using Kruskal-Wallis and chi-square tests. Ordinal logistic regression analysis was used to analyze the factors influencing preoperative frailty. A total of 212 patients were included in the analysis based on the inclusion and exclusion criteria, with an overall prevalence of frailty at 53 (25%). Ordinal logistic regression analysis results showed that current smoking (odds ratio [OR] = 2.584, $p = 0.006$) was an independent risk factor for preoperative frailty in elderly participants with HBP. In contrast, exercise habits (OR = 0.323, $p < 0.001$), two or more multimorbidity statuses (OR = 0.495, $p = 0.033$), and independent status (OR = 0.216, $p < 0.001$) were protective factors. Our results suggest that having good exercise habits, not smoking, and independent status can prevent frailty progression in older adults who require HBP surgery. Interventions for frail elderly patients should be supported preoperatively by strengthening exercises to improve tolerance to surgery.

***Keywords*:** frailty, hepatobiliary pancreatic surgery, aging, frailty assessment, influencing factor

Introduction

The global population is aging rapidly, with China having the world's largest aging population and Japan having the world's highest aging rate. The figures released by the Japanese Ministry of Internal Affairs and Communications in 2022 show that the population over 65 years of age has reached 36.23 million, accounting for 29.1% of the total population (*i.e.*, aging rate) (*1*). The number of Chinese adults aged 65 years and older reached 216.76 million by the end of 2023, accounting for 15.4% of the total population (*2*). Interestingly, this rapid rate of population aging has been outpaced by an increase in number of older patients needing surgical intervention as a main modality of treatment. Laparoscopic hepatobiliary pancreatic (HBP) surgery is a minimally invasive surgical method with many advantages in the treatment of HBP diseases (*3*). However, this type of surgery is difficult, especially with the long duration of pancreaticoduodenectomy, wide resection area, and high incidence of postoperative complications (*4*). To reduce hospital stay, hospital costs, and postoperative complications, it is particularly important to understand the status of patients during the perioperative period.

Fried *et al.* provided the first standardized definition of frailty as a geriatric syndrome characterized by multisystem physiological decline, increased vulnerability to stressors, and adverse clinical outcome (*5*). Frailty increases the risk of adverse outcomes, including mortality, major morbidity, and decreased functional status and quality of life (*5,6*). Although the risk of frailty increases with age, not all older adults are frail, and frailty is not exclusive to the aged (*7,8*). Most importantly, frailty is not a static state and can progressively improve depending on intervention (*7,9,10*).

A joint statement from the American College of

Surgeons and American Geriatrics Society recommends frailty assessment as part of the preoperative assessment of older surgical patients (*11*), and the recognition that frail patients have unique vulnerabilities and challenges is increasing in surgery. The relationship between frailty and post-operative outcomes in various surgical specialties has been a popular topic in recent years (*12*). Various approaches exist for measuring frailty; however, there is little agreement regarding the optimal frailty instrument. Agreement does exist that frailty measurement should be operationalized using a multidimensional approach, which is most often performed using either Fried's Frailty Phenotype or the Edmonton Frailty Scale (EFS) (*13*). Elderly patients undergoing surgery generally have been found to have a higher prevalence of frailty (25%-56%). Notably, most studies were performed on Caucasian patients in Canada and the United States (*14*). The outcomes of HPB surgery have improved tremendously over the past decade, with reduced postoperative mortality from 20% to less than 3% and 5%-6% for major liver and pancreatic surgeries, respectively. Therefore, frailty tools need to be incorporated into clinical practice to improve these outcomes (*15*). However, to date, no studies have specifically focused on the relationship between frailty and HBP among elderly patients in China. To address these important knowledge gaps, we conducted a population-based study of older adults who underwent common major HBP surgical procedures. The primary objective of this study was to understand the current status of frailty in elderly surgical patients with HBP and analyze the factors related to their debilitation.

Patients and Methods

Study design

This cross-sectional study was performed at two hospitals (First Affiliated Hospital of Chongqing Medical University and Peking University International Hospital) in China. We enrolled patients who were 65 years of age and above and had undergone HBP surgery from December 2023 to February 2024. As shown in Figure 1, 220 patients who underwent elective HBP surgery were prospectively enrolled. Written informed consent was obtained from all patients prior to enrolment in the study.

