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Symptom clusters and influencing factors in pancreatic cancer patients with adjuvant chemotherapy after surgery: a cross-sectional study

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Abstract

Pancreatic cancer patients receiving postoperative adjuvant chemotherapy experience multiple distressing symptoms. However, how these symptoms cluster by severity remains unclear. This study aimed to explore symptom clusters based on severity and identify their influencing factors. A convenience sample of 224 postoperative pancreatic cancer patients receiving adjuvant chemotherapy was recruited from a hospital in China from January to October 2025. Baseline demographic and clinical data were collected one day before chemotherapy. Nutritional status, symptom burden, and functional status were assessed using the Nutritional Risk Screening 2002, Memorial Symptom Assessment Scale, and Karnofsky Performance Status scale, respectively. Exploratory Factor Analysis identified symptom clusters, and multiple linear regression examined influencing factors. The results showed that the five most severe symptoms were nervousness (2.05 ± 1.55), feeling sad (1.92 ± 1.54), anxiety (1.90 ± 1.51), lack of energy (1.88 ± 1.60), and lack of appetite (1.76 ± 1.53). Five symptom clusters were identified: gastrointestinal, psychological, physiological energy depletion, neuromuscular, and body image disturbance, explaining 72.13% of variance. Education level, primary caregiver, time since diagnosis, disease stage, chemotherapy cycle, and nutritional risk score were significant influencing factors (all $p < 0.05$). In conclusion, patients undergoing adjuvant chemotherapy after pancreatic cancer surgery commonly experience severe symptom clusters, with psychological symptoms such as anxiety and depression being particularly prominent. Targeted measures based on identified factors are needed to alleviate symptom burden and optimize quality of life.

Keywords: Pancreatic cancer, Adjuvant chemotherapy, Symptom clusters, Exploratory factor analysis, Influencing factors

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Introduction

Pancreatic cancer (PC) is an aggressive gastrointestinal malignancy with an extremely poor prognosis. Although its 5-year survival rate has increased from 3% to 13%, it remains the lowest among all cancers[1]. Radical surgery is the only potentially curative treatment and the means to long-term survival. However, only 15%–20% of patients are eligible for resection[2]. This low resectability rate is largely due to the lack of specific early symptoms and reliable biomarkers, underscoring the urgent need for early diagnostic strategies[3]. Emerging molecular imaging techniques further highlight that early tumor identification is key to improving prognosis[4]. Adjuvant chemotherapy significantly reduces postoperative recurrence risk and prolongs survival. Regimens such as gemcitabine plus nab-paclitaxel (AG) and modified FOLFIRINOX are widely used but often cause toxic side effects[5] and, combined with surgical trauma and psychological distress, can trigger complex multiple symptoms that severely impair patients' quality of life.

Current evidence confirms that PC patients undergoing postoperative adjuvant chemotherapy bear a heavy symptom burden. Kristensen et al.[6] identified pain as a core chemotherapy-related symptom, with progressive increases in severity, accompanied by gastrointestinal symptoms such as nausea and vomiting, which severely undermine patients' ability to carry out daily activities. Similarly, a longitudinal assessment by Burrell et al.[7] of 143 postoperative patients receiving chemotherapy found that fatigue, sleep disturbance, appetite loss, and weight loss were widespread and severe. Expanding on this, Seelen et al.[8] conducted a multicenter prospective study and demonstrated that beyond physical complaints (e.g., pain, fatigue) and gastrointestinal symptoms (e.g., loss of appetite, diarrhea), patients commonly suffer from psychological complications including depression and anxiety throughout chemotherapy, resulting in a complex, multi-layered burden. Statistics show that PC patients on chemotherapy experience an average of 13.39 ± 5.83 symptoms, a burden markedly heavier than that of patients with other solid tumors such as breast or lung cancer[9,10]. Notably, addressing this complex symptom profile during chemotherapy represents a key clinical hurdle. Suboptimal symptom control often triggers treatment delays or early cessation, diminishes therapy adherence, and ultimately compromises survival outcomes[11].

In clinical practice, symptoms frequently do not occur in isolation but coexist as 'Symptom Clusters' (SCs)—defined as two or more concurrent, interrelated, relatively stable symptoms that exhibit statistical independence[12]. Although studies have explored SCs in pancreatic cancer patients (e.g., Burrell et al.[7] identified 16 SCs via exploratory and confirmatory factor analysis in stage II PC patients who underwent surgical resection or with subsequent chemoradiotherapy, with severity significantly associated with reduced overall quality of life). Yang[13] used the Memorial Symptom Assessment Scale (MSAS) to evaluate patients across chemotherapy cycles and identified seven SCs (pancreatic cancer-specific, treatment-related, psychological, gastrointestinal, body image disturbance, fatigue, and excretory SCs). Research focusing specifically on the postoperative adjuvant chemotherapy phase remains insufficient. The framework of

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SCs helps comprehensively assess patients' symptom burden and develop integrated intervention strategies. Unlike single symptom interventions, SC-oriented models not only improve intervention efficiency and rational allocation of medical resources but also reduce symptom severity and enhance patient-reported outcomes[14].

The Theory of Unpleasant Symptoms (TOUS) offers a framework for symptom experiences by describing four symptom dimensions—timing, severity, distress, and quality—emphasizing their dynamic, holistic nature[15]. Currently, SCs are identified based on occurrence, severity, and distress. Among these, severity is a core dimension that is directly associated with key outcomes, including physiological functional status, treatment adherence, and quality of life[16]. Occurrence offers epidemiological description, distress reflects psychological impact, whereas severity directly captures symptom intensity and burden. For instance, Lin et al.[17] found that the severity dimension showed excellent model fit in AML chemotherapy patients. Thus, identifying SCs via severity can precisely reveal the physiological state of patients during chemotherapy, providing clear targets for clinical intervention.

Notably, merely identifying SCs is insufficient to fully guide clinical practice, as their severity varies substantially among individuals and may be influenced by demographic characteristics, disease stage, treatment regimens, and other factors[18]. In-depth exploration of the factors influencing SCs is essential for developing individualized management strategies. Current research predominantly focuses on breast and lung cancer, having confirmed that factors such as BMI, age, self-efficacy, social support, and financial burden are associated with SCs burden[19,20]. However, research on SCs determinants in PC remains limited: Reyes-Gibby et al.[21] identified comorbidities, treatment phase, and regimens as influencing factors in PC patients undergoing chemoradiotherapy, while Burrell et al.[7] conducted a longitudinal study on surgical patients, highlighting preoperative anxiety and pain as predictors of postoperative SCs severity. Collectively, existing evidence primarily addresses patients receiving chemoradiotherapy or surgery alone, with a lack of systematic investigation into SCs determinants during adjuvant chemotherapy following PC surgery. Notably, this population endures dual burdens of surgical trauma and chemotherapy toxicity, potentially resulting in unique symptom patterns and influencing factors. Therefore, guided by the TOUS framework, this study aims to systematically describe postoperative PC patients' symptom experiences during adjuvant chemotherapy. It will focus on the severity dimension to identify SCs via exploratory factor analysis and to analyze factors influencing their severity, with the ultimate goal of developing timely, precise interventions based on SCs' peak severity periods.

Materials and methods

Study design

This was a single-center study conducted at the Pancreatic Center of a Grade A tertiary hospital in Nanjing, Jiangsu Province, China. This study was approved by the Institutional Review Board of the participating hospital and strictly adhered to the Declaration of Helsinki. All participants provided written informed consent for secondary data use. A pilot study (n = 20), completed in July 2024, indicated that symptom occurrence was significantly lower in patients undergoing their first chemotherapy cycle (n = 5) than in those who had received subsequent cycles (n = 15). Based on this finding, the main study protocol optimized the inclusion criteria to 'having completed at least one full cycle of chemotherapy' to focus on the phase with a more significant symptom burden. Recruitment for the main study (n = 224) officially commenced on January 20, 2025. Data from the pilot study were used solely for design optimization and were not included in the final analysis.

Study participants

Inclusion criteria: adult patients (≥ 18 years) with pathologically confirmed pancreatic cancer who had undergone surgery, were receiving adjuvant AG chemotherapy, and had completed at least one full chemotherapy cycle. Participants were required to be conscious, able to communicate verbally, and capable of providing signed informed consent.

All included stage IV patients were oligometastatic cases who underwent resection of both the primary tumor and metastatic lesions.

