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Research Article

Influencing Factors and a Predictive Nomogram of Frailty in Chinese Patients with Cancer: A Single-Center Retrospective Study

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Objective. The number of cancer survivors is increasing, and the high prevalence of frailty not only reduces quality of life but also affects the treatment of cancer patients. This study aimed to identify the prevalence and risk factors of frailty in cancer patients and to construct a nomogram to predict the probability of frailty. *Methods*. Nine hundred fifty-eight cancer patients were included in this retrospective study, randomly divided into a development set ($n = 680$) and a validation set ($n = 278$). Frailty was assessed using the Tilburg frailty indicator (TFI). Social support, medical coping styles, and psychological distress were assessed by the Social Support Self-Rating Scale (SSRS), Medical Coping Modes Questionnaire (MCMQ), and distress thermometer (DT), respectively. *Results*. The prevalence of frailty in cancer patients was 45.93%. Cancer patients who exercised regularly, ate a balanced diet, and actively coped with diseases were less likely to become frail. The risk factors for frailty identified by a multivariate analysis were parenteral nutrition, advanced TNM staging, vegetarian diet, unemployment, psychological distress ≥4, low physical activity, and negative coping styles. These risk factors were used to construct a nomogram, and the C-index, calibration curve, and decision curve analysis (DCA) were used to assess the performance of the nomogram. The C-index was 0.762, and the calibration curve showed satisfactory coherence. The net benefit of the nomogram was better between threshold probabilities of 17%–96% in DCA. *Conclusion*. Special focus needs to be placed on frail cancer patients due to their high prevalence and severe outcomes. Clinical medical workers could use this nomogram to identify high-risk patients and intervene early to prevent frailty.

1. Introduction

Cancer ranks as a leading public health problem worldwide. Nineteen million new cancers and ten million cancer deaths occurred in 2020, and the World Health Organization has estimated that there will be 28.4 million cases in 2040, which represents a significant global burden of cancer incidence and mortality [1]. With the development of therapeutic technologies and new drugs, individuals with cancer can live longer; thus, an increasing number of cancer patients focuses on quality of life instead of length of life. Surgical excision, radiotherapy, and chemotherapy are essential parts of multimodality therapy, and many cancer survivors have accepted these treatments. Despite satisfactory outcomes and treatment-related side effects that have been partly mitigated through the use of intensity-modulated techniques and medicine, these therapies can still induce cellular senescence in all kinds of cells and lead to extensive physical injury [2–4]. Cancer has reduced patient resistance, and coupled with the damage caused by the side effects of surgery, radiation, and chemotherapy, the reserves of cancer patients have decreased sharply [5].

Frailty is a complex, multidimensional, and reversible state of diminished physiological reversibility. It is a condition marked by a decline in multiple physiologic systems, decreased resiliency and adaptive capacity, and increased

vulnerability to stressors [6, 7]. Frailty impacts not only disease survival but also quality of life in cancer patients. Cancer is a highly stimulating stressor event, and the majority of patients with common malignancies are older adults. In addition to additional therapeutic side effects, the incidence of frailty in cancer patients can be as high as 86% [8]. Moreover, frailty could be a predictor for readmission, healthy resource use, chronic disease, risk of postoperative complications, and mortality [9–12]. Following an effective early warning and intervention, cancer patients might reverse their frail status. Therefore, it is essential to understand the impacts of frailty on the effective and correct management of nursing care.

Previous studies focused on the physical and disease factors of cancer patients and demonstrated that age, malnutrition, surgery, chronic diseases, and low physical activity could significantly influence their frailty [13–15]. Along with the deepening of research, few studies have reported that in addition to these disease-related indicators, psychological factors and social support were related to frailty [16–18]. To date, however, only a limited number of studies have investigated these factors in frailty. Therefore, the identification of risk factors and the construction of a prediction model for frail patients are imperative. The main objective of this study was to describe the morbidity of frailty in cancer patients and to assess psychosomatic and social factors associated with frailty. Then, these related influencing factors were used to construct a nomogram to identify high-risk patients.

2. Methods

2.1. Study Population. This retrospective study included cancer patients at the Department of Medical Oncology, Nanfang Hospital, from March 2021 to May 2022. The criteria for enrolment in this study were as follows: (1) pathological diagnosis of cancer, (2) age ≥18 years, and (3) informed consent and voluntary participation in this study. The exclusion criteria included (1) mental illness or major depression, (2) use of psychiatric medication within two weeks of the survey, and (3) incomplete medical records. Before initiating questionnaire collection, inform patients that their treatment or care will not be influenced by their participation. Ensuring the strict protection of patients' personal information and privacy, and questionnaire collection should only commence after obtaining informed consent. Establishing a standardized survey process and providing systematic training for investigators ensure consistency and adherence to the established standard. During questionnaire collection, investigators are advised to refrain from providing targeted explanations to patients to maintain the accuracy of responses. Following the survey, prompt data review is conducted by investigators. If any discrepancies or unusual values are identified, patients are promptly contacted to address and resolve any concerns. All procedures in this study conformed to ethical standards and the Declaration of Helsinki, and this study was approved by the Nanfang Hospital Ethics Committee (no. NFEC-202103-K5).

2.2. Demographic and Clinical Characteristics. A self-designed questionnaire was used to collect sociodemographic characteristics, including diet and sports habits, mode of nutrition, and other information obtained from the medical records by researchers, such as sex, age, TNM staging, height, weight, comorbidities, history of surgery, marital status, type of cancer, cancer duration, and cancer metastasis.