The inclusion criteria for this study were as follows: *i*) patients 65 years of age and older, *ii*) patients who were conscious and provided written informed consent, and *iii*) patients who were expected to survive for more than 3 months without serious cardiopulmonary, renal, or psychiatric disorders. The exclusion criteria were as follows: *i*) patients who did not consent to surgical treatment, *ii*) patients who died, and *iii*) patients who were transferred to another hospital before discharge. Sociodemographic data were obtained pre-operatively, and measures for evaluating self-care, nutritional risk screening, assessment of the patient's risk of depression, and frailty status were completed before surgery. Eight participants were excluded from the study because they could not be evaluated for frailty or their questionnaires were incomplete.

Prior to conducting the study, the approval from Ethics Committee of Hamamatsu University School of Medicine was obtained (NO. 23-250, 6 November 2023),

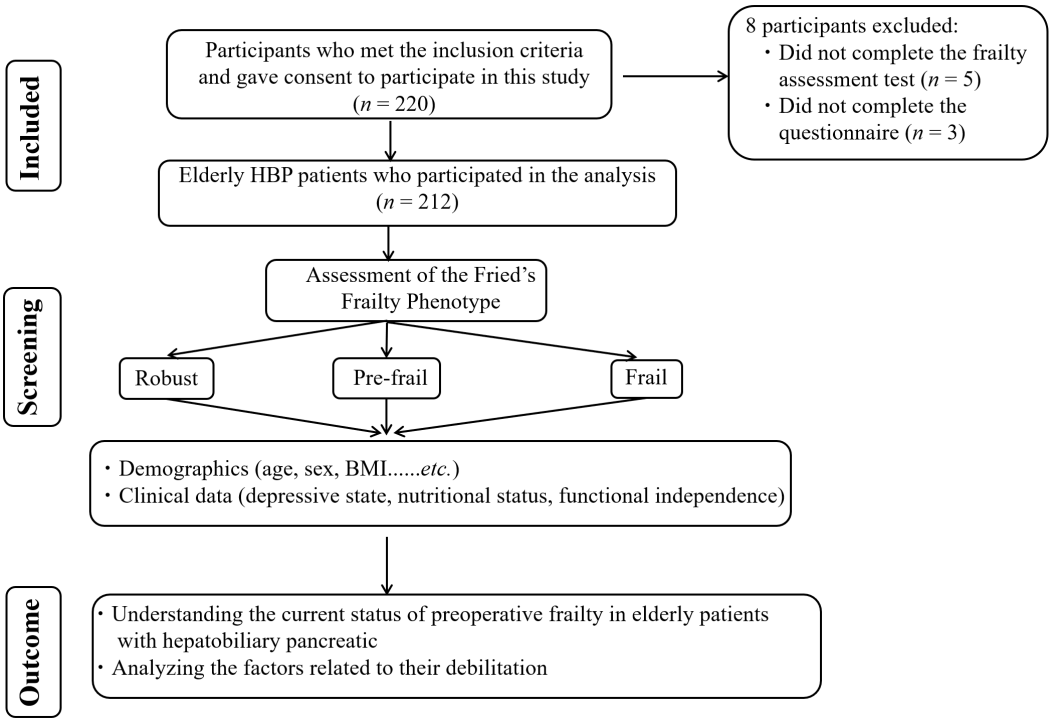

Figure 1. Study flowchart.

the First Affiliated Hospital of Chongqing Medical University (NO. 2023-337, 26 December 2023) and the Peking University International Hospital (NO. 2023-KY-0085-01, 12 December 2023). The participants' data were processed and electronically stored in accordance with the ethical principles of the Declaration of Helsinki for medical research involving human subjects. Data were stored and analyzed anonymously.

Sample size

This study is a cross-sectional design, and the sample size was calculated using the formula $n = [z^2 \alpha/2\ p(1-p)]/\delta^2$. Based on previous studies, where p = 25% (*14*), $\alpha = 0.05$, t = 1.96, and the allowable error = 0.06, the required sample size was determined to be 200 cases. Considering shedding and other factors, and additional 10% was added, bringing the total number of required cases to 220.

Research measures

Outcome parameters

Data collected preoperatively included the demographics of the participants, such as age, sex, body mass index (BMI), marital status, place of residence (rural/urban), level of education, annual tax-included income, alcohol and smoking status, sleep status, exercise habits, alone situation, and clinical data such as multimorbidity and polypharmacy, depressive state (assessed using the Patient Health Questionnaire-9 [PHQ-9]), nutritional status (by the Nutritional Risk Screening 2002), functional independence (by the Barthel Index), and frailty measures (by the Fried's Frailty Phenotype).

