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Original Article

Chemotherapy-related symptom networks in distinct subgroups of Chinese patients with gastric cancer

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ABSTRACT

Objective: This study aims to identify distinct subgroups among gastric cancer patients undergoing chemotherapy (CTX), delineate associated symptom networks, and ascertain the clinical and sociodemographic variables contributing to diverse symptom patterns.
Methods: Conducted in eastern China, our investigation involved gastric cancer patients receiving CTX. We gathered data using the M.D. Anderson Symptom Inventory Gastrointestinal Cancer Module along with clinical and sociodemographic variables. Subgroups were discerned based on symptom severity through latent profile analysis, and subsequent comparisons were made regarding the symptom networks in different subgroups.
Results: The analysis encompassed 677 eligible gastric cancer patients, revealing three profiles: "Profile 1: low class" (n = 354, 52.3%), "Profile 2: moderate class" (n = 222, 32.8%), and "Profile 3: all high class" (n = 101, 14.9%). Nausea—vomiting exhibited robust associations in the symptom networks of all subgroups, whereas sadness—distress, and taste change—lack of appetite were notably linked with Profile 1 and Profile 2. Distress emerged as a core symptom in Profile 1, lack of appetite dominated the symptom network in Profile 2, and fatigue attained the highest strength in Profile 3. Distinct symptom profiles were influenced by variables such as education level, CTX combined with surgical or herbal treatment, psychological resilience, and social support.
Conclusions: Patients within different subgroups manifest individualized patterns of symptom profiles. Analyzing demographics, disease characteristics, and psychosocial information among diverse subgroups facilitates healthcare providers in devising more personalized and targeted symptom management strategies, thereby alleviating the symptom burden on patients.

Introduction

Gastric cancer is a common type of malignant tumor that caused over 1 million cases and 768,000 deaths worldwide in 2020, with almost 50% of cases occurring in China.[1] Chemotherapy (CTX) is one of the primary treatments for gastric cancer, but it also causes patients to experience more than 10 related symptoms that interact to form clusters.[2]

There have been studies that examined the symptom clusters of gastrointestinal cancers. Han et al.[3] identified an average of 13 symptoms before and after the CTX cycle in 399 patients in the U.S. with gastrointestinal cancers. They identified four symptom clusters based on three symptom dimensions (occurrence, severity, and distress). Longitudinal comparisons revealed that the psychological, CTX-related, and weight change clusters were relatively stable across all three symptom dimensions and over time.[4] Fu et al.[5] investigated 322 gastric cancer patients undergoing CTX at three medical centers in China and identified five symptom clusters. In our previous research, Hu and Wang et al.[6,7] used exploratory factor analysis to identify five symptom clusters in a longitudinal survey of 113 and 213 gastric cancer patients, respectively, undergoing CTX in China: sickness symptom cluster, emotional symptom cluster, gastrointestinal symptom cluster, neurologic symptom cluster, and gastric cancer–specific symptom cluster.

The study of symptom clusters is regarded as an essential direction in the field of symptom science.[8] Identifying symptom clusters is

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instrumental in simplifying the complex relationships between symptoms and enhancing the efficacy of symptom management strategies. However, the approach to identifying symptom clusters may vary based on data collection methods and various statistical techniques.[9–11] Despite this, there is agreement in the conclusion that multiple symptom burden negatively affects quality of life for patients.

The appropriateness of using dimensionality reduction techniques to investigate symptom clusters is still under debate in today's clinical practice with huge amounts of data.[12] Symptom dimension reduction gives only a broad picture of which disease-specific or CTX-related symptoms share the same co-occurrence mechanism,[13] but they may not accurately reflect the complex reality of people with gastric cancer. Few studies have focused on differentiating clinical subtypes and symptom networks of CTX-related symptoms, rather than creating symptom clusters. The identification of subgroups of gastric cancer patients based on symptom clusters and severity of individual symptoms is crucial for the determination of person-centered symptom management.[14]

Latent profile analysis (LPA) is a person-centered method used to establish the correlations between interindividual differences and symptoms. Jing F et al.[15] investigated the symptom profiles of breast cancer patients and found that younger patients who paid out-of-pocket for health care, used aromatase inhibitors and that those who had a history of CTX were at greater risk of being in the high-symptom group. Oppegaard K et al.[16] investigated 3 subgroups of depressive symptoms in 1327 oncology patients and discovered that individual differences in depressive symptoms were associated with demographic and clinical characteristics and levels of psychological resilience, as well as the severity of multiple comorbid symptoms. These analyses could be particularly valuable for discerning similarities and disparities among various symptoms in a heterogeneous sample, where these attributes may manifest as prominent patterns or profiles.[17] The identification of symptom patterns and the analysis of their risk factors can help clinical practitioners identify high-risk patients and initiate more timely and supportive therapeutic interventions.