2.3. Tilburg Frailty Indicator Questionnaire—Chinese Version (TFI-C). Frailty was assessed with the Tilburg frailty i indicator (TFI). The TFI was originally compiled by Gobbens [19], and the Chinese version was translated by Dong et al. [20]. The Chinese TFI contains 15 items addressing three domains, including physical, psychological, and social aspects. Each item is scored 0 or 1, with a total score ranging from 0 to 15 points. A total score ≥5 is defined as frailty. The higher the total scores, the more severe the frailty is. The Chinese TFI has been used in patients with cancer and has proven to be extensively culturally adapted and validated [21, 22]. The overall internal consistency (Cronbach's α) of the TFI in this study was 0.778, and the internal consistencies of the physical, psychological, and social domains were 0.709, 0.745, and 0.796, respectively.

2.4. International Physical Activity Questionnaire—Chinese Version (IPAQ-C). Physical activity was measured by the International Physical Activity Questionnaire (IPAQ)—Chinese version, which is a self-report questionnaire originally compiled by the International Consensus Group on Physical Activity Measurement [23]. The Chinese version was translated by Qu and Li [24], and it has shown excellent reliability and validity when compared to other physical activity instruments [25]. The IPAQ-C contains 3 levels and 7 questions. We input the information from the questionnaire into an Excel file to calculate the physical activity intensity level automatically (available at https://sites.google.com/view/ipaq/home).

2.5. Social Support Self-Rating Scale (SSRS). The level of social support was assessed by the Social Support Self-Rating Scale. The SSRS was developed by Xiao [26], and it divides social support into material support and emotional support. The SSRS consists of 10 items measuring 3 dimensions, including subjective support, objective support, and utilization of support. The scoring method is a 4-point Likert scale ranging from 1 (never seek help) to 4 (regularly seek help) and the number of sources providing support. The three dimensions add up to the total score (range: 12–66). Higher total scores indicate stronger social support. It has become one of the most commonly used instruments for measuring social support in China due to its high reliability and validity [27]. The total internal consistency (Cronbach's α) of the SSRS scale in this study was 0.789, and the internal consistencies of the subjective support, objective support, and utilization of support domains were 0.756, 0.796, and 0.739, respectively.

2.6. Medical Coping Modes Questionnaire—Chinese Version (MCMQ-C). The medical coping style was evaluated using the Chinese version of the Medical Coping Modes Questionnaire, which was originally developed by Feifel et al. [28] and translated by Shen and Jiang [29]. It contains 20 questions across three domains: confrontation, avoidance, and acceptance. Among them, 12 items are scored 1 (never) to 4 (very often), and 8 items are scored reversely. The sum of the three subscales gives the total score, with higher scores indicating increased use of each coping strategy. The MCMQ-C has acceptable reliability and validity and high applicability in Chinese cancer patients [30, 31]. The global internal consistency (Cronbach's α) of the MCMQ-C questionnaire in this study was 0.778, and the internal consistencies of the confrontation, avoidance, and acceptance domains were 0.753, 0.789, and 0.769, respectively.

2.7. Distress Thermometer (DT). The distress thermometer and problem list were used to measure the degree of psychological distress, which was developed by Roth and translated by Tang et al. [32–34]. The DT is an 11-point visual analogue scale ranging from 0 (no distress) to 10 (extreme distress). The problem list is a 40-item self-reported list that covers 5 domains, including practical, social contact, emotional, spiritual, and physical. There is also an open-ended question at the end for patients to complete.

2.8. Statistical Analysis. Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the patients. Measurement data were reported as the mean ± SD, and count data were reported as *N* (%). Two independent Student's *t*-tests and Mann–Whitney *U* tests were used to test the differences between frail (total TFI score ≥5) and nonfrail (total TFI score <5) cancer patients. Categorical variables were compared using the chi-square analysis. Variables that were demonstrated to be significant ($p < 0.10$) in univariate regression were selected and entered into the multivariate logistic regression to identify influencing factors of frailty. Regression coefficients from the multivariate logistic models were used to construct the nomogram. Harrell's concordance index (C-index) and calibration curves were used to evaluate the performance of the nomogram. Decision curve analysis (DCA) and the receiver operating characteristic (ROC) curve were used to test the accuracy and goodness of fit of the nomogram. Differences were considered statistically significant when $p < 0.05$. All statistical analyses were performed using SPSS version 25 and R version 4.2.1.

3. Results

3.1. Patient Characteristics of Development and Validation Cohorts. The primary cohort comprised 958 patients, including 611 males (63.78%) and 347 (36.22%) females, and 440 (45.93%) patients were frail. Then, the original data were randomly divided into the development set ($n = 680$) and validation set ($n = 278$) according to a 7 : 3 ratio, and there was no significant difference in characteristics between these two sets (all $p > 0.05$). In the development set, statistically significant differences were observed between frail and nonfrail patients in terms of BMI, TNM staging, cancer duration, comorbidities, dietary habits, mode of nutrition, marital status, work status, mental state, social support, medical coping styles, and levels of physical activity (all $p < 0.05$). Sex, type of cancer, cancer metastasis, smoking history, drinking history, education level, and income were not statistically significantly different ($p > 0.05$) between the two groups. The detailed sociodemographic and clinical characteristics of the development cohort are shown in Table 1, and a comparison between the development and validation cohorts is shown in Supplementary Material Table S1.