The Fried's Frailty Phenotype (The Fried's FP)

The Fried's FP test was used to determine the presence and degree of frailty. Preoperatively, Fried's FP was completed by the participants under the supervision of specially trained nurses. Fried's FP is a multi-dimensional screening tool comprising five domains: slow walking speed (slowness), grip strength (weakness), weight loss (shrinking), fatigue (poor endurance/energy), and low physical activity. Slowness was assessed using the timed get-up-and-go test. The area for the timed get-up-and-go test was measured 3 m from the front legs of the straight-backed armchair. The subject was instructed as follows: "sit with your back against the chair and your arms on the arm rests. On the word "go", stand upright, then walk at your normal pace to the line on the floor, turn around, return to the chair, and sit down". The time required to complete the test was time from the word "go" to time when the subject returned to the starting position. Subjects who took > 10 seconds to complete the test were classified as frail. Grip strength was measured using a Camry hand dynamometer and compared with normative data adjusted for age and sex. Participants met the "weak grip strength" criterion if their grip strength was below the 20th percentile. The subject was seated with the forearm resting on the arm of a chair and instructed to hold the dynamometer upright and squeeze it as hard as possible. Three trials in the right hand, followed by three trials in the left hand, were recorded, and the highest reading of the six was taken as the final reading. The criterion for weight loss was met if the participants suffered an unintentional loss of 2 or 3 kg in half a year. Regarding fatigue, participants were asked if they felt exhausted without any reason in the previous month and if they exercised regularly once a week for low physical activity. The scores were summed, with a score of 0 classified as non-frail, a score of 1-2 classified as pre-frail, and a score of 3-5 classified as frail.

Nutritional risk screening 2002 (NRS 2002)

This scale is a nutritional risk-screening tool developed by Kondrup *et al.* (*16*) in 2002 based on the sequential medical method, which includes three items: disease severity score, nutritional impairment score, and age score. With a total score of 0 to 7, "3" is considered nutritional risk and "4" no nutritional risk. This scale is the most widely used and clinically validated nutritional risk screening tool, and has been recommended by several nutritional associations.

Barthel Index (BI)

The BI is an ordinal scale used to measure functional disability while performing ten daily activities (*17*). It is a validated 10-item instrument that measures a patient's independence in performing the main activities of daily living, including bathing, dressing, toileting, transferring, continence, and feeding. Functional status is defined as "independent" if the participant does not require any assistance from another person for any activities of daily living. The participant is considered "partially dependent" if they require some assistance from another person for activities of daily living and "totally dependent" if they require assistance for all activities of daily living. Scores range from 0-100, with a total score of 100 indicating the highest level of independence.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (*18*) was used as a self-administered screening tool to assess the severity of depressive symptoms. Unlike other depression scales, the PHQ-9 includes nine items that assess symptoms of Major Depressive Disorder (MDD), as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). The questionnaire assessed how often the subjects had been disturbed by any of the nine items during the immediately preceding two weeks. Each item of the PHQ-9 is scored on a scale of 0 to 3 (0 = not at all, 1 = several days, 2 = more than a week, 3 = nearly every day). The PHQ-9 total score ranges from

0 to 27 (scores of 0-4 indicate normal or no depressive symptoms; 5-9 indicate mild depression; 10-14 indicate moderate depression; 15-19 indicate moderately severe depression; and ≥ 20 indicate severe depression).

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics 29.0. Frailty was analyzed as a categorical variable. Patients were defined as robust, pre-frail, or frail based on their frailty scores, as noted above. Descriptive statistics of the baseline demographic and clinical variables were calculated using mean (standard deviation) or percentages (%). The Shapiro-Wilk test was used to assess normal distribution. Non-parametric Kruskal-Wallis and chi-square tests were used to compare continuous and categorical variables, respectively. Ordinal logistic regression was used for categorical variables to predict variables affecting frailty. Statistical comparisons were 2-sided and a p value <0.05 was considered statistically significant.

