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Risk factors for and a prediction nomogram of physical frailty in older patients hospitalized with acute calculous cholecystitis

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Abstract: Frailty increases the risk of complications and delays recovery in older patients with acute calculous cholecystitis (ACC). Early identification is crucial to improving outcomes. Subjects were 386 older inpatients with ACC at two hospitals who were randomly divided into a training set (n = 270) and validation set (n = 116). Patients were categorized into frail and non-frail groups. Binary logistic regression identified significant predictors, and a nomogram was developed. The incidence of frailty was 27% (n = 73). Smoking, a sleep disorder, impaired ADL, and malnutrition were independent predictors for frailty ($p < 0.05$). The nomogram showed good discrimination (AUC = 0.752), with a sensitivity of 82.6% and a specificity of 67.4%. Calibration was acceptable (Hosmer–Lemeshow χ^2 = 4.407, p = 0.732), and decision curve analysis demonstrated clinical utility. The developed nomogram reliably predicts the risk of frailty in older patients with ACC and may facilitate targeted early interventions in clinical practice.

***Keywords*:** physical frailty, acute calculous cholecystitis, elderly, influencing factors, prediction model

1. Introduction

Acute calculous cholecystitis (ACC) is one of the most common surgical acute abdominal conditions. With changes in lifestyle and dietary habits, the incidence of ACC has been increasing. ACC is highly prevalent in China, where it is closely linked to the widespread occurrence of gallstones and the prevalence of gallbladder stones among adults is estimated to be 4.2% to 21.7% (*1*). A study conducted in Liaoning Province reported that the annual prevalence of gallbladder stones increased from 1.59% in 2016 to 2.52% in 2020 (*2*). However, the exact etiology and pathogenesis of gallbladder stones remain unclear. They are generally believed to be associated with multiple factors, including genetic predisposition, metabolic abnormalities, biliary cholesterol supersaturation, impaired gallbladder motility, mucin hypersecretion, intestinal microbiota imbalance, dietary habits, and lifestyle (*3-5*). Due to the rapid progression of ACC, delayed treatment can lead to serious complications, including cholangitis, biliary peritonitis, and septic shock, which may be life-threatening (*6*). Thus, health management of older patients with ACC remains a considerable challenge for medical professionals.

The main treatment options for ACC include conservative management, surgical intervention, and cholecystostomy. Currently, laparoscopic cholecystectomy (LC) is considered to be the treatment of choice for ACC (*7*). It offers several advantages, including minimal surgical trauma, faster recovery, and shorter hospitalization (*8*). The evaluation of pros and cons for surgery in elderly suffering from ACC is more complex than in young people; in addition, old age is not a contraindication for surgery; but better identification of frailty could help lead to the best clinical decision by the surgeon (*9*). Although clinical guidelines emphasize the importance of preoperative frailty assessment in patients with ACC, only a limited number of studies have evaluated the role of frailty in preoperative risk assessment among patients with ACC (*10*), and they have provided evidence for the association between frailty and postoperative outcomes in patients with ACC. Thus, there is a need to identify preoperative clinical variables for older patients with ACC undergoing LC, with a particular focus on frailty.

Frailty is a geriatric syndrome characterized by a

multisystem physiological decline, increased vulnerability to stressors, and adverse clinical outcomes, such as disability, hospitalization, and mortality (*11-13*). The development of physical frailty in older patients is the result of a combination of multiple factors. By using internationally developed screening tools (*14*), potential factors influencing physical frailty can be identified. A review identified as many as 34 factors influencing frailty, encompassing physiological, psychological, social, and lifestyle domains (*15*). However, the development of physical frailty is reversible (*16*), thereby necessitating the development of a convenient and rapid early warning tool, which would improve the management of physical frailty in older patients with ACC, allow early identification of risk factors for physical frailty, and facilitate the adoption of effective intervention measures to prevent, delay, or reverse the progression of frailty.

Currently, research on physical frailty has paid insufficient attention to hospitalized older adults, and specific assessments of patients with ACC are still lacking. Nomogram models are extensively utilized in clinical research to aid clinical decision-making and generate a numerical probability of clinical events to assess patients' frailty (*17*). Although various frailty assessment tools and predictive models have been developed for elderly patients undergoing surgery or hospitalization, there are no existing models of the ACC population specifically.

Given the unique pathophysiological characteristics, surgical considerations, and recovery patterns in older patients with ACC, our study addresses this issue by establishing a tailored nomogram that integrates geriatric, nutritional, and functional domains. This model represents an innovative effort to facilitate the early identification of frailty in patients with ACC and to optimize clinical decision-making.

2. Patients and Methods

2.1. Study design

This was a retrospective cohort study. Convenience sampling was used to select inpatients at two hospitals (the First Hospital Affiliated with Chongqing Medical University and Peking University International Hospital) in China. Subjects were patients with ACC who were 65 years of age or older who were seen from December 2023 to April 2025. Prior to conducting the study, approval was received from the Ethics Committee of the School of Medicine, Hamamatsu University (No. 25-124), the First Hospital Affiliated with Chongqing Medical University (No. 2023-337) and the Peking University International Hospital (No. 2023-KY-0085-01). Subjects' data were processed and electronically stored in accordance with the ethical principles of the Declaration of Helsinki for medical research involving human subjects.