Exclusion criteria: patients who had received neoadjuvant therapy; were undergoing concurrent radiotherapy, immunotherapy, or targeted therapy; had a history of other malignancies; or suffered from severe cardiovascular or cerebrovascular diseases, organ dysfunction, or psychiatric/cognitive disorders; and those lacking key baseline laboratory data required for the study.

The sample size met two empirical criteria[22]: absolute $N \geq 100$, and a sample-to-variable ratio (N:K) of 5–10:1. Of the 32 symptoms assessed by the Memorial Symptom Assessment Scale, only those with occurrence rates between 20% and 80% were retained for factor analysis, yielding 21 symptoms (K = 21). The final sample comprised 224 valid cases, satisfying $N \geq 100$ and exceeding the recommended N:K upper limit ($224/21 \approx 10.7{:}1 > 10{:}1$).

Study instruments

General information questionnaire

Self-designed by the research group, the questionnaire collected demographic data (e.g., age, sex, education level, primary caregiver, smoking/alcohol use, comorbid chronic diseases) and clinical characteristics (e.g., body mass index [BMI], tumor location, American Joint Committee on Cancer [AJCC] stage, metastasis, time since diagnosis, chemotherapy cycles, HbA1c, complete blood count parameters, and aspartate aminotransferase [AST]). All data were retrieved from the hospital's electronic medical record system.

Memorial Symptom Assessment Scale (MSAS)

Developed by Portenoy et al. in 1994[23], this scale is designed to capture the multifaceted nature of the symptom experience in oncology populations. It has proven reliable, valid, and psychometrically robust across cancers—including pancreatic cancer—via extensive validation. It assesses the occurrence, severity, and distress of 32 symptoms, as well as the frequency of 24 of these symptoms. Occurrence was indicated as 'Yes' or 'No'. A four-point Likert scale was used to assess frequency and severity, while distress is rated on a scale from 0 to 4 points. The Chinese version of the MSAS (MSAS-Ch) used in this study was officially validated by Cheng et al. in 2009[24]. Cronbach's α ranged from 0.79 to 0.87, and it demonstrated a high content validity index (CVI) of 0.94, showing good reliability and validity.

Nutritional Risk Screening 2002 (NRS-2002)

Developed by Kondrup et al. in 2002[25], it is endorsed by the European Society for Clinical Nutrition and Metabolism (ESPEN) for identifying malnutrition risk among adult patients in hospital settings. The scoring stage covers nutritional status, disease severity, and age adjustment (≥ 70 years). Nutritional risk is assessed on a scale from 0 to 7 points, with a score of ≥ 3 considered indicative of risk. Studies show satisfactory diagnostic accuracy (sensitivity 0.98, specificity 0.77).

Consequently, this study used the Chinese version of NRS-2002, translated by Chen et al. in 2005[26], widely promoted and adopted in nutritional risk screening for Chinese cancer patients.

Karnofsky Performance Status (KPS) scale

First proposed by Karnofsky in 1948[27], it was used to assess patients' daily living abilities and quality of independent life. The scoring ranges from 0 (death) to 100 (normal). Higher scores indicate better functional status.

Procedures

All research personnel underwent uniform standardized training to familiarize themselves with the questionnaire content and master standardized investigation methods. All questionnaires were checked on-site and corrected as needed; no missing data were present in the final 224-patient sample.

Baseline data collection: at the time of enrollment, trained researchers completed the General Information Questionnaire by reviewing electronic medical records and conducting face-to-face interviews with patients or their family members. Nutritional status was assessed using the Nutritional Risk Screening 2002 (NRS-2002) tool.

Symptom and functional status assessment: on day 7 of the chemotherapy cycle, the MSAS and the KPS scale were administered to evaluate the patients' symptom experiences (with a focus on severity) and their functional status, respectively. To minimize subjective bias and ensure data accuracy, the researchers read each item in a neutral tone and recorded responses objectively based strictly on patient feedback. Questionnaires were collected on-site and reviewed immediately; any data identified as questionable were promptly verified and corrected.

Data analysis

Data were analyzed using SPSS software (v27.0). Categorical variables were presented as frequencies and percentages; continuous variables with normal distribution were described using mean ± standard deviation, while skewed variables were described using median and interquartile range. Correlation analysis was employed to examine the associations between nutritional indicators, biochemical indicators, and symptom clusters. Univariate analysis was performed using independent samples t-tests or analysis of variance (ANOVA). Bonferroni correction was applied for conservative interpretation of the univariate comparisons, but the univariate analysis itself was exploratory screening to avoid missing potential variables. Hence, all predictors with unadjusted $p < 0.05$ were entered into the multivariable linear regression to identify factors influencing symptom cluster severity, with $p < 0.05$ considered statistically significant for the final model. Bonferroni-adjusted significance level is provided for reference.

Exploratory Factor Analysis (EFA) with principal component analysis and varimax rotation was performed based on symptom severity to identify high-burden SCs. Following methodological recommendations[28], we excluded symptoms with an occurrence of < 20% or > 80% to ensure adequate variability and stable factor solutions, as symptoms with very low or very high occurrence provide limited variance for correlation estimation and may compromise the stability and interpretability of the factor structure. Prior to factor extraction, the Kaiser–Meyer–Olkin (KMO) and Bartlett's test of sphericity confirmed suitability for factor analysis (KMO > 0.5; Bartlett's test $p < 0.05$). Factors were extracted based on the criteria of eigenvalue ≥ 1, minimum number of items ≥ 2, and factor loading ≥ 0.4. Items displaying cross-loadings were assigned to the factor with the highest loading. Subsequently, Cronbach's α coefficient was calculated post-extraction to verify the reliability of each symptom cluster. Finally, clusters were named based on their constituent items, relevant literature, and clinical significance.

Cluster severity scores were calculated as the arithmetic mean of the symptom severities within each cluster. These raw scores (1–4 scale) were directly entered into regression models without standardization, given the common metric and confirmed normality (Shapiro–Wilk test, all $p > 0.05$).

Results

Demographic and clinical characteristics

This study ultimately included 224 pancreatic cancer patients. The mean age was 64.22 ± 7.93 years, and 132 patients (58.9%) were male. The majority of patients had an education level of junior high school or below (68.3%). Additionally, 58.9% of the patients had comorbid chronic diseases. Tumors were predominantly located in the head and neck of the pancreas (65.6%), with a mean time since diagnosis of 11.28 ± 11.28 months. AJCC stage was primarily stage II (62.5%). Detailed information is presented in Table 1.

Symptom occurrence and severity

Pancreatic cancer patients experienced an average of 14.88 ± 4.40 symptoms during chemotherapy. A total of 21 symptoms had an occurrence rate ≥ 20%. The five most prevalent symptoms were: nervousness (76.3%), anxiety (75.4%), feeling sad (75.0%), lack of energy (70.5%), and lack of appetite (67.0%). Nervousness was the most severe (2.05 ± 1.55) and the most distressing (2.02 ± 1.57) symptom. Detailed data are shown in Table 2.

Symptom clusters based on severity

EFA was performed on 21 symptoms, with the KMO measure of 0.761 and a significant Bartlett's test of sphericity ($p < 0.001$). Five common factors were extracted, accounting for a cumulative variance of 72.13%: Factor 1 (Gastrointestinal Symptom Cluster) included six symptoms. Factor 2 (Psychological Symptom Cluster) included four symptoms. Factor 3 (Physiological Energy Depletion Symptom Cluster) included five symptoms. Factor 4 (Neuromuscular Symptom Cluster) included four symptoms. Factor 5 (Body Image Disturbance Symptom Cluster) included two symptoms. Detailed results are presented in Table 3.

Univariate analysis of symptom cluster severity

The results revealed that the severity of the gastrointestinal symptom cluster was significantly associated with time since diagnosis, chemotherapy cycles, NRS-2002, and AST levels. The psychological symptom cluster was influenced by age, smoking history, comorbid chronic disease history, tumor location, AJCC stage, KPS score, and neutrophil count. The physiological energy depletion symptom cluster was associated with smoking history, comorbid chronic disease history, KPS score, and chemotherapy cycles. The neuromuscular symptom cluster was associated with alcohol consumption history, chemotherapy cycles, NRS-2002, and AST levels. Furthermore, education level, primary caregiver, and time since diagnosis were associated with the body image disturbance symptom cluster (all $p < 0.05$; for details, see Table 4).

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Table 1. Sociodemographic and clinical characteristics of the participants (N = 224).