Results

Baseline characteristics

The participant characteristics and demographic data are presented in Table 1. In total, 212 elderly patients with HBP were enrolled between December 2023 and February 2024. The mean (± standard deviation) patient age was 72.46 ± 5.94 years, and 116 (54.7%) were male. The BMI of the study subjects was 22.39 ± 3.47 kg/m^2; married individuals accounted for 163 (76.9%), while unmarried, divorced, or widowed account for 49 (23.1%). One hundred eighty-three patients (86.3%) had no postsecondary education. Sixty-two (29.2%) patients lived in rural areas, and 121 (57.1%) belonged to the middle- and low-income groups (annual tax-included income < 50,000 RMB). Forty-four (20.8%) patients continued to smoke and 168 (79.2%) were non-smokers or had quit smoking. Only 36 (17.0%) patients drank alcohol, with the vast majority abstaining from alcohol consumption. One hundred and thirty-two (62.3%) had exercise habits, 102 (48.1%) had 0-1 chronic disease, and 110 (51.9%) had two or more chronic diseases. One hundred and forty-one (66.5%) patients had normal sleep, 71 (33.5%) had sleep difficulties, 182 (85.8%) were taking three or fewer drugs, and 30 (14.2%) were taking four or more drugs. One hundred eighty-one patients (85.4%) had no symptoms of depression. Sixty-one (28.8%) patients were dependent on other people for help, 171 (80.7%) lived with their family, 41 (19.3%) lived alone or in nursing homes, and 180 (84.9%) had good nutritional status.

Preoperative frailty in elderly hepatobiliary and pancreatic patients and single factor analysis

As shown in Table 1, among the elderly participants with HBP disease, there were 53 cases in the frailty group (25%), 83 in the pre-frailty group (39.1%), and 76 in the non-frailty group (35.8%). Details of the frailty scale indicators are presented in Table 2. Fatigue (42.0%) was the most common, followed by low grip strength (31.1%), slow walking speed (30.7%), weight loss (26.9%), and low activity levels, which were reported by at least 50 (23.6%) participants. Univariate analysis showed statistically significant differences in age, education level, smoking status, alcohol status, exercise habits, activity of daily living (ADL), multimorbidity and polypharmacy, sleep status, and nutritional status in the incidence of preoperative frailty among the elderly participants ($p < 0.05$), as shown in Table 1.

Factors influencing preoperative frailty in elderly hepatobiliary and pancreatic patients

To study the factors influencing preoperative frailty, ordinal logistic regression analysis was performed. The results are summarized in Table 3. The preoperative frailty of elderly participants with HBP diseases (frailty group = 1, pre-frailty group = 2, robust group = 3) was used as the dependent variable. The result of the parallel line test was $p = 0.978$, > 0.05 and which is ensuring the accuracy and reliability of the ordinal logistic regression analysis results. The results showed that current smoking status (OR = 2.584, $p = 0.006$) was an independent risk factor for preoperative frailty in elderly participants with HBP. In contrast, exercise habits (OR = 0.323, $p < 0.001$), two or more multimorbidity statuses (OR = 0.495, $p = 0.033$), and independent status (OR = 0.216, $p < 0.001$) were protective factors. Age had no significant effect on preoperative frailty.

Discussion

This study showed that 25% of the 212 elderly HBP patients were frail. Komici *et al.* (*19*) showed that a total of 34,276 HBP cancer patients were identified, and the weighted prevalence of frailty was 39%. Therefore, the number of patients included in our study was lower than that of patients with HBP cancer in a previous study. This may be related to different research objectives and evaluation standards. Komici *et al.* included patients with HBP cancer who had been treated with surgery, chemotherapy, and radiotherapy, whereas the elderly patients in this study had not yet undergone invasive treatments such as surgery. At the same time, as many different instruments are used to measure frailty, it is difficult to reliably compare those results. To date, there is no consensus regarding the assessment of frailty. There are more than 60 validated tools for screening and measuring frailty with important similarities; however, there is no defined standard assessment tool for frailty assessment in HBP surgery. Nevertheless, this wide

Table 1. Characteristics of participants in the study cohort, stratified by whether they were determined to be frail or non-frail using the Fried's Frailty Phenotype instrument before surgery