In this study, the symptom network was used based on the LPA results. Symptom network involved a quantitative investigation of the structural composition, nodes, and network indicators encompassing individual symptoms.[18] The application of symptom networks can provide further differentiation of profiles and additional data that could not be found with patient-centered analysis methods. Using LPA and symptom networks together may have greater clinical implications. This could lead to the development of patient-centered precision care.

Therefore, this study was designed to 1) identify subgroups of gastric cancer CTX–related symptoms using LPA and 2) determine whether the subgroups differ on demographic and health-related characteristics and symptom network indicators.

Methods

Study design and participants

This was a cross-sectional survey study of patients in four tertiary class-A hospitals located in the Yangtze River Delta region of China. Participants at all study sites were eligible if they were (1) aged $\geq$18 years, (2) had a pathologically confirmed primary gastric cancer, (3) were receiving CTX, and (4) able to read and understand Chinese. Patients who had cognitive impairment or were unaware of their true diagnosis were not considered for enrollment. A total of 732 eligible participants were recruited between July 2021 and November 2022, using convenience sampling, of which 55 patients were excluded due to missing data, and data from 677 patients were included in the final analysis.

Instruments

Demographic and clinical characteristics questionnaire Patients' demographic and clinical characteristics were obtained from a self-administered questionnaire. The main items included sex, age, place of residence, marital status, education level, employment status, monthly income per capita, health insurance, comorbidities, duration of diagnosis, cancer stage, frequency of CTX, and combination therapy regimens. All demographic data were checked with the patient or family, and data on clinical characteristics were confirmed from the medical record.

Chinese Version of the M. D. Anderson Symptom Inventory Gastrointestinal Cancer Module (MDASI-GI-C) The incidence and severity of the patient's symptoms were assessed by MDASI-GI-C, which is a reliable and valid tool for assessing cancer-related symptoms in Chinese-speaking patients with digestive tract tumors (the construct validity was 0.784; Cronbach's α value was 0.842 and 0.859).[19] The scale was used to assess the severity of 13 common cancer symptoms and 5 gastrointestinal cancer–specific symptoms in the past 24 hours. The responses range from "no symptoms" (0) to "most severe" (10). The 18 symptoms included in the MDASI-GI were categorized into 5 symptom clusters: sickness symptom cluster (pain/fatigue/disturbed sleep), emotional symptom cluster (distress/shortness of breath/difficulty remembering/sadness), gastrointestinal symptom cluster (nausea/lack of appetite/dry mouth/-vomiting), neurologic symptom cluster (drowsiness/numbness), and gastric cancer–specific symptom cluster (constipation/diarrhea/difficulty swallowing/change in appetite/bloating).

Karnofsky Performance Status (*KPS*) KPS is widely used in oncology to evaluate the body's performance status. The total score of the scale ranges from 0 to 100, in 10 point increments with higher scores indicating better health status.

Connor and Davidson's Resilience Scale (*CD-RISC*) The resilience of gastric cancer survivors was measured using Chinese version of the CD-RISC.[20] The scale consists of three dimensions: resilience (13 items), self-reliance (8 items), and optimism (4 items). A 5-point Likert scale is used, ranging from 0 (never) to 4 (always), with a total score of 100. A higher score indicates better psychological resilience. The validity and reliability of the Chinese version of the CD-RISC is well established (Cronbach's α value = 0.91).[20]

Social Support Rating Scale(*SSRS*) A 10-item SSRS was utilized to assess the level of social support in gastric cancer survivors.[21] The scale contains three dimensions: objective support, subjective support, and social support utilization. The total score on the scale ranges from 12 to 66 points, with higher scores indicating higher levels of social support. A previous study has demonstrated that SSRS had good validity (the construct validity was 0.879) and internal consistency (Cronbach's α value = 0.865).[22]

Study procedures

After an eligible patient with gastric cancer was admitted to the hospital, a research assistant explained the study to the patients who were willing to participate in the trial. Questionnaires were distributed during the period after the start of CTX and before the patient was discharged from the hospital. The entire survey was completed independently by the patient. A researcher accompanied the whole process and explained items that were difficult to understand. Missing entries were confirmed with the patient on the spot to ensure data completeness.