Item		n/mean ± SD	Percentage (%)
Sex	Man	132	58.9
	Woman	92	41.1
Age		64.22 ± 7.93	
	< 65	111	49.6
	≥ 65	113	50.4
Education level	Primary school or below	72	32.1
	Junior high school	81	36.2
	Senior high school/ Technical secondary school	50	22.3
	Junior college or above	21	9.4
BMI	< 18.5	38	17.0
	18.5–23.9	145	64.7
	≥ 24	41	18.3
Primary caregiver	Spouse	129	57.6
	Parents	7	3.1
	Children	88	39.3
	Siblings	0	0
Smoking history	Yes	46	20.5
	No	178	79.5
Alcohol consumption history	Yes	72	32.1
	No	152	67.9
Comorbid chronic diseases history	Yes	132	58.9
	No	92	41.1
Tumor location	Head/neck of pancreas	147	65.6
	Body/tail of pancreas	77	34.4
AJCC Stage	I	28	12.5
	II	140	62.5
	III	39	17.4
	IV	17	7.6
Metastasis	Yes	87	38.8
	No	137	61.2
Time since diagnosis (months)		11.28 ± 11.28	
	≤ 12	148	66.1
	12–24	47	21.0
	> 24	29	12.9
Chemotherapy cycles		3.84 ± 2.44	
	≤ 3	113	50.4
	4–6	77	34.4
	> 6	34	15.2
KPS score		81.70 ± 7.97	
	70	55	24.6
	80	76	33.9
	90	93	41.5
NRS-2002 score		2.97 ± 1.43	
	< 3	92	41.1
	≥ 3	132	58.9
HbA1c (%)		6.67 ± 1.36	
WBC (× 10^9/L)		7.65 ± 5.95	
Hb (g/L)		103.80 ± 20.16	
Platelets (× 10^9/L)		252.30 ± 129.50	
AST (U/L)		31.31 ± 21.67	
Neutrophils (× 10^9/L)		5.55 ± 7.87	

Multiple linear regression analysis of symptom clusters

Variables significant in the univariate analysis were entered into multiple linear regression models. All five regression models were statistically significant (p < 0.001). The Durbin–Watson statistics (1.857–2.082) indicated no residual autocorrelation. Model diagnostics showed no multicollinearity (all VIF < 10), and residuals were approximately normally distributed (all p > 0.05). As detailed in Table 5, the severity of the gastrointestinal symptom cluster was independently associated with chemotherapy cycles, time since diagnosis, NRS-2002, and AST level (explaining 35.0% of variance). The psychological symptom cluster severity was associated with AJCC stage, tumor location, comorbid chronic disease history, and KPS score (explaining 9.0% of variance). Factors influencing the physiological energy depletion symptom cluster were comorbid chronic disease history, KPS score, and smoking history (explaining 16.5% of variance). The neuromuscular symptom cluster was associated with alcohol consumption history and chemotherapy cycles (explaining 16.6% of variance). The body image disturbance symptom cluster was associated with education level, primary caregiver, and time since diagnosis (explaining 13.4% of variance).

Sensitivity analysis

A sensitivity analysis excluding the 17 stage IV patients (Supplementary Tables S1, S2) confirmed the stability of the five symptom clusters and the majority of regression findings, with only minor changes in a few predictors (e.g., AST and nutritional risk score became non-significant). The cumulative variance explained was 72.19%.

Discussion

Symptom experience in pancreatic cancer patients undergoing chemotherapy

To the best of our knowledge, this is the first study to explore symptom clusters and the factors that influence them in PC patients receiving postoperative adjuvant AG chemotherapy. This study investigated the symptom experience of PC patients. Patients reported a mean of 15 symptoms. Nervousness showed the highest occurrence, severity, and distress. In contrast to lymphoma patients, who primarily experience fever and fatigue[29], this difference may be related to the poor prognosis, high recurrence rate, and chemotherapy side effects of pancreatic cancer[30]. Additionally, drowsiness and abdominal distension were also highly prevalent. These findings support TOUS, in which symptoms are multidimensional and linked by shared biopsychosocial mechanisms.

Note that this cross-sectional study did not measure inflammatory cytokines, hormones, or metabolic biomarkers. Therefore, the following discussion of potential mechanisms is based on the literature and should be considered hypothesis-generating rather than conclusive.

Composition and influencing factors of symptom clusters

Based on the severity dimension, this study identified five symptom clusters: gastrointestinal, psychological, physiological energy depletion, neuromuscular, and body image disturbance. Compared to prior symptom-cluster studies in gastric[31] and breast cancer[20], our findings reveal both overlapping domains and distinct configurations specific to pancreatic cancer. This population-level heterogeneity underscores the necessity of tailoring clinical interventions to disease-specific symptom severity profiles rather than applying generic management protocols.

The gastrointestinal symptom cluster is centered on lack of appetite, accompanied by nausea, vomiting, dry mouth, and abdominal

Table 2. Symptom occurrence, frequency, severity, and distress in pancreatic cancer patients ($N = 224$).

Item	Occurrence *n* (%)	Frequency (mean ± SD)	Severity (mean ± SD)	Distress (mean ± SD)
Difficulty concentrating	131 (58.5)	1.79 ± 1.72	1.59 ± 1.62	1.52 ± 1.67
Pain	135 (60.3)	1.54 ± 1.52	1.37 ± 1.45	1.16 ± 1.51
Lack of energy	158 (70.5)	2.26 ± 1.72	1.88 ± 1.60	1.72 ± 1.68
Cough	41 (18.3[a])	0.33 ± 0.80	0.29 ± 0.77	0.21 ± 0.76
Nervousness	171 (76.3)	2.28 ± 1.58	2.05 ± 1.55	2.02 ± 1.57
Dry mouth	140 (62.5)	1.60 ± 1.47	1.52 ± 1.45	1.59 ± 1.55
Nausea	136 (60.7)	1.36 ± 1.34	1.69 ± 1.60	1.77 ± 1.68
Drowsiness	141 (62.9)	1.71 ± 1.65	1.52 ± 1.53	1.39 ± 1.60
Numbness and tingling in hands/feet	117 (52.2)	1.37 ± 1.57	1.17 ± 1.37	1.22 ± 1.49
Difficulty sleeping	131 (58.5)	1.63 ± 1.62	1.33 ± 1.49	1.30 ± 1.54
Abdominal distension	144 (64.3)	1.53 ± 1.44	1.25 ± 1.25	1.29 ± 1.37
Difficulty urinating	33 (14.7[a])	0.32 ± 0.90	0.29 ± 0.84	0.22 ± 0.76
Vomiting	138 (61.6)	1.08 ± 1.05	1.66 ± 1.57	1.75 ± 1.66
Shortness of breath	36 (16.1[a])	0.30 ± 0.75	0.33 ± 0.87	0.30 ± 0.87
Diarrhea	128 (57.1)	1.31 ± 1.39	1.33 ± 1.38	1.43 ± 1.54
Feeling sad	168 (75.0)	1.81 ± 1.38	1.92±1.54	1.89 ± 1.56
Sweating	38 (17.0[a])	0.45 ± 1.07	0.38 ± 0.92	0.39 ± 0.99
Anxiety	169 (75.4)	2.24 ± 1.58	1.90 ± 1.51	1.87 ± 1.55
Loss of interest in sex/sexual difficulties	39 (17.4[a])	0.24 ± 0.63	0.20 ± 0.46	0.12 ± 0.36
Itchy skin	128 (57.1)	0.92 ± 1.05	1.00 ± 1.13	0.94 ± 1.30
Lack of appetite	150 (67.0)	1.82 ± 1.56	1.76 ± 1.53	1.85 ± 1.60
Dizziness	40 (17.9[a])	0.36 ± 0.86	0.36 ± 0.88	0.33 ± 0.90
Difficulty swallowing	40 (17.9[a])	0.46 ± 1.06	0.42 ± 0.99	0.42 ± 1.05
Irritability	134 (59.8)	1.52 ± 1.58	1.45 ± 1.51	1.44 ± 1.54
Mouth ulcers	30 (13.4[a])	–	0.18 ± 0.50	0.18 ± 0.61
Changes in taste	136 (60.7)	–	1.31±1.41	1.33 ± 1.47
Weight loss	39 (17.4[a])	–	0.24 ± 0.63	0.21 ± 0.68
Hair loss	130 (58.0)	–	1.26 ± 1.37	1.42 ± 1.59
Constipation	39 (17.4[a])	–	0.33 ± 0.87	0.29 ± 0.80
Swelling in arms or legs	107 (47.8)	–	1.05 ± 1.30	1.15 ± 1.45
Feeling 'I don't look like myself'	125 (55.8)	–	1.04 ± 1.21	1.17 ± 1.44
Skin changes (hyperpigmentation)	42 (18.8[a])	–	0.33 ± 0.82	0.25 ± 0.82