2.2. Quality control measures

i) Controlling selection bias: During the factor extraction phase, close communication with experts was maintained to develop a detailed, scientifically sound, and feasible research protocol. Subjects were selected strictly based on predefined inclusion and exclusion criteria.

ii) Standardizing research implementation: Prior to the study, all research team members underwent standardized training and assessments. Uniform instructions were used throughout the study. Informed consent was obtained from patients and their families. Investigators accompanied subjects throughout the process, answered questions in real time, and ensured timely collection and thorough verification of the authenticity and completeness of questionnaires.

iii) Controlling information bias: A double data entry method was used to ensure the accuracy of data input. Two researchers independently entered, verified, and analyzed the clinical data to maintain data reliability and consistency.

2.3. Subjects

The inclusion criteria for this study were as follows: *i*) patients with ACC who were 65 years of age and older, *ii*) using the diagnostic criteria for ACC as defined by the Tokyo Guidelines (TG18) (*18*), and *iii*) patients who were conscious and provided written informed consent.

The exclusion criteria were as follows: *i*) patients who have been clearly diagnosed with dementia or mental illness, *ii*) patients who could not assist in completing the survey, and *iii*) those with any known severe vision or auditory problems or who were unable to complete the questionnaire. Informed consent was obtained from all patients.

2.4. Sample size

Researchers were trained on the standard use of research tools before conducting the study. Subjects signed the informed consent form, completed the questionnaire individually, and submitted it immediately. When subjects were unable to complete the questionnaire on their own, the researchers assisted them by asking questions. After the questionnaires were collected, they were immediately checked for any omissions, which were corrected on the spot. Data were stored and analyzed anonymously. Based on the method of calculating the sample size for logistic regression (*19*), the sample size should be at least 5 to 10 times the number of independent variables, so the required sample size for modeling would be 138 to 276 patients. In this study, considering a potential loss to follow-up of approximately 40%, we initially planned to recruit 276 subjects but ultimately enrolled 392 individuals.

2.5. Instruments and measurements

Data collected included the demographics of the subjects, such as age, sex, body mass index (BMI), marital status, place of residence (rural/urban), level of education, annual income including tax, alcohol and smoking status, sleep disorder, exercise habits, and living alone, and clinical data such as multimorbidity and polypharmacy, nutritional status (assessed using the Nutritional Risk Screening 2002) (*20*), functional independence (assessed using the Barthel Index) (*21*), depressive state (assessed using the Patient Health Questionnaire-9 [PHQ-9]) (*22*), and frailty measures (Fried's Frailty Phenotype) (*11*). Postoperative data collected included operating time, duration of hospitalization, and postoperative complications. All data were recorded and managed using Microsoft Excel.

2.5.1. Fried's Frailty Phenotype (Fried's FP)

Specially trained nurses assessed frailty status based on functional status at the time of admission using Fried's FP (*13*). Fried's FP test is an easy-to-use and intuitive tool that demonstrates minor variations in performance across different healthcare professionals, countries, and source of data. Fried's FP is a multi-dimensional screening tool consisting of five domains: *i*) weight loss (shrinking): Unintentional weight loss: In the past year, unexpected weight loss > 4.5 kg or > 5% (excluding diet and exercise); *ii*) slow walking speed (slowness): This was assessed by recording the time required to walk 4.6 m; *iii*) grip strength (weakness): This was assessed using the mean of three consecutive measures of the dominant hand, and the cut-of points were adjusted for sex and BMI; *iv*) fatigue (poor endurance/energy): This was assessed with two questions from the Center for Epidemiological Studies–Depression. Elderly individuals were asked how many days a week "I feel I need to work hard to do everything" and "I feel I cannot continue my life," and any answer of more than 3 days a week was assigned 1 point; and *v*) low physical activity: Men exercising less than 383 kcal per week (about 2.5 hours / week) or women exercising less than 270 kcal per week (about 2 hours / week) according to the Minda Leisure Activity Questionnaire. The scores were summed, with a score of ≥ 3 classified as frail.

2.5.2. Nutritional Risk Screening 2002 (NRS 2002)

This scale is a nutritional risk-screening tool developed by Kondrup *et al.* (*20*) in 2002 that 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.

2.5.3. Barthel Index (BI)

The BI is an ordinal scale used to measure functional disability while performing ten daily activities (*21*). It is a validated 10-item instrument that measures a patient's independence in performing the main activities of daily living (ADL), including bathing, dressing, toileting, transferring, continence, and feeding. Functional status is defined as "independent" if the subject does not require any assistance from another person for any ADL. The subject is considered "partially dependent" if they require some assistance from another person for ADL and "totally dependent" if they require assistance for all ADL. Scores range from 0-100, with a total score of 100 indicating the highest level of independence.

2.5.4. Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (*22*) 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 on 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).

2.6. Statistical analyses

Statistical analyses were performed using the software IBM SPSS Statistics 29.0 and R version 4.5.0. Frailty was analyzed as a categorical variable. Descriptive statistics of the baseline demographic and clinical variables were calculated using the mean (standard deviation) or percentage (%). The Shapiro-Wilk test was used to assess normal distribution. The Mann–Whitney *U* test 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. The area under the receiver operating characteristic (ROC) curve and the area under the curve (AUC) of the ROC were used to evaluate the model's discriminative ability; the Hosmer-Lemeshow test and calibration curve were used to evaluate the model's goodness of fit; and decision curve analysis (DCA) was used to evaluate the clinical benefit of the model. The significance level was set at $\alpha = 0.05$, and statistical significance was defined as a p-value < 0.05.