Data analysis

LPA was performed using the Mplus 8.3 software to identify person-centered subtypes of symptoms. We calculated average severity scores for each cluster and constructed models starting from a single profile. The number of classifications was determined by comparing each model-fit metric. Smaller values of Bayesian information criterion (BIC), Akaike information criterion (AIC), and adjusted sample size BIC (ABIC) indicate better model fit. An entropy closer to 1 indicates higher accuracy. *P*-values of Lo–Mendell–Rubin likelihood ratio test (LMR), and bootstrap likelihood ratio test that are < 0.05 indicate that the k-model is superior to the k-1 model. The final model was selected by considering theoretical interpretability as well as clinical applicability.

Table 1
Latent profile model fit indices.

Model	LL	AIC	BIC	ABIC	Entropy	Relative frequency of smallest class (%)	LMR *P*-value	BLRT *P*-value
1	−6543.710	13,107.420	13,152.597	13,120.846	1	100	–	–
2	−5530.575	11,093.151	11,165.434	11,114.632	0.958	20.7	< 0.001	< 0.001
3	−5161.705	10,367.410	10,466.799	10,396.947	0.895	14.9	< 0.001	< 0.001
4	−5063.186	10,182.372	10,308.867	10,219.964	0.878	10.8	0.115	< 0.001

AIC, Akaike's information criteria; ABIC, adjusted BIC; BIC, Bayesian information criteria; BLRT, bootstrapped likelihood ratio test; LL, log likelihood; LMR, Lo–Mendel–Rubin.

The statistical analyses were performed using R version 4.2.1 and the qgraph package. We used Spearman correlations to assess the relationships (edges) between pairs of symptoms (nodes) in the full sample and subgroups. The Fruchterman–Reingold algorithm and spring layout were used to generate symptom networks. Node centrality serves as a mechanistic indicator for identifying core symptoms. We conducted a centrality analysis using three metrics (strength, betweenness, and closeness).[23] The strength metric measures node significance by calculating the sum of absolute correlation coefficient weights of edges. The higher the value, the stronger the influence of a symptom on other symptoms and its importance.[24] In this study, strength is used as the dominant indicator among the three indices.[25]

Ethical considerations

The Affiliated Hospital of Nanjing University of Chinese Medicine's Institutional Review Board approved this survey in July 2021 (IRB No. 2021NL-089-03). The study was conducted under the guidelines of the Declaration of Helsinki, and written informed consent was obtained from all study participants before the initiation of the survey.

Results

Symptom subgroups identified by LPA

For our study, four models were built, and the results of their LPA-fit indices are provided in Table 1. Model 2 had the highest entropy value (0.958), but its AIC, BIC, and ABIC values were higher, and its classification was too simplistic to be clinically significant. Model 4 got the lowest AIC, BIC, and ABIC values, but a high *P*-value for the LMR test, indicating that it did not surpass the three-level categorization. Model 3 had the second-greatest entropy value (0.895), and the LMR and bootstrap likelihood ratio test tests confirmed that it outperformed the other two profiles. We chose Model 3 as the best categorization based on all of the fit indices, and its average latent class probabilities for most likely latent class membership were 92.4%–98.1%, which provides better persuasion.

We plotted symptom-severity scores for the 3-profile model (Fig. 1). The blue graph reflects Profile 1, which includes 354 patients (52.3%) and depicts an overall low-severity symptom cluster that we named the "*low*" class. The purple graph shows the "*moderate*" class (Profile 2), with 222 patients (32.8%) presenting with a higher severity of the sickness symptom cluster such as fatigue and disturbed sleep; the yellow graph represents the "*all high*" class (Profile 3) with a higher severity of the gastrointestinal symptom cluster such as vomiting and lack of appetite, with 101 patients (14.9%) classified in this subgroup.