3.2. Univariate and Multivariate Analyses of Frailty. The univariate analysis revealed that the level of distress thermometer, dietary habits, mode of nutrition, level of physical activity, TNM staging, work status, medical coping styles, BMI, cancer duration, social support, marital status, and Charlson comorbidity index were associated with frailty ($p < 0.05$). A multivariate logistic regression analysis with a backwards method was applied to analyse the relationship between frailty and the significant factors that were identified in the univariate analysis. The multivariate analysis showed that the following predictors were recognized as significant risk factors for frailty: the level of distress thermometer, dietary habit, mode of nutrition, IPAQ-C, TNM staging, work status, and medical coping styles. The detailed results and assignments are described in Table 2.

3.3. Construction of the Nomogram. A nomogram was established based on the multivariate logistic model (see Figure 1). The significant variables associated with frailty were TNM staging, work status, mode of nutrition, dietary habits, level of distress thermometer (DT), physical activity, and medical coping styles. At the top of the nomogram was a single-point line for each predictor, and summing them all up yields the total score of probability. The online version is available at https://frail-nomo.shinyapps.io/dynnomapp/, as shown in Figure 2.

3.4. Performance Assessment of the Nomogram. The area under the ROC curve (AUC) was 0.762 (95% CI: 0.726–0.797) in the development set (see Figure 3(a)) and 0.747 (95% CI: 0.689–0.804) in the validation set (see Figure 3(b)), which indicated good predictive capacity of the prediction nomogram. In the development set, the cut-off value was 0.438 by maximizing the Youden index up to 0.406, and the sensitivity and specificity were 0.740 and 0.666, respectively. In the validation set, the cut-off value was 0.505, the Youden index was 0.386, and the sensitivity and specificity were 0.576 and 0.810, respectively. In addition, the C-index was 0.762, and the calibration curve was close to the diagonal line, which indicated good agreement between the predicted and real observations (see Figure 4(a)), demonstrating an adequate fit of the nomogram. The DCA curve

Table 1: Demographic and clinical characteristics of cancer patients in the development set.

	Nonfrail ($n = 365$)		Frail ($n = 315$)		$t/\chi^2/Z$	p value
Age (mean, SD)	55.88	11.74	57.39	12.79	−1.612	0.108
BMI kg/m^2 (mean, SD)	22.13	2.93	21.57	3.22	2.347	0.019*
Sex *N* (%)					1.732	0.188
Male	238	65.2	190	60.3		
Female	127	34.8	125	39.7		
Types of cancer *N* (%)					2.832	0.830
Lung cancer	82	22.5	77	24.5		
Colorectal cancer	94	25.7	90	28.6		
Stomach cancer	60	16.4	53	16.8		
Liver cancer	40	11.0	27	8.6		
Pancreatic cancer	36	9.9	25	7.9		
Oesophageal cancer	28	7.7	25	7.9		
Other	25	6.8	18	5.7		
TNM staging *N* (%)					21.733	<0.001**
I	78	21.4	35	11.1		
II	123	33.7	88	28.0		
III	98	26.8	105	33.3		
IV	66	18.1	87	27.6		
Cancer metastasis *N* (%)					1.820	0.403
No	130	35.6	97	30.8		
Local	55	15.1	53	16.8		
Distant	180	49.3	165	52.4		
Cancer duration *N* (%)					12.159	0.007*
1–3 months	85	23.3	111	35.2		
3–6 months	90	24.6	67	21.3		
6–12 months	70	19.2	46	14.6		
≥12 months	120	32.9	91	28.9		
Surgery *N* (%)					0.013	0.994
No	229	62.7	198	62.8		
Radical surgery	105	28.8	91	28.9		
Palliative surgery	31	8.5	26	8.3		
Charlson comorbidity index *N* (%)					12.698	<0.001**
<5	172	47.1	106	33.7		
≥5	193	52.9	209	66.3		
Dietary habit *N* (%)					18.797	<0.001**
Vegetarian	46	12.6	79	25.1		
Balanced	256	70.1	180	57.1		
Carnivorous	63	17.3	56	17.8		
Mode of nutrition *N* (%)					24.204	<0.001**
Oral feeding	360	98.6	284	90.2		
Enteral nutrition	3	0.8	18	5.7		
Parenteral nutrition	2	0.6	13	4.1		
Smoking history *N* (%)					1.198	0.274
Yes	160	43.8	125	39.7		
No	205	56.2	190	60.3		
Drinking history *N* (%)					0.610	0.435
Yes	106	29.0	83	26.3		
No	259	71.0	232	73.7		
Educational degree *N* (%)					0.475	0.789
Elementary school or below	78	21.4	67	21.3		
Middle or high school	150	41.1	137	43.5		
Bachelor degree or above	137	37.5	111	35.2		
Marital status *N* (%)					6.686	0.035*
Married	337	92.4	272	86.4		
Unmarried	14	3.8	19	6.0		
Divorced or widowed	14	3.8	24	7.6		
Work status *N* (%)					13.221	0.004*
Work	145	39.7	85	27.0		
Freelance	23	6.3	18	5.7		
Retirement	102	28.0	111	35.2		
Sick rest	95	26.0	101	32.1		

Table 1: Continued.