3. Results

3.1. Subject characteristics and the prevalence of frailty

A total of 392 elderly patients with ACC were interviewed, and six were excluded due to incomplete clinical data. Ultimately, 386 elderly patients with ACC were included. Of these, 270 served as the training set, while 116 served as the validation set. The prevalence of frailty in the two sets was 27% and 21.6%, respectively. The mean (± standard deviation) patient age in the training set was 71.86 ± 6.03 years. For the validation set, the average age was 70.18 years. The subjects' basic characteristics and univariate analysis data are shown in Table 1.

3.2. Related variables

Table 1. Univariate analysis of physical frailty in older patients with acute calculous cholecystitis

Variable	Training set			*p*-value	Validation set			*p*-value
	Total *n* = 270	Non-frail *n* = 197 (73%)	Frail *n* = 73 (27%)		Total *n* = 116	Non-frail *n* = 91 (78.4%)	Frail *n* = 25 (21.6%)	
Age (years, x ± s)	71.86 ± 6.03	71.85 ± 5.24	72.89 ± 7.80	0.102	70.18 ± 5.9	70.24 ± 6.35	69.96 ± 4.0	0.148
65 ≤ age < 70	33 (12.2%)	20 (60.6%)	13 (39.4%)		68 (58.6%)	57 (83.8%)	11 (16.2%)	
70 ≤ age < 80	116 (43%)	99 (85.3%)	17 (14.7%)		37 (31.9%)	25 (67.6%)	12 (32.4%)	
Age ≥ 80	121 (44.8%)	78 (64.5%)	43 (35.5%)		11 (9.5%)	9 (81.8%)	2 (18.2%)	
Sex (*n*, %)				0.273				0.316
Male	148 (54.8%)	104 (70.3%)	44 (29.7%)		64 (55.2%)	48 (75%)	16 (25%)	
Female	122 (45.2%)	93 (76.2%)	29 (23.8%)		52 (44.8%)	43 (82.7%)	9 (17.3%)	
BMI	22.64 ± 3.47	22.78 ± 3.36	22.26 ± 3.73	0.295	23.13 ± 3.54	22.94 ± 3.6	23.82 ± 3.27	0.358
Marital status (*n*, %)				0.158				0.583
Married	218 (80.7%)	155 (71.1%)	63 (28.9%)		98 (84.5%)	76 (77.6%)	22 (22.4%)	
Unmarried, divorced, or widowed	52 (19.3%)	42 (80.8%)	10 (19.2%)		18 (15.5%)	15 (83.3%)	3 (16.7%)	
Level of education (*n*, %)				0.063				0.138
No post-secondary	230 (85.2%)	163 (70.9%)	67 (29.1%)		106 (91.4%)	85 (80.2%)	21 (19.8%)	
Bachelor degree or above	40 (14.8%)	34 (85%)	6 (15%)		10 (8.6%)	6 (60%)	4 (40%)	
Place of residence (*n*, %)				0.643				0.327
Rural	83 (30.7%)	59 (71.1%)	24 (28.9%)		69 (59.5%)	52 (75.4%)	17 (24.6%)	
Urban	187 (69.3%)	138 (73.8%)	49 (26.2%)		47 (40.5%)	39 (83%)	8 (17%)	
Annual income including tax (*n*, %)				0.227				0.953
< 50,000	154 (57%)	108 (70.1%)	46 (29.9%)		69 (59.5%)	54 (78.3%)	15 (21.7%)	
≥ 50,000	116 (43%)	89 (76.7%)	27 (23.3%)		47 (40.5%)	37 (78.7%)	10 (21.3%)	
Smoking status (*n*, %)				< 0.001				0.003
Quit/non-smoker	217 (80.4%)	168 (77.4)	49 (22.6%)		32 (27.6%)	31 (96.9%)	1 (3.1%)	
Current smoker	53 (19.6%)	29 (54.7%)	24 (45.3%)		84 (72.4%)	60 (71.4%)	24 (28.6%)	
Alcohol status (*n*, %)				0.425				0.169
Quit/non-drinker	233 (86.3%)	168 (72.1%)	65 (27.9%)		102 (87.9%)	82 (80.4%)	20 (19.6%)	
Current drinker	37 (13.7%)	29 (78.4%)	8 (21.6%)		14 (12.1%)	9 (64.3%)	5 (35.7%)	
Exercise habits (*n*, %)				0.002				0.004
No	93 (34.4%)	57 (61.3%)	36 (38.7%)		63 (54.3%)	43 (68.3%)	20 (31.7%)	
Yes	177 (65.6%)	140 (79.1%)	37 (20.9%)		53 (45.7%)	48 (90.6%)	5 (9.4%)	
Multimorbidity (*n*, %)				0.048				0.026
0–1	134 (49.6%)	105 (78.4%)	29 (21.6%)		60 (51.7%)	52 (86.7%)	8 (13.3%)	
≥ 2	136 (50.4%)	92 (67.6%)	44 (32.4%)		56 (48.3%)	39 (69.6%)	17 (30.4%)	
Sleep disorder (*n*, %)				< 0.001				0.015
No	177 (65.6%)	141 (79.7%)	36 (20.3%)		37 (31.9%)	24 (64.9%)	13 (35.1%)	
Yes	93 (34.4%)	56 (60.2%)	37 (39.8%)		79 (68.1%)	67 (84.8%)	12 (15.2%)	
Polypharmacy (*n*, %)				0.024				< 0.001
0–3	232 (85.9%)	175 (75.4%)	57 (24.6%)		59 (50.9%)	50 (84.7%)	9 (15.3%)	
≥ 4	38 (14.1%)	22 (57.9%)	16 (42.1%)		57 (49.1%)	32 (56.1%)	25 (43.9%)	
Depressive state (*n*, %)				0.021				< 0.001
No	181 (67%)	140 (77.3%)	41 (22.7%)		66 (56.9%)	59 (89.4%)	7 (10.6%)	
Yes	89 (33%)	57 (64%)	32 (36%)		50 (43.1%)	32 (64.0%)	18 (36%)	
ADL (*n*, %)				< 0.001				0.025
Dependent	65 (24.1%)	34 (52.3%)	31 (41.7%)		93 (80.2%)	69 (74.2%)	24 (25.8%)	
Independent	205 (75.9%)	163 (79.5)	42 (20.5%)		23 (19.8%)	22 (95.7%)	1 (4.3%)	
Living alone (*n*, %)				0.111				0.186
No	220 (81.5%)	156 (70.9%)	64 (29.1%)		98 (84.5%)	79 (80.6%)	19 (19.4%)	
Yes	50 (18.5%)	41 (82%)	9 (18%)		18 (15.5%)	12 (66.7%)	6 (33.3%)	
Malnutrition (*n*, %)				< 0.001				0.010
No	186 (68.9%)	148 (79.6%)	38 (20.4%)		68 (58.6%)	59 (86.8%)	9 (13.2%)	
Yes	84 (31.1%)	49 (58.3%)	35 (41.7%)		48 (41.4%)	32 (66.7%)	16 (33.3%)	