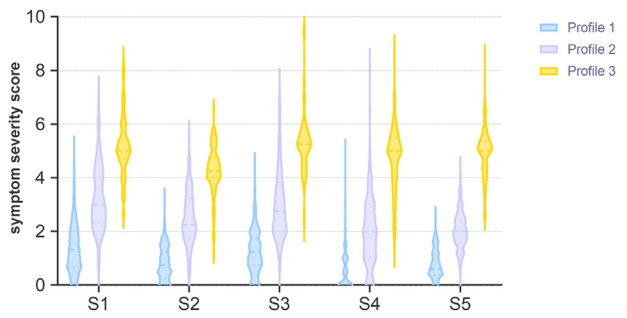

Fig. 1. Symptom severity score of the three latent profiles for five symptom clusters. S1: sickness symptom cluster; S2: emotional symptom cluster; S3: gastrointestinal symptom cluster; S4: neurologic symptom cluster; S5: gastric cancer-specific symptom cluster.

Demographic and clinical disease characteristics

In our sample, 73.0% patients were male, and 27.0% patients were female, with a mean age of 61.75 ± 10.50 years. In the total sample, patients had an average KPS score of 87.43 ± 9.83, a psychological resilience score of 54.08 ± 16.68, and a social support score of 52.56 ± 14.33. More demographic characteristics are detailed in Table 2.

Distinctions in demographic and health-related indicators among the three subgroups

Table 2 compares the demographic and health-related features of the three subgroups. Except for education level ($P = 0.003$), the differences in demographic factors among the three subgroups were not statistically significant ($P > 0.05$). In terms of disease-related characteristics, there were significant differences in the distribution of cancer stage, CTX frequency, CTX combined with radical surgery, and CTX combined with traditional Chinese medicine (TCM) treatments among patients in different subgroups ($P < 0.05$). In addition, psychological resilience and level of social support exhibited equally significant differences ($P < 0.001$). In terms of functional status, patients in Profile 3 had significantly lower KPS scores than those in the other two subgroups ($P < 0.001$). Table 3 shows the results of the multivariate regression analysis, with Profile 1 selected as the control. Compared to Profile 1, the patients in Profile 2 were more likely to receive CTX combined with Chinese herbal therapy (odds ratio [OR] = 1.907) and had lower psychological resilience (OR = 0.972). The patients in Profile 3 were less likely to have junior high school education (OR = 0.309), less likely to receive radical surgery (OR = 0.308), and more likely to receive CTX combined with Chinese herbal therapy (OR = 3.027) and had lower social support levels (OR = 0.963).

Symptom networks and centrality indices of subgroups

Fig. 2 shows the symptom networks for the full sample and the three subgroups. The network analysis was performed for 18 symptoms consisting of the five aforementioned symptom clusters in the full sample and subgroups. Based on the thickness of the edges in the symptom network, in the full sample, the top three symptom pairs with the strongest correlation were the following: change in taste—lack of appetite ($r = 0.794$), sadness—distress ($r = 0.791$), and nausea—vomiting ($r = 0.766$). The most strongly associated symptoms in the three subgroups were nausea and vomiting, whereas sadness—distress, and change in taste—lack of appetite were closely related in Profiles 1 and 2. Possibly due to the small number of people, only nausea—vomiting ($r = 0.692$) in Profile 3 shows thicker edges.

Fig. 3 displays the centrality indices (strength, closeness, and betweenness) for the full sample and three subgroups. Testing found that

Table 2
Demographic and health-related characteristics difference among subgroups.