	Nonfrail ($n = 365$)		Frail ($n = 315$)		$t/\chi^2/Z$	p value
Income N (%)					5.747	0.125
<3000 yuan	26	7.1	25	7.9		
3000–5000 yuan	169	46.3	130	41.3		
5001–10000 yuan	138	37.8	115	36.5		
>10000 yuan	32	8.8	45	14.3		
Distress thermometer N (%)					62.725	<0.001**
<4	171	46.8	57	18.1		
≥4	194	53.2	258	81.9		
IPAQ-C N (%)					40.003	<0.001**
Low	99	27.1	157	49.8		
Moderate	219	60.0	140	44.5		
High	47	12.9	18	5.7		
SSRS score (mean, SD)						
Subjective social support	7.56	2.448	6.71	1.810	5.193	<0.001**
Objective social support	19.82	4.085	17.95	3.843	6.125	<0.001**
Utilization of support	7.01	2.302	6.69	2.264	1.831	0.068
Total	34.40	6.898	31.36	5.888	6.209	<0.001**
MCMQ-C score (mean, SD)						
Confrontation	19.37	4.062	17.48	5.386	5.111	<0.001**
Avoidance	15.90	4.657	17.25	4.435	−3.867	<0.001**
Yielding	10.88	2.966	11.98	2.911	−4.873	<0.001**
Total	46.15	7.994	46.71	9.022	−0.863	0.388

Note. Asterisk (*) indicates p value <0.05 and asterisk (**) indicates p value <0.001. SD, standard deviation; IPAQ-C, International Physical Activity Questionnaire-Chinese version; SSRS, Social Support Rating Scale; MCMQ-C, Medical Coping Modes Questionnaire—Chinese version.

Table 2: Univariate and multivariate logistic regression analyses for frailty in cancer patients.

Variables	Univariate analysis			Multivariate analysis		
	β	OR (95% CI)	p value	β	OR (95% CI)	p value
Distress thermometer						
<4	Ref			Ref		
≥4	1.384	3.990 (2.803, 5.678)	<0.001**	1.142	3.132 (2.124, 4.620)	<0.001**
Dietary habit			<0.001**			0.010*
Vegetarian	Ref			Ref		
Balanced	−0.893	0.409 (0.272, 0.617)	<0.001**	−0.745	0.475 (0.294, 0.767)	0.002*
Carnivorous	−0.659	0.518 (0.310, 0.863)	0.012*	−0.577	0.562 (0.311, 1.013)	0.055
Mode of nutrition			<0.001**			0.022*
Oral feeding	Ref			Ref		
Enteral nutrition	2.029	7.606 (2.218, 26.076)	0.001**	1.245	3.471 (0.912, 13.212)	0.068
Parenteral nutrition	2.109	8.239 (1.844, 36.809)	0.006*	1.712	5.538 (1.123, 27.306)	0.036*
IPAQ-C			<0.001**			0.041*
Low	Ref			Ref		
Moderate	−0.909	0.403 (0.290, 0.560)	<0.001**	−0.457	0.633 (0.434, 0.923)	0.017*
High	−1.421	0.241 (0.133, 0.439)	<0.001**	−0.613	0.542 (0.268, 1.096)	0.088
TNM staging			<0.001**			0.086
I	Ref			Ref		
II	0.467	1.594 (0.983, 2.586)	0.059	0.422	1.526 (0.899, 2.589)	0.117
III	0.870	2.388 (1.471, 3.876)	<0.001**	0.597	1.817 (1.068, 3.090)	0.028*
IV	1.078	2.938 (1.762, 4.898)	<0.001**	0.690	1.993 (1.126, 3.529)	0.018*
Work status			0.004*			0.037*
Work	Ref			Ref		
Freelance	0.289	1.335 (0.682, 2.615)	0.400	0.216	1.241 (0.601, 2.564)	0.559
Retirement	0.619	1.856 (1.270, 2.713)	0.001*	0.541	1.718 (1.120, 2.635)	0.013*
Sick rest	0.595	1.814 (1.231, 2.672)	0.003*	0.561	1.753 (1.123, 2.736)	0.014*
MCMQ-C score						
Confrontation	−0.085	0.918 (0.888, 0.949)	<0.001**	−0.074	0.929 (0.892, 0.967)	<0.001**
Yielding	0.127	1.136 (1.077, 1.198)	<0.001**	0.127	1.136 (1.061, 1.216)	<0.001**
Avoidance	0.065	1.068 (1.032, 1.104)	<0.001**			
Total	0.008	1.008 (0.990, 1.026)	0.388			

Table 2: Continued.