Data are expressed as the mean ± standard deviation or median (interquartile range) unless indicated otherwise; statistical significance was defined as a *p*-value < 0.05. BMI: body mass index; ADL: activities of daily living.

Table 2. Logistic regression analysis of physical frailty in older patients with acute calculous cholecystitis for development of a predictive model

Variable	Group	*B*	SE	Wald χ^2	*p*-value	OR	95% CI	
							Lower limit	Upper limit
Smoking status	Quit/non-smoker				Reference			
	Current smoker	0.985	0.36	7.501	0.006	2.678	1.323	5.42
Exercise habits	No				Reference			
	Yes	-0.508	0.349	2.126	0.145	0.602	0.304	1.191
Multimorbidity	0–1				Reference			
	≥ 2	0.324	0.358	0.817	0.366	1.383	0.685	2.791
Sleep disorder	No				Reference			
	Yes	0.575	0.329	3.058	0.08	1.778	0.933	3.389
Polypharmacy	0–3				Reference			
	≥ 4	0.683	0.426	2.572	0.109	1.981	0.859	4.566
Depressive state	No				Reference			
	Yes	0.104	0.373	0.078	0.078	1.11	0.534	2.306
ADL	Dependent				Reference			
	Independent	-1.067	0.368	8.422	0.004	0.344	0.167	0.707
Malnutrition	No				Reference			
	Yes	0.985	0.379	6.756	0.009	2.677	1.274	5.626

Statistical significance was defined as a p-value < 0.05. SE: standard error; OR: odds ratio; CI: confidence interval; ADL: activities of daily living.

In the modeling group, univariate analysis revealed that smoking status, exercise habits, multimorbidity, sleep disorder, polypharmacy, depressive state, ADL, and malnutrition were significant influencing factors (p < 0.05), as shown in Table 1.

3.3. Logistic regression of patients with ACC

Logistic regression analysis was performed using physical frailty (no = 0, yes = 1) as the dependent variable and variables with statistical significance in univariate analysis as independent variables. The results of the multivariate regression analysis indicated that smoking status, ADL, and malnutrition were independent factors influencing physical frailty in older patients with ACC (p < 0.05), as shown in Table 2.

3.4. Development of an individualized prediction model

Figure 1 shows the constructed nomogram using the software R. In practical application, healthcare professionals first locate the corresponding scores for each predictive indicator on the first row (Points) of the nomogram based on the patient's specific condition, they sum the scores and draw a vertical line intersecting the last row of the nomogram from the marked total score (Total Points). At this intersection point, the value represents the patient's probable risk of physical frailty.

3.5. Validation and evaluation of the predictive model

The prediction model achieved an AUC of 0.752 (95% CI: 0.685–0.812) in the training set with a specificity of 67.1% and a sensitivity of 73.6%, as shown in Figure 2A. The Hosmer- Lemeshow-show test yielded a χ^2 value of 4.407 and a p-value of 0.732 as shown in Figure 3A. The DCA curve did not intersect with the two extreme curves, implying that the net return rate of the nomogram prediction model is higher than that intervention and non-intervention, underscoring the model's clinical applicability, as shown in Figure 4A. Collectively, these results indicate that the nomogram model is suitable for predicting the risk of frailty in older patients who were hospitalized for ACC.

For external validation, 116 patients with ACC were used. The AUC of the model was 0.873 (95% CI: 0.778–0.968) and is shown in Figure 2B. The results of the Hosmer–Lemeshow test were χ^2 = 14.379 and p = 0.0724. The accuracy and specificity of the model were 68% and 97.8%, respectively, indicating that the model performed well in its predictive efficacy in the external validation set. Both the calibration curve (Figure 3B) and DCA (Figure 4B) further affirmed the model's discriminating ability and clinical utility.