'–' indicates that the frequency of the symptom was not assessed. [a] Symptoms with an occurrence rate < 20%.

distension. This contrasts with prior studies where nausea and diarrhea predominated[32,33]. We hypothesize this reflects PC's unique physiology: postoperative reductions in digestive enzyme secretion and glucose dysregulation may delay gastric emptying and suppress hypothalamic appetite regulation. Notably, greater severity of appetite loss may be associated with poorer nutritional status (malnutrition prevalence: 42.4%–88.0%)[34]. We found that longer chemotherapy cycles were associated with higher cluster scores, consistent with the cycle-dependent toxic effects of chemotherapy[35]. However, Li et al.[36] found more severe GI symptoms in children with leukemia at initial chemotherapy, likely due to the high-intensity 'induction remission' regimen. The AG regimen (gemcitabine plus nab-paclitaxel) is speculated to cause symptom exacerbation via gastrointestinal mucosal injury, chronic inflammation, and neuroregulatory imbalance. This inflammatory link is indirectly supported by glioma research showing FBXL16 mediates cytokine release to regulate macrophage recruitment[37,38]. Additionally, a longer time since diagnosis positively correlates with GI symptom severity, consistent with the conclusions of Wei et al.[39], possibly due to higher tumor burden aggravating digestive tract compression or infiltration and mucosal damage from multiple chemotherapies. Secondly, a higher NRS-2002 score is linked to more severe GI symptoms. This differs from the report by Shi[40] showing no such correlation in glioma patients, possibly because the pancreas (a core digestive organ) is intimately linked to nutrition, and the AG regimen's significant damage to GI mucosa usually forms a malnutrition-related vicious cycle[41]. However, this hypothesis remains to be supported by direct evidence. Furthermore, higher AST levels are associated with worse GI symptoms, matching[42] findings in brain tumors, potentially due to chemotherapy-induced hepatocellular injury (manifested as elevated AST), reducing bile secretion (impairing fat digestion), and decreasing protein synthesis (weakening digestive enzyme function).

The psychological symptom cluster includes sadness, anxiety, nervousness, and irritability, with sadness symptoms being the most severe. The findings are highly consistent with the cluster (worry, anxiety, sadness, irritability) summarized by Harris et al.[43], suggesting that psychological symptom clusters with high negative emotional burden are common across cancer types. However, its presentation exhibits notable cancer-type heterogeneity, related to cancer site, treatment modality, and psychosocial stressors. For example, in lung cancer, clusters tend to center on sadness and distress linked to prognosis-related worry and dyspnea[44]. We found that AJCC stage III patients exhibited more psychological symptoms than stage I, consistent with Tie et al.[45], likely due to the advanced stage's increased tumor burden, complex treatments, and prognostic uncertainty exacerbating psychological distress. Secondly, head/neck cancer patients experienced a greater psychological burden than those with body/tail, echoing Wei et al.[39], potentially due to head/neck tumors inducing more visible physical symptoms (e.g., jaundice, pain) as well as appearance changes and impaired social functioning, amplifying stress. A KPS score was negatively correlated with psychological severity, corroborating the conclusions of Zhang et al.[18] in lung cancer

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Table 3. Symptom clusters in patients with pancreatic cancer based on severity.

Symptom	Factor loading				
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Lack of appetite	**0.932**	−0.086	0.032	0.025	0.079
Nausea	**0.912**	−0.123	0.024	−0.056	0.131
Vomiting	**0.884**	−0.135	−0.003	−0.027	0.134
Dry mouth	**0.828**	−0.074	0.066	0.118	−0.033
Diarrhea	**0.608**	0.137	0.058	0.239	−0.019
Abdominal distension	**0.569**	0.181	0.008	0.247	−0.105
Feeling sad	−0.007	**0.928**	0.128	0.066	−0.049
Anxiety	−0.035	**0.922**	0.103	−0.002	−0.064
Nervousness	0.01	**0.859**	0.241	0.091	0.043
Irritability	−0.093	**0.721**	0.009	−0.052	0.177
Drowsiness	−0.024	0.157	**0.897**	0.095	−0.048
Difficulty concentrating	−0.019	0.164	**0.865**	0.154	0.042
Lack of energy	0.013	0.122	**0.85**	−0.049	0.014
Changes in taste	0.394	−0.092	**0.592**	0.052	0.172
Difficulty sleeping	0.051	0.496	**0.566**	0.093	−0.24
Swelling in arms or legs	0.082	0.073	0.078	**0.913**	0.05
Numbness and tingling in hands/feet	0.136	0.111	0.114	**0.868**	0.094
Itchy skin	0.023	−0.09	0.078	**0.724**	0.333
Pain	0.157	−0.013	−0.005	**0.626**	−0.256
Feeling 'I don't look like myself'	0.071	0.155	0.021	0.121	**0.859**
Hair loss	0.082	−0.066	−0.003	0.012	**0.851**
Eigenvalue	4.776	4.261	2.309	2.068	1.733
Percentage of variance (%)	19.479	16.394	14.593	12.931	8.731
Cumulative percentage of variance (%)	19.479	35.873	50.467	63.397	72.129
Cronbach's α	0.892	0.898	0.846	0.807	0.760

A factor loading of 0.40 was used as the cutoff criterion. Rotation converged in five iterations. Bold values indicate factor loadings with an absolute value ≥ 0.40, which was the prespecified cutoff for symptom-cluster assignment.

patients. Reduced functional status (e.g., inability to work or perform self-care) often triggers helplessness and negative emotions. Additionally, patients with chronic diseases had more severe psychological symptoms, consistent with the report by Burger & Okkenhaug[46] in hematological cancers. Prior models hypothesize that chronic disease–tumor coexistence drives persistent inflammation, which disrupts hypothalamic–pituitary–adrenal (HPA) axis function through cytokines, thereby inducing sickness behaviors such as depression and anxiety[38]. Notably, although psychological symptoms formed a distinct cluster, reporting bias warrants consideration. Grounded in the symptom perception hypothesis, elevated negative affect heightens hypervigilance, amplifying somatic complaints. It also correlates strongly with self-reported severity but only weakly with clinician-assessed severity[47]. Thus, the high psychological symptom burden observed may reflect both genuine distress and an affective amplifier of gastrointestinal and fatigue symptoms. This does not invalidate the cluster structure; rather, it implies that targeting negative affect may yield cross-domain benefits. Future studies require objective measures to disentangle amplification from true burden.

The physiological energy depletion symptom cluster is characterized by lack of energy, difficulty concentrating, and drowsiness. The prevalence of cancer-related fatigue (CRF) in this study (70.54%) was lower than that detected by disease-specific tools like FACT-F[7], yet slightly higher than the 60.1% in Chen et al.[48], where low loading of lack of energy in an 'emotional-illness' cluster suggests that methodological and cultural differences may lead to underestimation. Mechanistically, the high severity of this cluster is associated with platinum-based chemotherapy-induced myelosuppression, inflammation, and reduced oxygen-carrying capacity of red blood cells (leading to tissue hypoxia)[49]. This same inflammatory mechanism is also observed in CAR-T cell therapy, where cytokine release syndrome induces fatigue and cognitive impairment, supporting immune activation as a common pathway underlying energy depletion across treatment modalities[50]. Given its high clinical relevance, the more severe the CRF, the faster the decline in patients' physical function and quality of life, and concurrent gastrointestinal and psychological symptoms further amplify fatigue. We found that patients with comorbid chronic diseases had lower energy levels, which aligns with Ma et al.[51]. Chronic diseases are speculated to not only exacerbate fatigue by depleting physiological reserves, superimposing chemotherapy toxicity, and mediating inflammation, but also to contribute to symptom development via immune-metabolic dysregulation[52]. Additionally, lower KPS scores correlated with more severe physiological symptoms, aligning with reports by Dodd et al.[12] in adult cancer patients, and linked to reduced exercise tolerance and increased energy burden from chemotherapy. Furthermore, smokers exhibited greater physiological symptom severity. Smoking may impair cardiopulmonary function and metabolism, amplifying chemotherapy-related energy depletion[53].