Variables	Univariate analysis			Multivariate analysis		
	β	OR (95% CI)	p value	β	OR (95% CI)	p value
Age (years)	0.010	1.010 (0.998, 1.023)	0.108			
BMI (kg/m^2)	−0.059	0.942 (0.897, 0.990)	0.019*			
Cancer duration			0.007*			
1–3 months	Ref					
3–6 months	−0.562	0.570 (0.373, 0.871)	0.009*			
6–12 months	−0.687	0.503 (0.315, 0.803)	0.004*			
≥12 months	−0.544	0.581 (0.392, 0.860)	0.007*			
SSRS score						
Subjective social support	−0.183	0.833 (0.774, 0.896)	<0.001**			
Objective social support	−0.119	0.887 (0.853, 0.924)	<0.001**			
Utilization of support	−0.062	0.940 (0.879, 1.005)	0.068			
Total	−0.074	0.928 (0.905, 0.952)	<0.001**			
Marital status			0.039*			
Married	Ref					
Unmarried	0.520	1.681 (0.828, 3.415)	0.151			
Divorced or widowed	0.753	2.124 (1.078, 4.185)	0.029*			
Charlson comorbidity index						
<5	Ref					
≥5	0.564	1.757 (1.287, 2.399)	<0.001**			
Sex						
Male	Ref					
Female	0.209	1.233 (0.902, 1.684)	0.188			
Smoking history						
Yes	Ref					
No	0.171	1.186 (0.874, 1.611)	0.274			
Drinking history						
Yes	Ref					
No	0.135	1.144 (0.816, 1.603)	0.435			
Cancer metastasis			0.403			
No	Ref					
Local	0.256	1.291 (0.815, 2.046)	0.276			
Distant	0.206	1.229 (0.877, 1.721)	0.232			
Educational degree			0.789			
Elementary school or below	Ref					
Middle or high school	0.061	1.063 (0.713, 1.587)	0.764			
Bachelor degree or above	−0.058	0.943 (0.625, 1.423)	0.781			
Surgery			0.994			
No	Ref					
Radical surgery	0.002	1.002 (0.714, 1.407)	0.989			
Palliative surgery	−0.030	0.970 (0.557, 1.689)	0.914			
Income			0.130			
<3000 yuan	Ref					
3000–5000 yuan	−0.223	0.800 (0.441, 1.450)	0.462			
5001–10000 yuan	−0.143	0.867 (0.475, 1.583)	0.641			
>10000 yuan	0.380	1.462 (0.718, 2.980)	0.295			
Types of cancer			0.831			
Lung cancer	Ref					
Colorectal cancer	0.019	1.020 (0.667, 1.559)	0.929			
Stomach cancer	−0.061	0.941 (0.580, 1.525)	0.804			
Liver cancer	−0.330	0.719 (0.403, 1.282)	0.264			
Pancreatic cancer	−0.302	0.740 (0.407, 1.344)	0.322			
Oesophageal cancer	−0.050	0.951 (0.510, 1.772)	0.874			
Others	−0.266	0.767 (0.388, 1.515)	0.445			

Note. Asterisk (*) indicates p value <0.05 and asterisk (**) indicates p value <0.001. IPAQ-C, International Physical Activity Questionnaire—Chinese version; MCMQ-C, Medical Coping Modes Questionnaire—Chinese version; SSRS, Social Support Rating Scale; Hosmer–Lemeshow = 0.605.

showed that if the threshold probability of a patient was between 17 and 96%, using this nomogram to predict frailty risk for cancer patients is more beneficial than the intervention-all-patients or intervention-none-patients scheme (see Figure 5(a)). All of these results show the appropriate calibration capability of this nomogram.

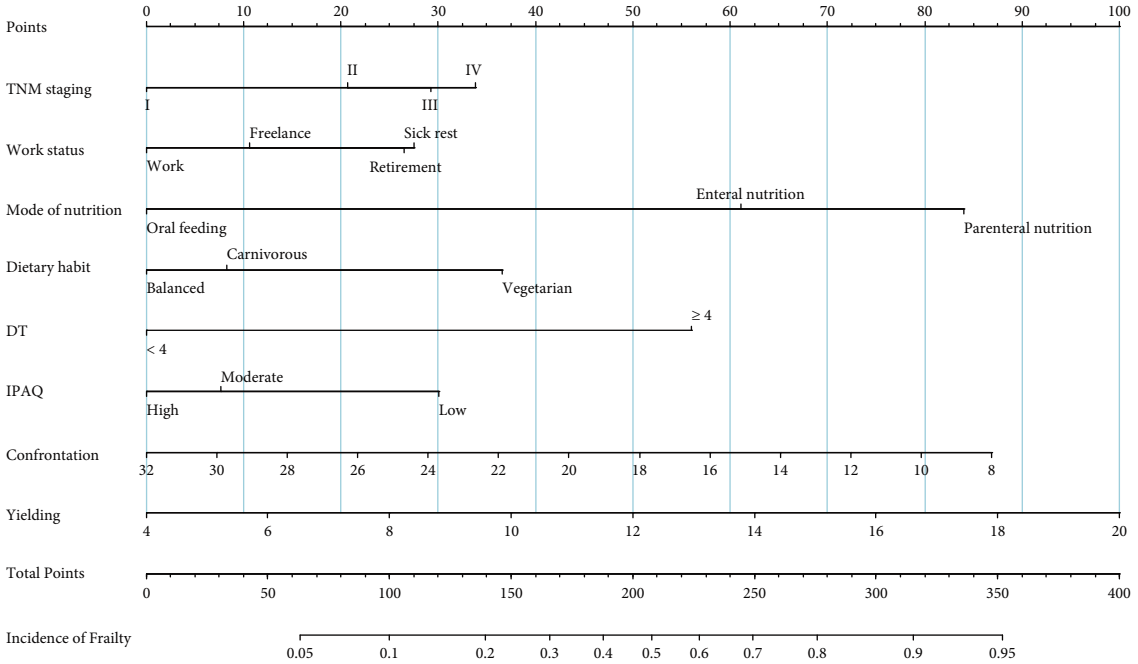

FIGURE 1: A nomogram for predicting frailty in cancer patients. On the left is the name of each assessed item, the middle is the specific option in these items, and each option corresponds to the score top line (points). The individual score of each item is added together to obtain the total points, which correspond to the incidence of frailty in cancer patients (%).