4. Discussion

4.1. An elevated risk of physical frailty in older patients with ACC

Presently, there are few studies on physical frailty in hospitalized patients with ACC, and there is no risk prediction model for physical frailty in patients with ACC. In our study population, the prevalence of physical frailty among hospitalized elderly patients with ACC was found to be 27.0%, indicating a high level of physical frailty in this population. Physical frailty can affect the quality of life of older people, leading to postoperative complications, readmission, and even death (*23-25*). Therefore, an urgent task is to develop a risk prediction model for early identification of physical frailty in elderly individuals with ACC and timely intervention.

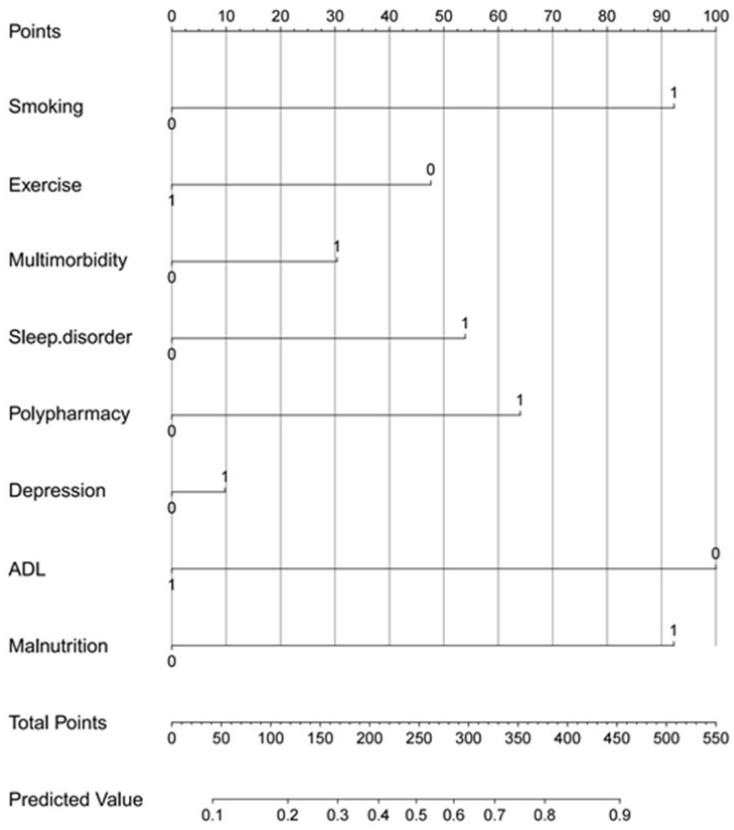

Figure 1. Nomogram to predict the risk of physical frailty in older patients with acute calculous cholecystitis. This nomogram includes smoking, exercise, multimorbidity, sleep disorder, polypharmacy, depression, sleep disorders, ADL, and malnutrition. The horizontal scale labeled "Points" reflects the impact of each variable. A line was drawn up to the points axis for each variable. The total score was calculated by summing all of the variables. Then, the probability of non-frailty and frailty was determined by drawing a line down from the total points axis to the horizontal axis "Risk of non-frailty" and "Risk of frailty" below.

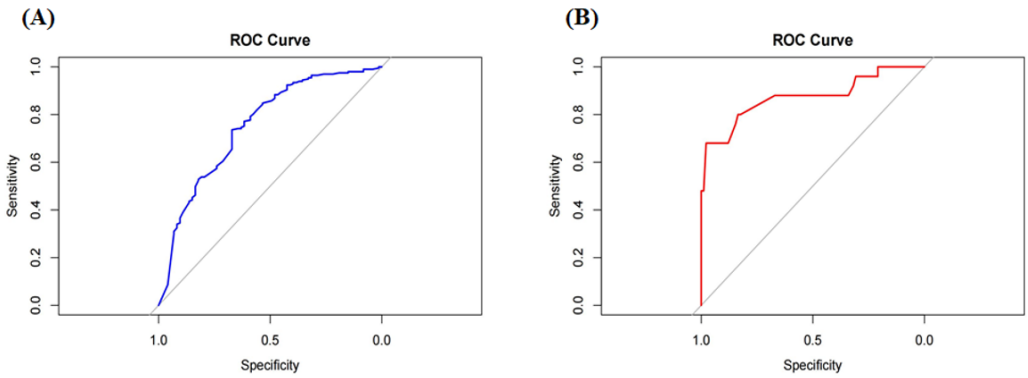

Figure 2. The receiver operator characteristic (ROC) curve for the model to predict the risk of frailty. (A) Training set; **(B)** Validation set.