Variable	All participants *n* = 212	Robust (0) *n* = 76 (35.8%)	Pre-Frail (1-2) *n* = 83 (39.1%)	Frail (3-5) *n* = 53 (25%)	*p*-value
Age (years, x ± s)	72.46 ± 5.94	72.46 ± 5.95	71.90 ± 5.38	71.94 ± 7.68	0.018*[a]
65 ≤ age < 70 years old	83 (39.2%)	21 (25.4%)	31 (37.3%)	31 (37.3%)	< 0.001*[b]
70 ≤ age < 80 years old	101 (47.6%)	46 (45.5%)	43 (42.6%)	12 (11.9%)	
Age ≥ 80 years	28 (13.2%)	9 (32.1%)	9 (32.1%)	10 (35.8%)	
Sex (*n*, %)					0.441[b]
Male	116 (54.7%)	40 (34.5%)	43 (37.1%)	33 (28.4%)	
Female	96 (45.3%)	36 (37.5%)	40 (41.7%)	20 (20.8%)	
BMI (kg/m^2, x ± s)	22.39 ± 3.47	21.88 ± 2.72	23.11 ± 3.76	22.02 ± 3.83	0.081[a]
Marital status (*n*, %)					0.433[b]
Married	163 (76.9%)	58 (35.6%)	61 (37.4%)	44 (27.0%)	
Unmarried, divorced or widowed	49 (23.1%)	18 (36.7%)	22 (44.9%)	9 (18.4%)	
Level of education (*n*, %)					0.019*[b]
No post-secondary	183 (86.3%)	60 (32.8%)	72 (39.3%)	51 (27.9%)	
Bachelor's degree or above	29 (13.7%)	16 (55.2%)	11 (37.9%)	2 (6.9%)	
Place of residence (*n*, %)					0.925[b]
Rural	62 (29.2%)	23 (37.1%)	23 (37.1%)	16 (25.8%)	
Urban	150 (70.8%)	53 (35.3%)	60 (40.0%)	37 (24.7%)	
Annual tax-included income (RMB) (*n*, %)					0.191[b]
< 50,000	121 (57.1%)	38 (31.4%)	48 (39.7%)	35 (28.9%)	
≥ 50,000	91 (42.9%)	38 (41.7%)	35 (38.5%)	18 (19.8%)	
Smoking status (*n*, %)					0.004*[b]
Quit/non-smoker	168 (79.2%)	67 (88.2%)	67 (80.7%)	34 (64.2%)	
Current smoker	44 (20.8%)	9 (20.5%)	16 (36.4%)	19 (43.1%)	
Alcohol status (*n*, %)					0.024*[b]
Quit/non-drinker	176 (83.0%)	69 (39.2%)	62 (35.2%)	45 (25.6%)	
Current drinker	36 (17.0%)	7 (19.5%)	21 (58.3%)	8 (22.2%)	
Exercise habits (*n*, %)					< 0.001*[b]
Yes	132 (62.3%)	57 (43.2%)	54 (40.9%)	21 (15.9%)	
No	80 (37.7%)	19 (23.8%)	29 (36.2%)	32 (40.0%)	
Multimorbidity (*n*, %)					0.023*[b]
0~1	102 (48.1%)	39 (38.2%)	46 (45.1%)	17 (16.7%)	
≥ 2	110 (51.9%)	37 (33.6%)	37 (33.6%)	36 (32.8%)	
Sleep status (*n*, %)					0.003*[b]
Good	141 (66.5%)	59 (41.8%)	56 (39.7%)	26 (18.5%)	
Bad	71 (33.5%)	17 (23.9%)	27 (38.0%)	27 (38.0%)	
Polypharmacy (*n*, %)					0.038*[b]
0~3	182 (85.8%)	69 (37.9%)	73 (40.1%)	40 (22.0%)	
≥ 4	30 (14.2%)	7 (23.4%)	10 (33.3%)	13 (43.3%)	
Depressive state (*n*, %)					0.062[b]
Yes	31 (14.6%)	6 (19.4%)	13 (41.9%)	12 (38.7%)	
No	181 (85.4%)	70 (38.7%)	70 (38.7%)	41 (22.6%)	
ADL (*n*, %)					< 0.001*[b]
Independent	151 (71.2%)	69 (45.7%)	57 (37.7%)	25 (16.6%)	
Dependent	61 (28.8%)	7 (11.5%)	26 (42.6%)	28 (45.9%)	
Alone situation (n, %)					0.183[b]
Yes	41 (19.3%)	15 (36.6%)	20 (48.8%)	6 (14.6%)	
No	171 (80.7%)	61 (35.7%)	63 (36.8%)	47 (27.5%)	
Nutritional status (*n*, %)					< 0.001*[b]
Bad	32 (15.1%)	6 (18.8%)	9 (28.1%)	17 (53.1%)	
Good	180 (84.9%)	70 (38.9%)	74 (41.1%)	36 (20.0%)	

*Data are presented as mean ± standard deviation or median (interquartile range) unless indicated otherwise; represents statistical significance ($p < 0.05$). a: The value obtained by Kruskal-Wallis test; b: The value obtained by chi-square test. BMI, body mass index; ADL, activity of daily living.

range of scores and scales allows physicians to find the scale that fits their needs according to the type of surgery, local population, and resources.