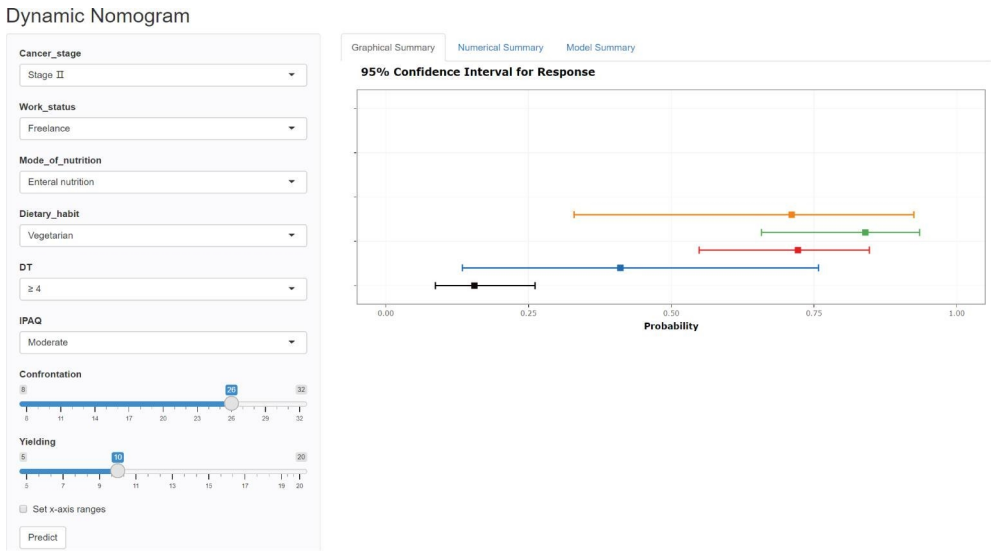

FIGURE 2: Online nomogram. On the left is the name of the items that need to be evaluated. Select the estimated result from the drop-down box or vernier calliper and then click predict at the bottom to obtain the prediction result. Click the two buttons above the figure ("Numerical Summary" and "Model Summary") to display the detailed results of the prediction model. After using the model, click the "Quit" button at the bottom to exit the program (available at https://frail-nomo.shinyapps.io/dynnomapp/).

4. Discussion

In this study, we assessed the incidence and analysed influencing factors of frailty in cancer patients. The results showed that the prevalence of frailty in cancer patients was 45.93%, which was higher than that reported in community-dwelling older adults and other disease patients [35, 36]. This discrepancy may be explained by differences in disease and therapeutic factors. The mechanism of cancer is dysregulated cell growth, and radiation and chemotherapy can also lead to free radical formation, cellular senescence, and telomere shortening, all of which could result in cellular damage and accelerate the process of frailty [37]. In addition, treatment-related side effects, such as pain, nausea, and dyspepsia, may lead to decreased oral food intake and increase the risk of malnutrition [38, 39]. Lack of nutrition can lead to a vicious

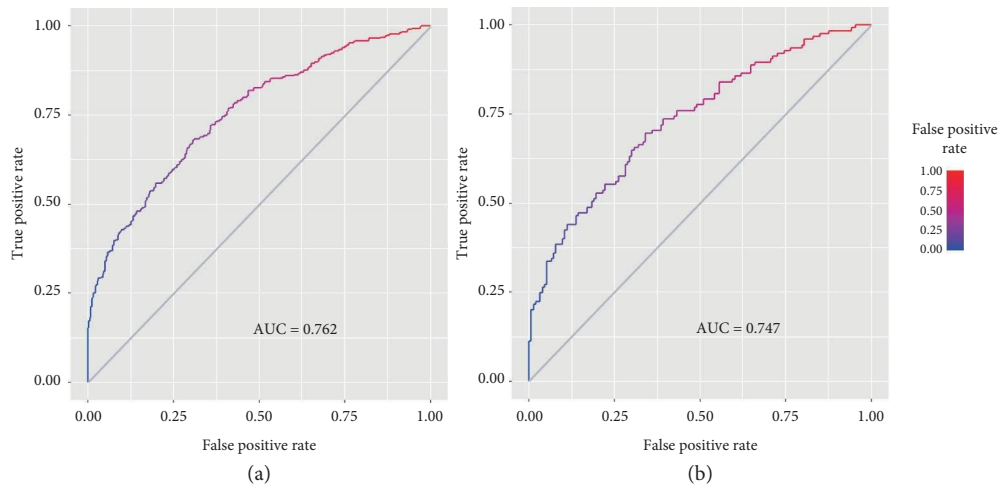

FIGURE 3: ROC curves of the nomogram for predicting the probability of frailty in the development set (a) and the validation set (b). The horizontal axis is "1-specificity," also known as the false positive rate. The closer the horizontal axis is to zero, the higher the accuracy is. The vertical axis is sensitivity, also known as the true positive rate, and the larger the vertical axis is, the better the accuracy. According to the position of the curve, the whole figure is divided into two parts. The area under the curve is AUC, which is used to indicate the prediction accuracy. The higher the AUC value is, the closer the curve is to the top left corner (the smaller the horizontal axis is, the larger the vertical axis is), both mean a higher prediction accuracy. ROC: receiver operating characteristic curve; AUC: area under the curve.