In addition, Li *et al*. (*26*) reported that the incidence of frailty among hospitalized patients with hemodialysis was approximately 34.7%, which is about 10% higher than the risk of frailty observed in our study. Ramos *et al*. (*27*) also used the Frailty Phenotype (FP) in a study of patients undergoing asymptomatic aortic stenosis, and they reported that the prevalence of frailty was high as 59.6%. Additionally, Goh *et al*. (*28*) used the Clinical Frailty Scale (CFS) to evaluate the frailty status of 233 elderly patients undergoing emergency laparotomy and found a 26.0% incidence of frailty risk. These data suggest that greater attention should be paid to the risk of frailty in older adults with diseases. Early screening and identification of high-risk individuals are essential,

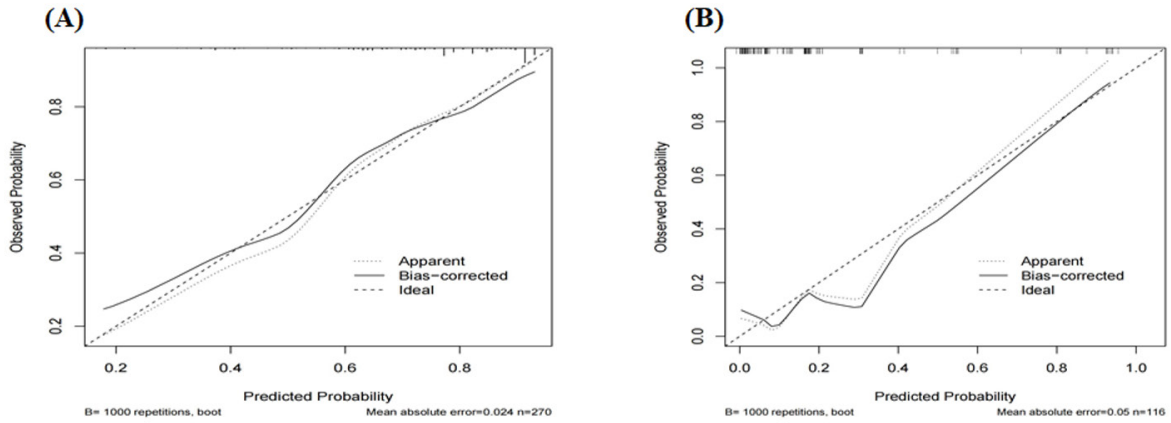

Figure 3. Calibration curve for the frailty risk model in training and validation sets of older patients with acute calculous cholecystitis. (A) Calibration curves for the training group show that the apparent curve closely matches the ideal curve, indicating predictive probability. **(B)** Calibration curves for the test group also show that the apparent curve aligns well with the ideal curve, confirming the model's strong predictive performance. Note: The X-axis represents the predicted possible risk of physical frailty in patients with ACC. The Y-axis represents the actual diagnosed ACC. The dashed line represents the original performance, and the solid dashed line represents the performance during internal validation by Bootstrapping (*B* =1,000 repetitions).

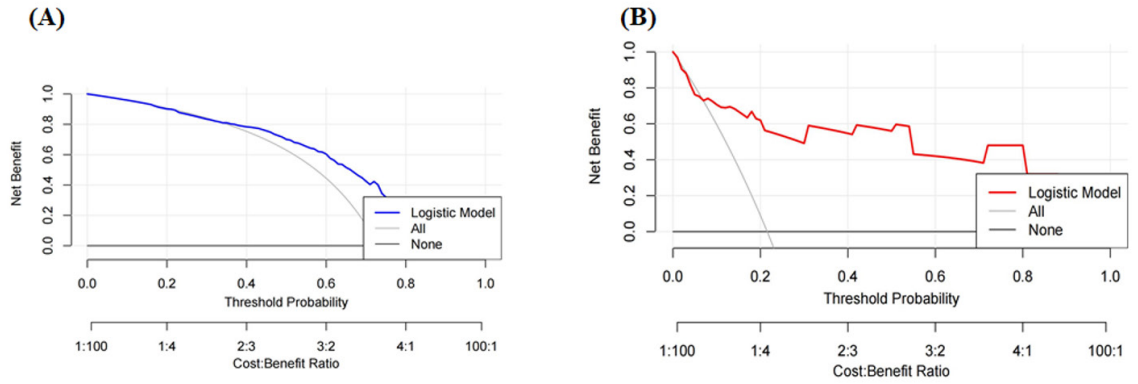

Figure 4. Decision curve analysis (DCA) of the nomogram to predict frailty risk in training and validation sets.

Table 3. Comparison of existing models to predict frailty and our ACC-specific model

Name of model	Applicable population	Predictive factors	Method of prediction	Applicability to ACC
Clinical Frailty Scale (CFS)	General elderly	Functional status	Clinical scoring	Not disease-specific
Frailty Index (FI)	General elderly	> 30 variables (deficit accumulation)	Continuous index	Complex and non-specific
Hospital Frailty Risk Score	Inpatients	ICD code-based	Risk stratification	Not personalized; lacks functional data
This study's nomogram	Elderly patients with ACC	Smoking, ADL, malnutrition, sleep disorder	Logistic regression + nomogram	High specificity and tailored to ACC

ACC: acute calculous cholecystitis; ADL: activities of daily living.

along with timely and effective interventions to prevent or delay the onset and progression of frailty.

As shown in Table 3, compared to existing frailty models such as the CFS, Frailty Index (FI), and general nomograms developed for surgical patients, our model features several innovations. First, it is the first frailty prediction model specifically designed for elderly patients with ACC, incorporating clinical variables closely related to their perioperative status. Second, it integrates modifiable and multidimensional risk factors

such as impaired ADL, malnutrition, smoking, and sleep disorders — factors that are both clinically relevant and targetable for intervention. Third, the model exhibits strong external validation performance (AUC = 0.873), underscoring its predictive reliability. A comparative summary is provided in Figure 2B.