As illustrated in Figure 2, fatigue was the most prevalent physical frailty factor. The prevalence values in the cases of fatigue, one of the factors of frailty, were 50 (56.2%) and 39 (43.8%) in HBP older adults with prefrailty and frailty, respectively. Of the participants in the study by Uslu *et al.*, 63.8% were frail with physical and cognitive fatigue. The higher the frailty, the higher is the fatigue (*20*). Fatigue is an often-neglected symptom that is frequently reported by older people, leading to an inability to continue functioning at a normal level. Fatigue reflects the exhaustion of physiological reserves in older individuals. Despite its clinical relevance, fatigue is typically underestimated by healthcare professionals,

Table 2. Percentage of each factor of frailty in pre-frailty and frailty participants

Item	All participants *n* (%)[a]	Pre-frailty group (*n* = 83) *n* (%)[b]	Frailty group (*n* = 53) *n* (%)[b]
Weight loss	57 (26.9%)	22 (38.6%)	35 (61.4%)
Grip strength	66 (31.1%)	21 (31.8%)	45 (68.2%)
Fatigue	89 (42.0%)	50 (56.2%)	39 (43.8%)
slow walking speed	65 (30.7%)	21 (32.3%)	44 (67.7%)
Low activity level	50 (23.6%)	24 (48.0%)	26 (52.0%)

*a: Percentage of participants in all participants; b: Percentage of participants in the pre-frail or frail groups.

Table 3. Ordinal logistic regression analysis to identify influencing factors of frailty before hepatobiliary pancreatic surgery

Variables	Groups	*B*	*SE*	*Wald* X^2	*P-Value*	*OR*	95% CI	
							lower limit	upper limit
Age	65 ≤ age < 70 years old				Reference			
	70 ≤ age < 80 years old	-1.094	0.296	13.62	< 0.001	0.335	0.188	0.596
	Age ≥ 80 years old	-0.511	0.428	1.425	0.233	0.6	0.251	1.434
Smoking status	Quit/non-smoker				Reference			
	Current smoker	0.949	0.344	7.603	0.006	2.584	1.313	5.085
Have exercise habits	No				Reference			
	Yes	-1.13	0.32	12.448	< 0.001	0.323	0.172	0.606
Multimorbidity	0~1				Reference			
	≥ 2	-0.703	0.329	4.563	0.033	0.495	0.259	0.947
ADL	Dependent				Reference			
	Independent	-1.533	0.351	19.136	< 0.001	0.216	0.109	0.427

*Represents statistical significance ($p < 0.05$), SE, standard error; OR, odds ratio; CI, confidence interval; ADL, activity of daily living.

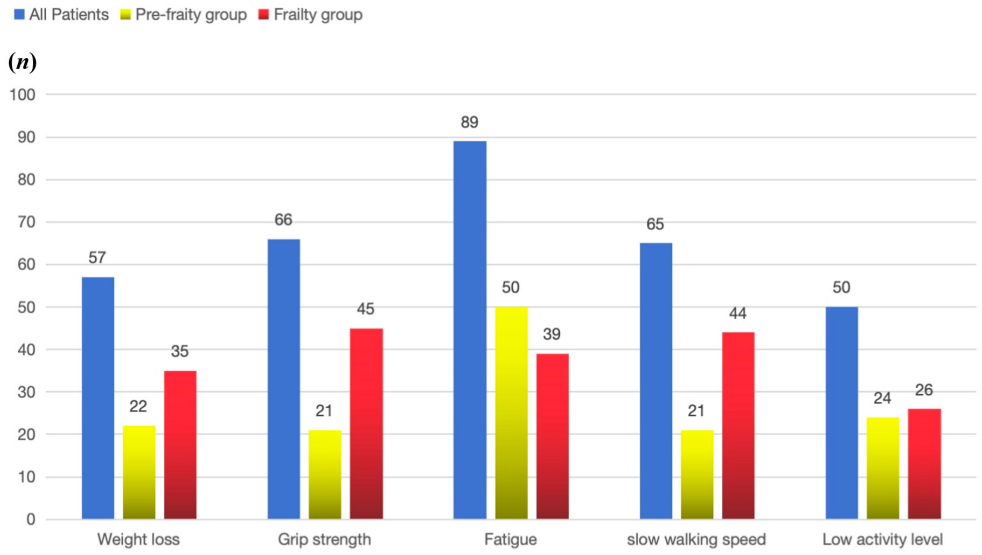

Figure 2. Overview of population of each factor of frailty in pre-frailty and frailty in elderly hepatobiliary and pancreatic patients (by the Fried's Frailty Phenotype).

mainly because reduced stamina is considered an unavoidable corollary of aging.