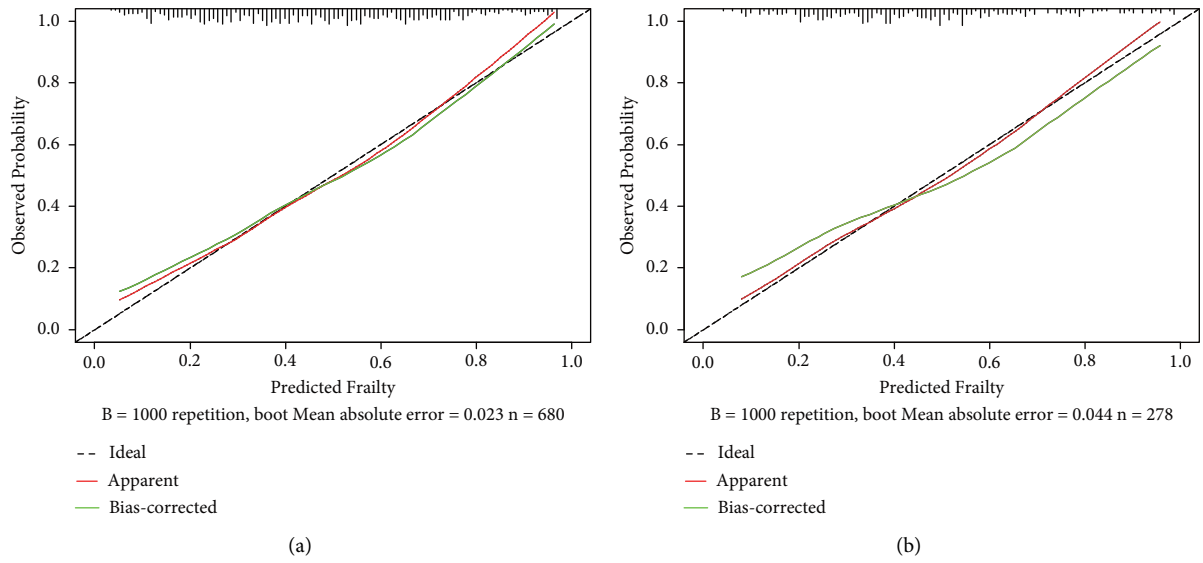

FIGURE 4: Calibration curves of the nomogram for predicting the probability of frailty in the development set (a) and validation set (b). The horizontal axis shows the predicted frailty probability, the vertical axis shows the actual frailty probability, and the dashed line shows the best-case scenario predicted. The green line shows the prediction of this nomogram, and the closer it is to the diagonal, the better the prediction performance is.

cycle that reduces the tolerance and effectiveness of treatments. All of these factors can increase the risk of frailty and reduce life quality; thus, cancer patients have a higher incidence of frailty.

The historical literature has reported several factors that could affect the frailty of cancer patients, such as age, sex, sedentary behaviour, type of cancer, and comorbidities [40–42]. Our study confirmed most of the previous findings and identified eight predictors of frailty: advanced TNM staging, no work status, parenteral nutrition, vegetarianism, high level psychological distress, low physical activity, avoidance, and yielding medical coping styles. However, age was excluded from our model. Indeed, previous studies have mentioned that even young adult cancer survivors may experience frailty and low health-related quality of life [43, 44]. For cancer patients, the effects of illness and negative emotions are more striking than age; thus, age as a general objective indicator may not be applicable in cancer patients [45]. In addition, we found that lower levels of psychological distress and positive medical coping styles are positively related to a better prognosis. A similar association between medical coping styles and poor prognosis has been

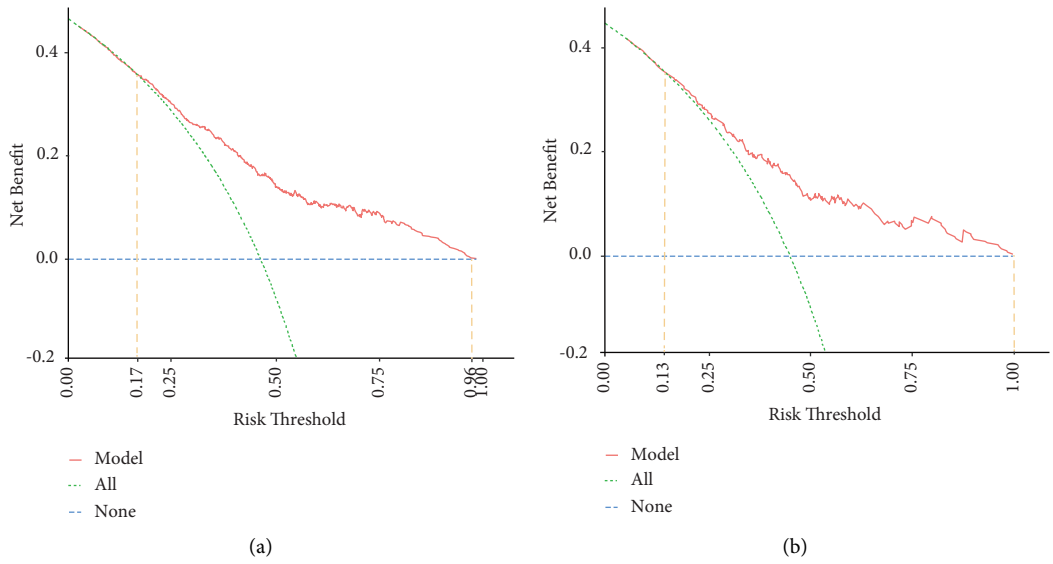

FIGURE 5: DCA curves of the nomogram for predicting the probability of frailty in the development set (a) and validation set (b). The horizontal axis represents the threshold probability, and the vertical axis represents the net benefit. The blue horizontal line indicates that all cancer patients are considered to have no frailty (the net benefit is zero). The green line indicates that all cancer patients are considered frail, and the red line represents the nomogram in this study. The higher the red line is (the farther it is from the blue and green lines), the better the model is applied. DCA: decision curve analysis.

shown in Cho's study [46]. One possible explanation is that a diagnosis of cancer is one of the most stressful events in one's life. The physical, psychological, and social pressures, especially the cancer stigma culture in Chinese society, can lead to the patient's psychological distress [47]. Higher levels of psychological distress also led to "fatalism" and lowered expectations of treatment effectiveness. The heavy psychological burden can make cancer patients feel that they cannot do things on their own, thus reducing their quality of life and increasing their risk of frailty. Therefore, these effects on the physical and mental state, along with treatment side effects, appear easier to understand than directly evaluating cancer patients by age.