4.2. Analysis of risk factors for physical frailty

This study established a model encompassing smoking status, exercise habits, multimorbidity, sleep disorder, polypharmacy, depressive state, sleep disorders, ADL, and malnutrition to forecast the risk of frailty in older patients with ACC. The results of this study indicate that impaired ADL increases the risk of physical frailty in older patients with ACC. Previous research has demonstrated a bidirectional relationship between ADL and frailty (*29,30*), wherein frailty may lead to functional decline and increased dependence in ADL, while limitations in ADL may in turn exacerbate frailty by reducing physical activity and social engagement. This reciprocal dynamic underscores the importance of early identification and intervention for older adults exhibiting even minor impairments in ADL. From a clinical perspective, healthcare providers should not only encourage patients to maintain regular physical activity within their functional capacity but also promote engagement in cognitively stimulating and socially interactive activities. A comprehensive, multidimensional approach to rehabilitation may help mitigate the progression of frailty and thus preserve independence.

A depressive state, characterized by persistent low mood and diminished interest, is a prevalent psychological concern among the elderly (*31*). Although our study did not find a statistically significant association between depressive symptoms and physical frailty, several previous studies have reported a strong link between the two (*32,33*). Depression may contribute to reduced appetite, poor nutritional intake, and decreased physical activity, all of which are recognized contributors to the onset and progression of frailty. These observations underscore the importance of incorporating mental health assessments and timely psychological support into comprehensive geriatric care. Moreover, although regular physical exercise has been widely acknowledged as a protective factor against frailty (*18*), this association was not confirmed in our study. A possible explanation lies in the clinical context of our subjects, many of whom were in the active treatment phase of their illness, potentially limiting their engagement in physical activity. Therefore, interpretation of such findings requires consideration of the subjects' functional status and disease stage, and future longitudinal studies are warranted to further clarify these associations.

A study has indicated that smoking is a significant risk factor for increased physical frailty (*34*), a finding that aligns with the results of our study. Chronic tobacco use is known to impair cardiopulmonary function, reduce exercise capacity, and exacerbate systemic inflammation, all of which may contribute to decreased physical performance and an accelerated decline in functional reserve among older adults. This cumulative physiological burden promotes the development and progression of frailty. Given that smoking is a modifiable behavioral risk factor, incorporating smoking cessation into comprehensive frailty prevention and intervention strategies has substantial clinical value. Smoking cessation interventions, including counseling, nicotine replacement therapy, and behavioral strategies, have been shown to improve not only cardiopulmonary function but also physical performance and quality of life in older adults (*35*). Incorporating structured cessation programs into perioperative care pathways could thus directly contribute to a reduced risk of frailty. Cessation programs tailored to the elderly population may not only delay the onset of frailty but also contribute to improved overall health outcomes and a reduction in long-term healthcare resource utilization.

This study found that sleep disorders are significant risk factors for physical frailty in older patients with ACC. A recent systematic review analyzing 13 cross-sectional and 4 longitudinal studies found that insomnia symptoms, both short and long sleep durations, and perceived poor sleep quality were independently associated with physical frailty (*36*). Mounting evidence confirms the significant role of sleep quality in the development and progression of frailty. From a clinical standpoint, routine screening for sleep disturbances should be integrated into geriatric assessments. Moreover, comprehensive interventions — including behavioral strategies and psychological support — may not only alleviate sleep-related symptoms but also mitigate negative emotional states, thereby improving sleep quality and potentially slowing the trajectory of physical decline. Future studies should explore individualized, multifactorial interventions to optimize sleep health as a key component in frailty prevention.

Although multimorbidity, polypharmacy, and exercise habits were not significantly associated with physical frailty in our multivariate analysis, they remain clinically important factors that should not be disregarded. Numerous studies have consistently reported strong associations between these variables and frailty. For instance, a Japanese cohort study found that individuals taking five or more medications had nearly twice the odds of being frail (adjusted OR: 1.89, 95% CI: 1.40–2.57), particularly presenting with components such as weight loss, weakness, and slowness (*37*). Similarly, a multicenter cohort study in China demonstrated that polypharmacy among hospitalized patients age 65 and older was a significant predictor of frailty progression over a two-year period (*38*). In addition, a hospital-based study in Nepal revealed that the presence of comorbidities increased the risk of frailty by more

than threefold (*39*). These findings suggest a complex interplay wherein multimorbidity necessitates the use of multiple medications, which may lead to adverse drug reactions, reduced physiological resilience, and ultimately increased frailty. From a clinical perspective, this underscores the importance of implementing structured medication reviews and targeted deprescribing protocols as part of routine frailty management. Even in the absence of significant associations in a given study, the underlying biological plausibility and consistent evidence from prior research highlight the need for continued vigilance in managing these factors to prevent the exacerbation of frailty in older adults.

Given that our study population consisted of hospitalized older adults, opportunities for regular physical activity were inherently limited. Nevertheless, the influence of exercise on the development and progression of frailty should not be underestimated. Emerging evidence suggests that the type, mode, intensity, and duration of physical activity significantly affect both the onset and potential reversal of frailty. A community-based study in Taiwan reported that engaging in 31–60 minutes of daily exercise reduced the risk of frailty by 59%, while exercising for more than 60 minutes led to a 69% risk reduction (*40*). Conversely, another study has noted that high-frequency exercise, including intensive resistance training, may be associated with more severe frailty in certain populations (*41*). These findings underscore the necessity of individualized exercise programs that account for an older adult's baseline physical capacity, comorbidities, and recovery stage. From a clinical perspective, tailoring exercise interventions to meet functional needs and avoid overexertion is critical to maximizing benefit and minimizing harm. Thus, incorporating structured yet adaptable physical activity programs into frailty management protocols may offer a safe and effective strategy to improve outcomes in older adults.