The neuromuscular symptom cluster is characterized by hand/foot swelling, numbness, and tingling. It is closely associated with AG chemotherapy-induced peripheral neuropathy (CIPN) caused by drugs like paclitaxel[49], severely affecting patients' daily activities and quality of life. However, its composition and severity ranking vary across cancer types: lung cancer exhibits a psycho-neurological cluster with psychological symptoms more severe than somatic ones[54], whereas breast cancer shows a fatigue-pain dominant cluster[20]. This variation may reflect the significantly different chemotherapy regimen used for pancreatic cancer. Analysis revealed alcohol consumption history positively correlated with neuromuscular symptoms, differing from the findings by Zhang et al.[55] (milder symptoms in drinkers)—possibly due to varied definitions of drinking history (our study did not limit drinking duration to examine long-term effects). Notably, Mellion et al.[56] demonstrated that alcohol and its metabolites can directly damage neuromuscular tissues, causing myasthenia and pain, which explains our result. We also found chemotherapy cycles positively correlated with neuromuscular symptom severity, consistent with the previous study[39] on gastric cancer patients—attributed to drug toxicity, tissue damage, and reduced body repair capacity in association with higher cycle counts.

The body image disturbance symptom cluster centers on two core symptoms: 'I do not look like myself' and hair loss, consistent with previous findings[57]. In our study, 58% of patients experienced hair loss, similar to the 58.1% reported by Nozawa et al.[58] as the leading treatment-related appearance change. Although not directly life-threatening, such changes can blur identity and disrupt self-continuity, leading to self-perception distress and reduced self-esteem. This study found that patients with lower education experienced more severe image disturbance, consistent with the lung cancer study by Ma et al.[59], potentially due to weak cognitive restructuring ability and the inability to actively utilize social resources through multiple channels to participate in body image management. Patients with spouses as primary caregivers scored higher in distress, similar to the study by Fang et al.[60], likely because intimate relationships intensify attractiveness anxiety and fear of being disliked or a burden[51]. Additionally, patients diagnosed for over 12 months reported more disturbance, aligning with previous studies[35,39], linked to disrupted body integrity and impaired dignity from disease burden and chemotherapy-related damage.

Table 4. Univariate analysis for symptom clusters in patients with pancreatic cancer ($N = 224$).

Item		Gastrointestinal SCs (mean ± SD)	Psychological SCs (mean ± SD)	Physiological energy depletion SCs (mean ± SD)	Neuromuscular SCs (mean ± SD)	Body image disturbance SCs (mean ± SD)
Sex	Man	1.56 ± 1.20	1.89 ± 1.31	1.47 ± 1.22	1.21 ± 1.05	1.13 ± 1.12
	Woman	1.50 ± 1.17	1.74 ± 1.38	1.60 ± 1.19	1.06 ± 1.05	1.18 ± 1.21
	Test statistic	0.346[a]	0.830[a]	−0.768[a]	1.013[a]	−0.293[a]
	p value	0.730	0.407	0.443	0.312	0.770
Age	< 65	1.57 ± 1.14	1.65 ± 1.34	1.49 ± 1.18	1.28 ± 1.08	1.11 ± 1.18
	≥ 65	1.51 ± 1.23	2.00 ± 1.32	1.56 ± 1.24	1.02 ± 1.00	1.19 ± 1.14
	Test statistic	0.389[a]	−1.977[a]	−0.440[a]	1.882[a]	−0.501[a]
	p value	0.697	0.049[*]	0.660	0.061	0.617
Education level	Primary school or below	1.59 ± 1.19	1.93 ± 1.37	1.52 ± 1.15	1.25 ± 1.14	1.39 ± 1.27
	Junior high school	1.61 ± 1.16	1.84 ± 1.34	1.47 ± 1.17	1.12 ± 1.04	1.35 ± 1.11
	Senior high school/ technical secondary school	1.43 ± 1.23	1.81 ± 1.35	1.64 ± 1.36	1.08 ± 0.96	0.81 ± 1.04
	Junior college or above	1.32 ± 1.20	1.50 ± 1.26	1.50 ± 1.23	1.05 ± 0.95	0.38 ± 0.65
	Test statistic	0.527[b]	0.564[b]	0.205[b]	0.394[b]	6.861[b]
	p value	0.664	0.639	0.893	0.757	< 0.001[**†]
BMI	< 18.5	1.71 ± 1.09	2.02 ± 1.41	1.69 ± 1.25	1.03 ± 0.88	1.20 ± 1.19
	18.5–23.9	1.49 ± 1.22	1.79 ± 1.28	1.44 ± 1.17	1.13 ± 1.07	1.21 ± 1.17
	≥ 24	1.56 ± 1.16	1.80 ± 1.48	1.68 ± 1.30	1.32 ± 1.10	0.89 ± 1.08
	Test statistic	0.534[b]	0.468[b]	1.080[b]	0.787[b]	1.285[b]
	p value	0.587	0.627	0.341	0.456	0.279
Primary caregiver	Spouse	1.61 ± 1.16	1.87 ± 1.30	1.60 ± 1.15	1.11 ± 0.95	1.37 ± 1.23
	Parents	1.55 ± 1.37	1.86 ± 1.57	1.17 ± 1.63	1.57 ± 1.30	0.79 ± 1.32
	Children	1.42 ± 1.21	1.77 ± 1.39	1.44 ± 1.25	1.17 ± 1.16	0.86 ± 0.97
	Siblings	0	0	0	0	0
	Test statistic	0.682[b]	0.150[b]	0.763[b]	0.684[b]	5.746[b]
	p value	0.506	0.861	0.467	0.506	0.004[*]
Smoking history	Yes	1.64 ± 1.13	2.22 ± 1.35	2.09 ± 1.30	1.30 ± 1.09	1.02 ± 1.06
	No	1.51 ± 1.20	1.73 ± 1.32	1.38 ± 1.14	1.11 ± 1.04	1.19 ± 1.18
	Test statistic	−0.673[a]	−2.265[a]	−3.639[a]	−1.143[a]	0.853[a]
	p value	0.501	0.024[*]	< 0.001[**†]	0.254	0.394
Alcohol consumption history	Yes	1.56 ± 1.19	1.94 ± 1.37	1.67 ± 1.24	1.68 ± 1.14	1.07 ± 1.18
	No	1.53 ± 1.18	1.78 ± 1.33	1.46 ± 1.19	0.90 ± 0.90	1.19 ± 1.15
	Test statistic	−0.166[a]	−0.841[a]	−1.229[a]	−5.134[a]	0.731[a]
	p value	0.868	0.401	0.220	< 0.001[**†]	0.465
Comorbid chronic diseases history	Yes	1.54 ± 1.21	1.99 ± 1.34	1.81 ± 1.23	1.19 ± 1.05	1.10 ± 1.13
	No	1.53 ± 1.16	1.59 ± 1.31	1.13 ± 1.05	1.09 ± 1.04	1.23 ± 1.20
	Test statistic	−0.060[a]	−2.246[a]	−4.430[a]	−0.688[a]	0.883[a]
	p value	0.952	0.026[*]	< 0.001[**†]	0.492	0.378
Tumor location	Head/neck of pancreas	1.47 ± 1.20	2.00 ± 1.33	1.51 ± 1.20	1.16 ± 1.04	1.08 ± 1.11
	Body/tail of pancreas	1.66 ± 1.15	1.50 ± 1.30	1.56 ± 1.23	1.12 ± 1.07	1.29 ± 1.24
	Test statistic	−1.113[a]	2.665[a]	−0.292[a]	0.247[a]	−1.315[a]
	p value	0.267	0.008[*]	0.771	0.805	0.190
AJCC stage	I	1.69 ± 1.23	1.58 ± 1.37	1.50 ± 1.21	1.25 ± 1.18	1.23 ± 1.09
	II	1.51 ± 1.14	1.67 ± 1.27	1.54 ± 1.22	1.13 ± 1.04	1.15 ± 1.19
	III	1.58 ± 1.22	2.49 ± 1.29	1.74 ± 1.26	1.35 ± 1.06	1.06 ± 1.11
	IV	1.36 ± 1.42	2.04 ± 1.57	0.98 ± 0.80	0.65 ± 0.72	1.21 ± 1.15
	Test statistic	0.312[b]	4.576[b]	1.606[b]	1.888[b]	0.130[b]
	p value	0.816	0.004[*]	0.189	0.133	0.942
Metastasis	Yes	1.51 ± 1.18	1.73 ± 1.31	1.45 ± 1.16	0.99 ± 0.96	1.21 ± 1.21
	No	1.55 ± 1.19	1.89 ± 1.36	1.57 ± 1.23	1.25 ± 1.09	1.12 ± 1.13
	Test statistic	0.251[a]	0.849[a]	0.745[a]	1.820[a]	−0.566[a]
	p value	0.802	0.397	0.457	0.070	0.572
Time since diagnosis (months)	≤ 12	1.26 ± 1.15	1.82 ± 1.35	1.48 ± 1.19	1.13 ± 1.03	1.07 ± 1.11
	12–24	1.82 ± 1.07	1.81 ± 1.36	1.56 ± 1.25	1.02 ± 0.97	1.09 ± 1.07
	> 24	2.51 ± 0.87	1.91 ± 1.29	1.71 ± 1.22	1.47 ± 1.21	1.66 ± 1.45
	Test statistic	17.737[b]	0.055[b]	0.462[b]	1.833[b]	3.208[b]
	p value	< 0.001[**†]	0.947	0.630	0.162	0.042[*]
Chemotherapy cycles	≤ 3	0.94 ± 1.03	1.62 ± 1.26	1.33 ± 1.12	0.95 ± 0.98	1.07 ± 1.08
	4–6	1.99 ± 1.01	2.03 ± 1.40	1.79 ± 1.26	1.31 ± 1.05	1.13 ± 1.19
	> 6	2.49 ± 0.96	2.07 ± 1.38	1.57 ± 1.26	1.43 ± 1.14	1.49 ± 1.31