Although the link between marital status and frailty was not demonstrated in our study, it remains worthy of attention. In a study by Trevisan *et al.* (*21*), unmarried/divorced/widowed elderly people had no partner and needed to take care of themselves; therefore, they may pay more attention to their health status and take timely intervention measures when discovering health problems, resulting in better health conditions than married elderly people. At the same time, unmarried/divorced/widowed older adults are more likely to participate in community activities to relieve negative emotions, such as loneliness, which is beneficial for their physical health and reduces

the incidence of frailty.

Our study did not show that nutritional status is a risk factor for frailty in older adults. Both quantitative (energy intake) and qualitative (nutrient quality) assessments are important because the lack of micronutrients (Vitamin D or leucine) and macronutrients (proteins) are considered risk factors for frailty, while certain diets (*e.g.*, Mediterranean diet) can prevent or reverse frailty (*22,23*). In addition, nutrition-related biomarkers may be used to assess the nutritional status and frailty in elderly patients. Patients with better nutritional status and higher serum transferrin, total protein, and albumin levels are less likely to develop frailty (*24*). Rather than focusing on the link between nutrition and frailty, we should consider what the best options are for realistic and lasting dietary changes or what the barriers and potential solutions are to improve nutritional status in older people. Undernutrition is not the only nutritional state related to frailty; high BMI and body fat percentage can also increase the risk of aging.

BMI is known to affect the severity of frailty. A cross-sectional study of Dutch subjects showed that BMI has a U-shaped relationship with frailty prevalence (*25*). A Japanese study found that the BMI range for which the prevalence of frailty was the lowest was 21.4-25.7 kg/m^2 (*26*). These findings highlight the need to evaluate the risk of frailty in both underweight and overweight individuals. Although the association between BMI and frailty was not analyzed in our study, future studies should focus on BMI in older adults. Age is considered to be one of the independent risk factors for frailty, and the prevalence of frailty increases exponentially with age. Kojima *et al.* (*27*) investigated the age-stratified meta-analyses of four studies and showed the pooled prevalence of frailty was 1.9%, 3.8%, 10.0%, 20.4%, and 35.1% for those aged 65-69, 70-74, 75-79, 80-84, and ≥ 85 years, respectively. However, our results differ from those of previous studies. Our research results showed that the pooled prevalence of frailty was 37.3%, 11.9%, and 35.8% for those aged 65-69, 70-79, and ≥ 80 years, respectively. Therefore, the prevalence of frailty did not increase with age in the present study. Notably, old age itself does not define frailty because some patients are active despite advanced age, whereas others experience functional decline in the absence of apparent stress factors or failure to rebound following hospitalization or illness (*28*).

This study supports smoking as a causal risk factor of frailty. Liu *et al.* (*29*) also confirmed this finding. Their study indicated that a genetic predisposition to smoking is associated with the risk of frailty in aging, which supports the potential causal role of smoking in the risk of frailty. In addition, the mechanisms underlying the potential association between smoking and frailty remain unclear. The most commonly suggested explanation is chronic inflammation induced by various toxic chemicals produced by tobacco smoking, which is supported by findings of positive associations between increased levels of inflammatory markers, such as CRP and IL-6, and higher prevalence and incidence of frailty (*30*). Further studies are required to elucidate the underlying biological mechanism. However, our study did not determine whether alcohol consumption played a causal role in frailty. As this study only collected information on whether the study participants had a habit of alcohol drinking at the time of the survey, the effect of alcohol consumption against frailty may also be due to the fact that the study participants in poorer health conditions did not drink alcohol themselves or chose to abstain from alcohol when they were in poor health due to alcohol consumption, and the relationship between alcohol consumption and frailty in older adults needs to be further studied.

Regarding exercise habits, older people who did not exercise were associated with a higher frailty severity. On September 30, 2019, the International Conference of Frailty and Sarcopenia Research (ICFSR) released the International Clinical Practice Guidelines: The Recognition and Management of Physical Frailty, stating that the management of frailty should include a multi-component physical activity program with a resistance-based training component (*7*). Our study focused only on whether elderly patients had exercise habits, and did not investigate the duration, frequency, and content of exercise, which are involved in preventing frailty severity. However, there are also studies showing that a high frequency of exercise, including resistance training, are associated with exacerbation of frailty severity (*31*). This shows that it is important to choose the right type of exercise according to the physical condition of the elderly person.