Malnutrition has been widely recognized as a critical and modifiable risk factor for physical frailty among older adults. Numerous studies have demonstrated a strong association between malnutrition and frailty, particularly among inpatients or surgical patients. For instance, a recent systematic review reported that older adults at risk of malnutrition were 2.5 to 4 times more likely to be frail compared to well-nourished individuals (*30*). This relationship is often bidirectional: frailty may lead to reduced appetite and food intake due to fatigue, depression, or swallowing difficulties, while malnutrition accelerates sarcopenia and worsens the severity of frailty (*42*). In the present study, malnutrition, assessed with the NRS-2002, was identified as an independent risk factor for frailty in elderly patients with ACC. This finding corroborates previous findings and highlights the importance of routine nutritional assessment and intervention in frailty prevention strategies. Early identification of nutritional risk followed by individualized dietary counseling, oral nutritional supplements, and, when appropriate, enteral nutrition support may mitigate the progression of frailty and improve postoperative outcomes. Given that nutritional interventions are relatively low-cost and easily implementable, integrating structured nutritional screening into routine care — particularly in high-risk populations such as elderly patients with ACC — should be a clinical priority.

Although a depressive state, polypharmacy, and lack of exercise were not statistically significant in the multivariate model, they were retained in the final predictive nomogram based on their established clinical relevance and corroboration in previous studies. Even in the absence of statistical significance, the inclusion of these variables enhances the clinical interpretability and comprehensiveness of the model, aligning with the goal of early identification and prevention. This approach is also consistent with previous nomogram studies that emphasize clinical plausibility over strict statistical thresholds when selecting predictive variables (*43,44*). The model we propose represents an interdisciplinary framework that integrates physical, psychological, and lifestyle-related dimensions in understanding frailty. While each domain may be analyzed independently, in real-world clinical settings, these factors interact in complex and tightly interwoven ways to influence overall health outcomes. Moreover, this predictive model equips clinical healthcare professionals with a practical tool for assessment of the risk of frailty. After brief training, they can use this model to forecast the risk of frailty in patients with ACC. This proactive approach facilitates early risk identification, enabling timely interventions. Such early actions can mitigate deteriorations in patients' frailty status during therapeutic procedures.

4.3. Limitations

The limitations of this study are as follows: First, in this study, the variables included in the model were not limited to those identified in the multivariate analysis. To develop a comprehensive predictive model, we also incorporated psychological factors that displayed significance in univariate analysis. Future research should conduct multicenter studies with larger sample sizes to enhance the reliability of the findings. Second, the predictive factors involved in this study were limited and primarily based on self-reported data. Future research should include more objective measurement predictors to identify risk factors for physical frailty more comprehensively and objectively. Third, the nomogram developed in this study was mainly based on data from elderly patients with ACC in two Chinese cities, and its generalizability may be influenced by patients' demographic characteristics, disease presentation, and regional differences in medical practice; the model requires external validation in other regions. Fourth,

age is a risk factor for physical frailty, and there may be differences in risk factors between different age groups (older and young people). Future research should explore and predict physical frailty in cancer patients across different age groups. Fifth, this study provides an initial nomogram tool to predict physical frailty in elderly patients with ACC. To enhance its practicality and convenience, future research could consider developing a dynamic nomogram or an online calculator to establish a predictive platform that facilitates the screening, prevention, and management of physical frailty in elderly patients with ACC.

4.4. Clinical implications and prospects for application

This frailty prediction model has potential for broad clinical applicability, particularly in preoperative evaluation and emergency triage of elderly patients with ACC. Since frailty is a crucial determinant of postoperative outcomes and treatment tolerance, the model may assist surgeons and geriatricians in stratifying surgical risk, guiding perioperative decision-making, and tailoring individualized care plans. For example, patients identified as high-risk can receive early interventions such as nutritional supplementation, physiotherapy, or closer postoperative monitoring.

Moreover, the simplicity of the model and the limited number of predictors facilitate its integration into electronic medical record (EMR) systems, allowing automated alerts about the risk of frailty during hospitalization. With further validation, this model also has the potential to be developed into a mobile app or web-based calculator for bedside or outpatient use by clinicians, enhancing its efficiency and accessibility in busy hospital settings. These future directions would greatly enhance the real-time utility of the model in both acute care and routine management.

An important point worth noting, however, is that several predictors in the model — such as smoking status, sleep quality, and depressive symptoms — are based on self-reported information. While self-reported data can be subject to recall bias or subjective misinterpretation, many of these variables (*e.g.*, ADL, PHQ-9, NRS2002) have been widely validated and are commonly used in clinical assessments. Nevertheless, the reliability of the model in real-world use may vary depending on the accuracy of patient-reported inputs. To address this limitation, future work should focus on developing standardized data collection interfaces, possibly incorporating patient-reported outcome measures (PROMs) *via* EMRs or apps, and conducting prospective studies to evaluate the model's real-time performance across diverse clinical settings.

5. Conclusions

Older patients with ACC are at a higher risk of frailty. This risk is intricately associated with various factors. By identifying high-risk individuals and implementing tailored interventions to alleviate frailty, the exacerbation of disease symptoms can be mitigated in patients with ACC. Moreover, this nomogram should be validated and widely used across diverse populations and healthcare settings in the future.

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