(to be continued)

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Table 4. (continued)

Item		Gastrointestinal SCs (mean ± SD)	Psychological SCs (mean ± SD)	Physiological energy depletion SCs (mean ± SD)	Neuromuscular SCs (mean ± SD)	Body image disturbance SCs (mean ± SD)
Chemotherapy cycles	Test statistic	41.946[b]	2.886[b]	3.391[b]	4.473[b]	1.741[b]
	p value	< 0.001[**†]	0.058	0.035[*]	0.012[*]	0.178
KPS score	Test statistic	0.097[c]	−0.162[c]	−0.275[c]	0.030[c]	0.025[c]
	p value	0.147	0.015[*]	< 0.001[**†]	0.651	0.705
NRS-2002 score	Test statistic	0.229[c]	−0.042[c]	0.020[c]	0.166[c]	0.025[c]
	p value	< 0.001[**†]	0.530	0.770	0.013[*]	0.705
HbA1c (%)	Test statistic	0.030[c]	0.045[c]	0.058[c]	−0.027[c]	0.025[c]
	p value	0.651	0.501	0.388	0.688	0.712
WBC (× 10^9/L)	Test statistic	0.023[c]	−0.118[c]	−0.051[c]	0.061[c]	−0.004[c]
	p value	0.737	0.079	0.452	0.362	0.958
Hb (g/L)	Test statistic	0.014[c]	0.020[c]	−0.048[c]	0.082[c]	−0.032[c]
	p value	0.840	0.768	0.473	0.222	0.633
AST (U/L)	Test statistic	0.223[c]	0.066[c]	−0.014[c]	0.152[c]	−0.032[c]
	p value	< 0.001[**†]	0.324	0.835	0.023[*]	0.634
Neutrophils (× 10^9/L)	Test statistic	0.014[c]	−0.138[c]	−0.045[c]	0.007[c]	0.017[c]
	p value	0.831	0.040[*]	0.502	0.919	0.803

[a] t-value, [b] F-value, [c] correlation coefficient *r*. Unadjusted univariate analysis: * $p < 0.05$, ** $p < 0.001$. †: significant after Bonferroni correction for multiple comparisons within each cluster (adjusted $\alpha = 0.05/20 = 0.0025$). For reference only; variable selection for the regression models used unadjusted $p < 0.05$.

Table 5. Multiple linear regression for symptom clusters ($N = 224$).

Variable		*B*	*SE*	*β*	*t*	*P*	Tolerance	*VIF*
Gastrointestinal symptom cluster	Constant	−0.728	0.225	–	−3.234	0.001	–	–
	Chemotherapy cycles	0.636	0.094	0.393	6.772	< 0.001	0.866	1.155
	Time since diagnosis	0.440	0.093	0.266	4.730	< 0.001	0.925	1.081
	NRS-2002	0.121	0.046	0.147	2.665	0.008	0.958	1.044
	AST	0.007	0.003	0.123	2.224	0.027	0.953	1.049
Psychological symptom cluster	Constant	3.511	0.978	–	3.589	< 0.001	–	–
	AJCC stage	0.276	0.115	0.155	2.405	0.017	0.985	1.015
	Tumor location	−0.505	0.182	−0.180	−2.778	0.006	0.975	1.025
	Comorbid chronic diseases history	0.455	0.175	0.168	2.602	0.010	0.981	1.019
	KPS score	−0.023	0.011	−0.137	−2.134	0.034	0.991	1.010
Physiological energy depletion symptom cluster	Constant	3.889	0.788	–	4.936	< 0.001	–	–
	Comorbid chronic diseases history	0.622	0.150	0.254	4.147	< 0.001	0.994	1.006
	KPS score	−0.035	0.009	−0.230	−3.694	< 0.001	0.967	1.034
	Smoking history	0.535	0.185	0.180	2.887	0.004	0.965	1.036
Neuromuscular symptom cluster	Constant	0.215	0.196	–	1.097	0.274	–	–
	Alcohol consumption history	0.785	0.137	0.351	5.739	< 0.001	0.998	1.002
	Chemotherapy cycles	0.251	0.089	0.175	2.820	0.005	0.967	1.034
	NRS-2002	0.090	0.045	0.123	1.972	0.050	0.966	1.035
Body image disturbance symptom cluster	Constant	2.088	0.278	–	7.514	< 0.001	–	–
	Education level	−0.345	0.076	−0.285	−4.561	< 0.001	0.992	1.008
	Primary caregiver	−0.283	0.075	−0.237	−3.784	< 0.001	0.992	1.008
	Time since diagnosis	0.204	0.101	0.126	2.015	0.045	0.998	1.002

Model: Gastrointestinal symptom cluster: *D-W* = 1.989, $R^2 = 0.362$, adjusted $R^2 = 0.350$. Psychological symptom cluster: *D-W* = 1.901, $R^2 = 0.107$, adjusted $R^2 = 0.090$. Physiological energy depletion symptom cluster: *D-W* = 1.857, $R^2 = 0.176$, adjusted $R^2 = 0.165$. Neuromuscular symptom cluster: *D-W* = 2.082, $R^2 = 0.177$, adjusted $R^2 = 0.166$. Body image disturbance symptom cluster: *D-W* = 1.883, $R^2 = 0.146$, adjusted $R^2 = 0.134$.

Clinical implications

Leveraging symptom cluster profiling, we developed a risk-stratified, proactive nursing model. For the gastrointestinal cluster, NRS-2002 screening was intensified every two cycles; oral nutritional supplements (ONS) were triggered preemptively for scores ≥ 3, coupled with AST-guided hepatoprotection and pancreatic enzyme replacement therapy (PERT). Psychological and neuromuscular clusters utilized targeted surveillance: MSAS screening for AJCC stage III or head/neck tumors, and intensified neurotoxicity monitoring for those with a drinking history or ≥ 4 cycles. Screen-positive patients received immediate nurse-led cognitive restructuring and prophylactic neuroprotection (e.g., gabapentin). Physiological energy depletion management featured KPS-tailored exercise and nocturnal hypoxemia screening for smokers/COPD patients, optimizing medication timing and glycemic control. For body image disturbance, culturally adapted interventions—including visual aids, spousal involvement, and narrative therapy—facilitated identity reconstruction. This integrated approach shifts the paradigm from reactive management to proactive, multi-cluster governance.