This study established a link between the number of chronic diseases and the risk of frailty. Previous studies have established a link between a single disease and frailty. For example, frailty prevalence in patients with inflammatory bowel disease (IBD) was 18% (*32*) and that for patients with chronic obstructive pulmonary disease (COPD) was 36% (*33*). Interactions among diseases in patients with multimorbidity may increase the risk of frailty. The British Biological Database (*34*) showed that patients with four or more chronic diseases have a significantly increased risk of frailty. However, our study showed that multimorbidity may protect against frailty in older populations. This may be because our criteria included two or more diseases. However, most of our patients had mild hypertension or diabetes mellitus. When you have a mild disease, more attention should be paid to your physical condition, but it should become a protective factor against frailty. Future studies should focus on the number and types of diseases that cause frailty.

Our study found that self-reliance of ADL was a protective factor against frailty. If self-care is limited, it can lead to a decrease in health-promoting behavior and

motivation to exercise in the elderly and a decrease in physical activity, resulting in a decline in overall health status. At the same time, the eating ability of people with self-care abilities is affected, which can easily cause adverse events such as insufficient daily energy intake and long-term bed rest, eventually leading to frailty. A previous study (*35*) indicated that disability in ADL is an adverse outcome of frailty that places a burden on frail elderly individuals. The functional status of hospitalized older adults can be improved through multi-domain interventions. Wang *et al.* (*36*) confirmed that participation in a multidomain intervention program during hospitalization improved the functional status and decreased the length of hospitalization, medical costs, and readmission rates of frail older people. Therefore, more attention should be paid to rehabilitation training for daily activities of the elderly to achieve life independence.

The strengths and limitations of this study must be considered. As this is a population-based study, our findings may be generalizable to similarly structured healthcare systems. We also based our data on validated, accurate, and complete measures of exposure and outcomes. To our knowledge, this is the first assessment of HBP patient-centered frailty rates and influencing factors. The present study has several limitations. First, the Fried FP was used as an assessment tool to determine preoperative frailty. The questionnaire only requires five minutes to complete, yet it covers physical functioning tests. Due to the time required for completion, it is unsuitable for use in busy outpatient settings. Despite testing physical function, it is a self-reported questionnaire that contains patient-reported outcomes. Due to individual interpretations, patients may overestimate or underestimate the actual problems that exist. Second, the sample size was relatively small. It would be difficult to extrapolate our study findings to cognitively impaired patients who do not have caregivers and to potentially high-risk patients because we could not recruit them for the study. We believe that the results of this study may have been influenced by systematic selection bias. Third, our study did not identify specific diseases in the patients who underwent surgery. Depending on the disease, the frailty factors affecting the patient may be different. Fourth, our study subjects are Chinese people, and whether the same conclusions will be drawn for older people with HBP disease in different countries. Finally, we only studied the Fried's FP and its association with HBP surgery patients; future research will be required to determine if similar effect sizes are found with related frailty tools (*e.g.* the Clinical Frailty Scale), as different frailty assessment tools typically only have moderate agreement in terms of who is identified as having frailty.

The surgical population is aging, and frailty is increasingly being observed. With an increasing number of frail patients undergoing surgery, healthcare professionals should be aware of the effects of frailty and develop improved and focused preoperative management strategies for stratified frail patients. The focus of future research and the implementation of science should be threefold. First, achieving a consensus on which frailty tool should be used for screening and diagnosis in HBP surgical settings, rather than developing frailty tools, is paramount. Unfortunately, there is a lack of standardized frailty assessment criteria, and the predictive efficacy, which is also a challenge in neurosurgical procedures (*37*). Future development of objective tools to identify/measure frailty based on the newest biological and computerized technologies is indispensable (*38*). Second, the development of interventions comprising treatment goals and plans that consider preoperative frailty as a risk factor for poor functional recovery may be an important cornerstone of preoperative management. In addition, effectively managing frailty can help alleviate the economic burden of an aging population (*39*). Future research should focus on the development and implementation of interventions that can potentially improve functional and adverse outcomes in frail patients. Third, these research findings should be translated into routine clinical care through the development of collaborative pathways and evaluated using scientific implementation methodologies.

In conclusion, our study shows that good exercise habits, lack of smoking, and good nutrition can prevent the exacerbation of frailty in older adults with HBP.

Acknowledgements

We would like to extend our gratitude to all the medical staff from the Department of Hepatobiliary and Pancreatic Surgery at the First Affiliated Hospital of Chongqing Medical University and Peking University International Hospital in China for their support in data collection.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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Received December 3, 2024; Revised December 14, 2024; Accepted December 16, 2024.

Released online in J-STAGE as advance publication December 17, 2024.

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