Medical coping styles are a patient's cognitive and behavioural effort to manage the demands of a cancer diagnosis. Svensson et al. [48] conducted a 10-year prospective cohort study and found that positive medical coping styles were associated with early cancer screening and better prognosis, and our results show that different medical coping styles can influence the occurrence of frailty. Confrontation strategies such as problem solving and help seeking can solve the problem at its root and boost confidence in fighting cancer. At the same time, seeking help from medical staff and family members can help patients better understand the disease and increase treatment compliance. In contrast, avoidance and acceptance of medical coping styles might lead to more vulnerability, since patients using negative coping strategies tend to view cancer as overpowering and give up their hope of treatment. However, it is not known whether psychological distress affects medical coping styles. Therefore, large, randomized, prospective, and multicenter studies are needed to confirm these results.

Among the lifestyle-related factors, our results showed that moderately active patients had a lower risk of frailty. Physical activity can increase immunity, improve muscle strength, and reduce therapeutic side effects, all of which can reduce the risk of frailty and improve quality of life [49, 50]. Similarly, work status may have the same effect. The amount of physical activity required for work, for example, commutes to companies and communications with work partners, could increase one's physical activity levels. This also explains why cancer patients with jobs have a lower risk of frailty and suggests that clinical health workers should encourage cancer patients to participate in more physical exercise and provide accurate information according to guidelines, such as the appropriate exercise dose, frequency, and modality.

Dietary habits were also considered an influencing factor of frailty in our results, given that patients with a balanced diet appeared to have a lower risk of developing frailty than those with a vegetarian diet. The highest category of red meat consumption is associated with higher levels of dietary fat and chemical carcinogens during the cooking of meat, which may cause a poor prognosis [51]. However, proper meat consumption rather than a vegetarian diet has shown to be beneficial in preventing frailty and is possibly related to the nutritional status. Cancer patients require sufficient nutrition to maintain reserves for a better prognosis because wasting disease and treatment side effects increase their energy needs [52]. Therefore, appropriate consumption of high-protein meat can improve their nutritional status.

In addition, a nomogram was developed based on previous results, which performed well in both the development and validation sets and demonstrated satisfactory discrimination and prediction performance. This nomogram

included both physical and psychological factors, which can better predict the risk of frailty than tools that only included physical dimensions. In addition, this nomogram was constructed by modifiable factors, which means it can provide insight for early intervention. In addition, we provided an electronic version of the patient's frailty risk that can be predicted after selecting the appropriate options. Based on the convenient and practical characteristics of the nomogram, it could be efficiently employed by clinical health workers.

4.1. Study Limitations. Inevitably, this study has several limitations. Firstly, selection bias was inevitable as we only included adult cancer patients from a single hospital. Secondly, we excluded patients with severe physical deficits and cognitive impairment, which may lead to a low identification of frailty, and the frailty prevalence predicted by the nomogram might be lower than the actual frailty prevalence. Lastly, insurance status may be associated with patients' frailty. However, this study did not evaluate the insurance status, potentially influencing the results. Despite this limitation, samples in this study could still be considered as representative of the target population due to a large number of selected cancer patients. Therefore, longitudinal and multicenter studies should be conducted to validate our results.

4.2. Clinical Implications. The number of cancer survivors is increasing, and a considerable proportion of them have reported frailty. The high prevalence of frailty not only reduces quality of life but also affects the treatment and prognosis of cancer patients. If clinical health workers can recognize frailty early and take preventive measures, the frailty of cancer patients may be reduced or even reversed. It is already known that disease and physical factors can impact frailty; however, little has been reported about the psychological effects of frailty in cancer patients. The results of this paper demonstrated that both psychological and physical factors can cause frailty. Thus, adding psychological factors to the assessment of frailty is crucial for early identification. In addition, a simple and quick tool for screening frail cancer patients, such as the nomogram, could help in the early prevention and intervention of frailty.

5. Conclusions

In conclusion, our study highlighted the significant prevalence of frailty among cancer patients. Through our analysis, we identified key risk factors associated with frailty, including parenteral nutrition, advanced TNM staging, adherence to a vegetarian diet, low physical activity, and unemployment. In addition, our research emphasized the impact of psychological factors on frailty in cancer patients. Experiencing psychological distress beyond a threshold of 4 and adopting negative coping styles were found to play crucial roles in influencing the development of frailty. These findings suggested that healthcare practitioners could consider early prevention and intervention strategies based on the identified risk factors. Moreover, we developed a quick and practical nomogram for frailty prediction, offering a promising tool for the early identification of cancer patients at a heightened risk of frailty.

Data Availability

Data are available on request due to privacy/ethical restrictions.

Ethical Approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Nanfang Hospital Ethics Committee (NFEC-202103-K5).

Disclosure

The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of Interest

The authors hereby declare that they have no conflicts of interest.

Authors' Contributions

Zhihui Yang and Yuanyuan Luo contributed equally to this work.

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Supplementary Materials

Table S1: sociodemographic and clinical characteristics of the development set and the validation set. (*Supplementary Materials*)

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