Limitations

This study provides valuable empirical evidence on symptom clusters and influencing factors in pancreatic cancer patients receiving AG

adjuvant chemotherapy. However, several limitations should be noted. First, the single-center design and convenience sampling may limit the generalizability of the findings and introduce selection bias; although sensitivity analysis supported robustness, future studies in non-metastatic or stage IV cohorts are needed and should also conduct sensitivity analyses to assess selection bias. Second, symptom assessment was only conducted on day 7 post-chemotherapy, failing to capture the dynamic trajectory of symptom clusters across chemotherapy cycles, particularly the differences between acute and delayed toxicities. Thus, no causal or temporal interpretations can be drawn from these data. Third, while the 20%–80% prevalence threshold for symptom inclusion is methodologically sound, it may exclude rare but clinically significant symptoms that could impact patient outcomes. Fourth, the adjusted R^2 values of the regression models were relatively low; future research should expand the range of predictor variables to improve the explanatory power of the model. Last, due to the lack of an independent validation sample, confirmatory factor analysis could not be performed in a strict sense. Future multicenter, longitudinal studies should track the trajectories of symptom progression, validate the identified symptom cluster structure, and assess its stability and replicability across populations and regimens (e.g., modified FOLFIRINOX).

Conclusions

This study identified a distinct symptom severity profile in post-operative pancreatic cancer patients receiving AG chemotherapy, with nervousness being the most severe symptom. Five major symptom clusters were recognized. The severity of these clusters was associated with factors such as chemotherapy cycles, nutritional risk, and tumor stage, highlighting the need for targeted interventions including nutritional support, psychological care, and functional exercise. Future research should focus on identifying potential predictors of symptom severity and exploring both common mechanisms and tailored management strategies across symptom clusters to advance symptom science.

Ethical statements

Ethics approval and consent to participate: This study was approved by the Clinical Research Ethics Committee of BenQ Hospital Affiliated to Nanjing Medical University (Pre-approval No.: 2024-KL005; Main Study Approval No.: 2025-KL002). The research was conducted in strict accordance with the principles of the Declaration of Helsinki and relevant ethical guidelines. Written informed consent was obtained from all enrolled participants prior to their participation. During the preparation of this work, the author(s) did not use any generative artificial intelligence or AI-assisted writing tools. Large Language Models (e.g., ChatGPT) do not satisfy our authorship criteria due to lack of accountability for the work. Their use was properly documented as none in the Methods section.

Author contributions

The authors confirm their contributions to the paper as follows: contributed to conceptualization, data curation, formal analysis, investigation, methodology, and writing of the original draft: Ding LL; contributed to investigation, data curation, and visualization: Wang Y; contributed to investigation and writing – review and editing: Shi N; contributed to investigation, resources, validation, and writing – review and editing: Xia NN; contributed to project administration, resources, supervision, funding acquisition, and writing – review and editing: Pan KC. All authors reviewed the results and approved the final version of the manuscript.

Data availability

The data that support the findings of this study are available on request from the corresponding author, Pan KC. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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Conflict of interest

The authors declare that they have no conflict of interest.

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References

[1] Elmadani M, Mokaya PO, Omer AAA, Kiptulon EK, Klara S, et al. 2025. Cancer burden in Europe: a systematic analysis of the GLOBOCAN database (2022). *BMC Cancer* 25:447

[2] Boubaddi M, Rossi J, Marichez A, Marty M, Amintas S, et al. 2025. Preoperative prognostic factors in resectable pancreatic cancer: state of the art and prospects. *Annals of Surgical Oncology* 32:4117–4127

[3] Cao Y, Zhao R, Guo K, Ren S, Zhang Y, et al. 2022. Potential metabolite biomarkers for early detection of stage-I pancreatic ductal adenocarcinoma. *Frontiers in Oncology* 11:744667

[4] Guo K, Ren S, Zhang H, Cao Y, Zhao Y, et al. 2023. Biomimetic gold nanorods modified with erythrocyte membranes for imaging-guided photothermal/gene synergistic therapy. *ACS Applied Materials & Interfaces* 15:25285–25299

[5] Neoptolemos JP, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, et al. 2017. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. *The Lancet* 389:1011–1024

[6] Kristensen A, Vagnildhaug OM, Grønberg BH, Kaasa S, Laird B, et al. 2016. Does chemotherapy improve health-related quality of life in advanced pancreatic cancer? A systematic review. *Critical Reviews in Oncology/Hematology* 99:286–298

[7] Burrell S, Yeo T, Smeltzer S, Leiby B, Lavu H, et al. 2018. Symptom clusters in patients with pancreatic cancer undergoing surgical resection: part I. *Oncology Nursing Forum* 45:E36–E52

[8] Seelen LWF, Augustinus S, Stoop TF, Bouwense SAW, Busch OR, et al. 2025. Quality of life among patients with locally advanced pancreatic cancer: a prospective nationwide multicenter study. *Journal of the National Comprehensive Cancer Network* 23:97–104

[9] Ploukou S, Papakosta-Gaki E, Panagopoulou E, Benos A, Smyrnakis E. 2024. Unmet needs in the process of chemotherapy provision in pancreatic cancer patients from the healthcare provider perspective: a phenomenological study in Greece. *Slovenian Journal of Public Health* 63:73–80

[10] Cass SH, Williams LA, Rajaram R, Hirata Y, Rice D, et al. 2024. Patient-reported outcome measures in surgical patients with upper gastrointestinal cancers: a qualitative interview study. *Journal of Surgical Oncology* 130:117–124

[11] Potiaumpai M, Schleicher EA, Wang M, Campbell KL, Sturgeon K, et al. 2023. Exercise during chemotherapy: friend or foe? *Cancer Medicine* 12:10715–10724

[12] Dodd MJ, Miaskowski C, Paul SM. 2001. Symptom clusters and their effect on the functional status of patients with cancer. *Oncology Nursing Forum* 28:465–470

[13] Yang Y. 2020. *Study on the status of symptom burden and its influencing factors in patients with pancreatic cancer*. Master's Thesis. Shanghai University of Traditional Chinese Medicine. http://doi.org/10.27320/d.cnki.gszyu.2020.000886 (in Chinese)

[14] Olsson C, Larsson M. 2024. Evidence-based and person-centered symptom cluster management in cancer care: the value of symptom theory. *Cancer Nursing* 47:423–424

[15] Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F. 1997. The middle-range theory of unpleasant symptoms: an update. *ANS Advances in Nursing Science* 19:14–27

[16] Fu L, Feng X, Jin Y, Lu Z, Li R, et al. 2022. Symptom clusters and quality of life in gastric cancer patients receiving chemotherapy. *Journal of Pain and Symptom Management* 63:230–243

[17] Lin DM, Yin XX, Wang N, Zheng W, Wen YP, et al. 2019. Consensus in identification and stability of symptom clusters using different symptom dimensions in newly diagnosed acute myeloid leukemia patients undergoing induction therapy. *Journal of Pain and Symptom Management* 57:783–792

[18] Zhang G, Weng H, Li Y, Li P, Gong Y, et al. 2022. Symptom clusters and their predictors in patients with lung cancer and treated with programmed cell death protein 1 immunotherapy. *Asia-Pacific Journal of Oncology Nursing* 9:100103

[19] Mao D, Luo Y, Zhang L, Zhu B, Yang Z, et al. 2025. Status and influencing factors of fatigue-pain-sleep disturbance symptom cluster in patients with lung cancer: a latent profile analysis. *Research in Nursing & Health* 48:626–639

[20] Liang M, Li J, Xiang J, Zeng Y, Li S, et al. 2025. Contemporaneous and temporal symptom drivers during breast cancer chemotherapy: a prospective repeated-measures cohort study. *European Journal of Oncology Nursing* 78:102944

[21] Reyes-Gibby CC, Chan W, Abbruzzese JL, Xiong HQ, Ho L, et al. 2007. Patterns of self-reported symptoms in pancreatic cancer patients receiving chemoradiation. *Journal of Pain and Symptom Management* 34:244–252

[22] Sapnas KG, Zeller RA. 2002. Minimizing sample size when using exploratory factor analysis for measurement. *Journal of Nursing Measurement* 10:135–154

[23] Portenoy RK, Thaler HT, Kornblith AB, McCarthy Lepore J, Friedlander-Klar H, et al. 1994. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer* 30:1326–1336

[24] Cheng KKF, Wong EMC, Ling WM, Chan CWH, Thompson DR. 2009. Measuring the symptom experience of Chinese cancer patients: a validation of the Chinese version of the memorial symptom assessment scale. *Journal of Pain and Symptom Management* 37:44–57

[25] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. 2003. ESPEN guidelines for nutrition screening 2002. *Clinical Nutrition* 22:415–421

[26] Chen W, Jiang ZM, Zhang YM, Wang XR, Chen CM, et al. 2005. 欧洲营养不良风险调查方法在中国住院患者的临床可行性研究 [Evaluation of European Nutritional Risk Screening method in Chinese hospitalized patients practice]. *中国临床营养杂志 [Chinese Journal of Clinical Nutrition]* 13:137–141 (in Chinese)

[27] Crooks V, Waller S, Smith T, Hahn TJ. 1991. The use of the karnofsky performance scale in determining outcomes and risk in geriatric outpatients. *Journal of Gerontology* 46:M139–M144

[28] Kim E, Jahan T, Aouizerat BE, Dodd MJ, Cooper BA, et al. 2009. Changes in symptom clusters in patients undergoing radiation therapy. *Supportive Care in Cancer* 17:1383–1391

[29] He J, Feng LN, Tian JL, Zhu XM, Xu XT. 2025. The changes of core symptoms and nursing implications for lymphoma patients with chemotherapy. *Chinese Journal of Nursing* 60:2492–2498

[30] Li W, Xu YH, Wang JN, Hong SS, Yang ZC, et al. 2025. 胰腺癌病人术后真实体验质性研究的 Meta 整合 [Qualitative study on the real experience of pancreatic cancer patients after surgery: a Meta-integration]. *循证护理 [Chinese Evidence-Based Nursing]* 11:210–216 (in Chinese)

[31] Hu Y, Duan PB, Hou QM, Wang X. 2017. 胃癌术后化疗患者症状严重度与困扰度调查研究 [Symptom severity and distress in patients with gastric cancer undergoing chemotherapy]. *护理学杂志 [Journal of Nursing Science]* 32:18–21 (in Chinese)

[32] Wang K, Diao M, Yang Z, Salvador JT, Zhang Y. 2025. Identification of core symptom cluster in patients with digestive cancer: a network analysis. *Cancer Nursing* 48:E55–E63

[33] Ju X, Bai J, She Y, Zheng R, Xu X, et al. 2023. Symptom cluster trajectories and sentinel symptoms during the first cycle of chemotherapy in patients with lung cancer. *European Journal of Oncology Nursing* 63:102282

[34] Whitcomb DC, Buchner AM, Forsmark CE. 2023. AGA clinical practice update on the epidemiology, evaluation, and management of exocrine pancreatic insufficiency: expert review. *Gastroenterology* 165:1292–1301

[35] Lopes-Júnior LC, Grassi J, Freitas MB, Trigo FES, Aguilar Jardim F, et al. 2025. Cancer symptom clusters in children and adolescents with cancer undergoing chemotherapy: a systematic review. *Nursing Reports* 15:163

[36] Li R, Ma J, Chan Y, Yang Q, Zhang C. 2020. Symptom clusters and influencing factors in children with acute leukemia during chemotherapy. *Cancer Nursing* 43:411–418

[37] Sonis ST. 2004. The pathobiology of mucositis. *Nature Reviews Cancer* 4:277–284

[38] Fang Z, Li J, Xiong Y, Luo P, Lu Q, et al. 2025. FBXL16 regulates TAMs recruitment by mediating cytokine release in gliomas. *Cancer Genetics* 298:285–294

[39] Wei L, Lv F, Luo C, Fang Y. 2023. Study on sentinel symptoms and influencing factors of postoperative chemotherapy in patients with gastric cancer. *European Journal of Oncology Nursing* 64:102318

[40] Shi XH. 2022. *胶质瘤患者化疗期间症状群的影响因素及其对生活质量的影响* [*Influencing factors of symptom clusters and their effects on quality of life in patients with glioma during chemotherapy*]. Master's thesis. Shandong University, Jinan, China. doi: 10.27272/d.cnki.gshdu.2022.001028 (in Chinese)

[41] Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, et al. 2017. ESPEN guidelines on nutrition in cancer patients. *Clinical Nutrition* 36:11–48

[42] Hao Y, Wu H, Huang Y. 2025. Symptom clusters in patients with brain tumors: a systematic review. *Seminars in Oncology Nursing* 41:151815

[43] Harris CS, Kober KM, Conley YP, Dhruva AA, Hammer MJ, et al. 2022. Symptom clusters in patients receiving chemotherapy: a systematic review. *BMJ Supportive & Palliative Care* 12:10–21

[44] Ma JS, Xu H, Liu S, Wang AP. 2022. 肺癌术后病人化疗初期症状群内前哨症状的调查 [Investigation of sentinel symptoms in the initial symptom group of patients with lung cancer after chemotherapy]. *护理研究 [Chinese Nursing Research]* 36:3528–3533 (in Chinese)

[45] Tie H, Shi L, Wang L, Hao X, Fang H, et al. 2023. Symptom clusters and characteristics of cervical cancer patients receiving concurrent chemoradiotherapy: a cross-sectional study. *Heliyon* 9:e22407

[46] Burger JA, Okkenhaug K. 2014. Idelalisib – targeting PI3Kδ in patients with B-cell malignancies. *Nature Reviews Clinical Oncology* 11:184–186

[47] Hong Y, Yang Z, Luo N, Busschbach J. 2026. Anxiety and depression may amplify self-reported physical health problems: evidence from EQ-5D-5L data. *Health and Quality of Life Outcomes* 24:45

[48] Chen DD, Qiao TT, Zheng W, Zhang W, Wang ZG, et al. 2016. 胃肠道肿瘤患者首次辅助化疗后症状群的调查研究 [Symptom clusters of patients with gastroenteric tumor after first adjuvant chemotherapy]. *中国全科医学 [Chinese General Practice]* 19:3215–3218 (in Chinese)

[49] Lai Y, Qiu G, Zheng Z, Huang X, Guo P, et al. 2026. Platinum accumulation in chemotherapy: toxicity mechanisms, challenges, and mitigation strategies. *BioMetals* 2026:1–21

[50] Singh SB, Bhandari S, Siwakoti S, Kumar M, Singh R, et al. 2024. PET/CT in the evaluation of CAR-T cell immunotherapy in hematological malignancies. *Molecular Imaging* 23:15353508241257924

[51] Ma HY, Zheng DL, Guo SP, Mao YJ, Wang HR, et al. 2023. Investigation of symptom clusters recognition and its influencing factors in patients after coronary artery bypass grafting. *Chinese Journal of Nursing* 58:158–164

[52] Liao H, Ma Q, Chen L, Guo W, Feng K, et al. 2025. Machine learning analysis of CD4+ T cell gene expression in diverse diseases: insights from cancer, metabolic, respiratory, and digestive disorders. *Cancer Genetics* 290:56–60

[53] Sørensen LT, Jørgensen S, Petersen LJ, Hemmingsen U, Bülow J, et al. 2009. Acute effects of nicotine and smoking on blood flow, tissue oxygen, and aerobe metabolism of the skin and subcutis. *Journal of Surgical Research* 152:224–230

[54] Luo Y, Luo J, Su Q, Yang Z, Miao J, et al. 2024. Exploring central and bridge symptoms in patients with lung cancer: a network analysis. *Seminars in Oncology Nursing* 40:151651

[55] Zhang W, Wang WL, Zhang XQ. 2016. 化疗期消化道癌症患者症状群及影响因素研究 [Symptom clusters of patients with digestive tract cancers undergoing chemotherapy and the influencing factors]. *中国全科医学 [Chinese General Practice]* 19:59–62,77 (in Chinese)

[56] Mellion M, Gilchrist JM, De La Monte S. 2011. Alcohol-related peripheral neuropathy: nutritional, toxic, or both? *Muscle & Nerve* 43:309–316

[57] Huang J, Gu L, Zhang L, Lu X, Zhuang W, et al. 2016. Symptom clusters in ovarian cancer patients with chemotherapy after surgery: a longitudinal survey. *Cancer Nursing* 39:106–116

[58] Nozawa K, Toma S, Shimizu C. 2023. Distress and impacts on daily life from appearance changes due to cancer treatment: a survey of 1, 034 patients in Japan. *Global Health & Medicine* 5:54–61

[59] Ma DY, Rong XX, Su CY, Tong JJ, Hong SK, et al. 2025. 恶性肿瘤患者化疗相关症状群的共性影响因素 [Common influences on chemotherapy-related symptom clusters in cancer patients]. *中华疾病控制杂志 [Chinese Journal of Disease Control and Prevention]* 29:487–491 (in Chinese)

[60] Fang J, Wong CL, Liu CQ, Huang HY, Qi YS, et al. 2023. Identifying central symptom clusters and correlates in children with acute leukemia undergoing chemotherapy: a network analysis. *Frontiers in Oncology* 13:1236129