Characteristic	Total $n = 677$	Profile 1 $n = 354$	Profile 2 $n = 222$	Profile 3 $n = 101$	F/χ^2	P
	M ± SD or *n* (%)					
Gender					3.565	0.168
Male	494 (73.0)	269 (76.0)	156 (70.3)	69 (68.3)		
Female	183 (27.0)	85 (24.0)	66 (29.7)	32 (31.7)		
Age (years)	61.75 ± 10.50	62.04 ± 10.01	61.34 ± 10.69	61.62 ± 11.78	0.315	0.730
Place of residence					4.467	0.107
Rural	244 (36.0)	133 (37.6)	84 (37.8)	27 (26.7)		
Urban	433 (64.0)	221 (62.4)	138 (62.2)	74 (73.3)		
Marital status					2.490	0.288
Married or partnered	649 (95.9)	342 (96.6)	213 (95.9)	94 (93.1)		
Single	28 (4.1)	12 (3.4)	9 (4.1)	7 (6.9)		
Education level					16.292	0.003
Junior school and below	422 (62.3)	211 (59.6)	130 (58.6)	81 (80.2)		
Senior or technical school	180 (26.6)	102 (28.8)	64 (28.8)	14 (13.9)		
College and above	75 (11.1)	41 (11.6)	28 (12.6)	6 (5.9)		
Employment status					3.890	0.143
Employed	377 (55.7)	207 (58.5)	122 (55.0)	48 (47.5)		
Otherwise	300 (44.3)	147 (41.5)	100 (45.0)	53 (52.5)		
Monthly income per capita					3.738	0.443
<¥4000	243 (35.9)	130 (36.7)	77 (34.7)	36 (35.6)		
¥4000~¥8000	371 (54.8)	185 (52.3)	127 (57.2)	59 (58.4)		
>¥8000	63 (9.3)	39 (11.0)	18 (8.1)	6 (5.9)		
Pay with health insurance (yes)	646 (95.4)	340 (96.0)	209 (94.1)	97 (96.0)	1.232	0.540
Comorbidity with other chronic diseases (yes)	455 (67.2)	235 (66.4)	149 (67.1)	71 (70.3)	3.674	0.452
Duration of diagnosis (months)					2.525	0.638
< 6	560 (82.7)	298 (84.2)	182 (82.0)	80 (79.2)		
6–12	112 (16.5)	53 (15.0)	38 (17.1)	21 (20.8)		
> 12	5 (0.7)	3 (0.8)	2 (0.9)	0 (0.0)		
Cancer stage					17.119	0.009
I	34 (5.0)	22 (6.2)	8 (3.6)	4 (4.0)		
II	132 (19.5)	57 (16.1)	52 (23.4)	23 (22.8)		
III	307 (45.3)	171 (48.3)	104 (46.8)	32 (31.7)		
IV	204 (30.1)	104 (29.4)	58 (26.1)	42 (41.6)		
Frequency of chemotherapy (times)					11.471	0.022
≤ 3	469 (69.3)	248 (70.1)	143 (64.4)	78 (77.2)		
4–6	136 (20.1)	61 (17.2)	57 (25.7)	18 (17.8)		
> 6	72 (10.6)	45 (12.7)	22 (9.9)	5 (5.0)		
Treatment with chemotherapy combinations						
Radical surgery (yes)	530 (78.3)	280 (79.1)	194 (87.4)	56 (55.4)	41.951	< 0.001
Radiotherapy (yes)	9 (1.3)	4 (1.1)	2 (0.9)	3 (3.0)	2.403	0.229
Targeted therapy (yes)	46 (6.8)	28 (7.9)	15 (6.8)	3 (3.0)	3.028	0.220
Immunotherapy (yes)	54 (8.0)	27 (7.6)	20 (9.0)	7 (6.9)	0.532	0.7671
Chinese herbal therapy (yes)	127 (18.8)	47 (13.3)	44 (19.8)	36 (35.6)	26.038	< 0.001
KPS	87.43 ± 9.83	90.31 ± 6.95	86.98 ± 9.53	78.32 ± 12.97	71.02	< 0.001
CD-RISC	54.08 ± 16.68	57.55 ± 16.34	49.93 ± 17.20	51.09 ± 13.79	16.938	< 0.001
SSSR	52.56 ± 14.33	54.06 ± 16.66	51.92 ± 13.28	48.71 ± 9.27	5.888	0.003

CD-RISC, Connor and Davidson's Resilience Scale; KPS, Karnofsky Performance Status; M, mean; SSRS, Social Support Rating Scale; SD, standard deviation.

Table 3
Multivariate logistic regression analysis of three profiles.

Variable	Profile 2 versus Profile 1	P	Profile 3 versus Profile 1	P
	OR (95% CI)		*OR* (95% CI)	
Educational level (compared to junior school and below)				
Senior or technical school	1.096 (0.733, 1.638)	0.655	**0.309 (0.160, 0.598)**	**< 0.001**
College and above	1.339 (0.759, 2.363)	0.313	0.518 (0.201, 1.337)	0.174
Cancer stage (compared to I)				
II	2.114 (0.836, 5.348)	0.114	3.363 (0.946, 11.957)	0.061
III	1.398 (0.580, 3.368)	0.456	1.460 (0.428, 4.980)	0.545
IV	1.459 (0.585, 3.639)	0.418	2.097 (0.604, 7.155)	0.246
Chemotherapy frequency (compared to ≤3 times)				
4~6	1.424 (0.922, 2.199)	0.111	1.151 (0.608, 2.177)	0.666
> 6	0.851 (0.477, 1.519)	0.585	0.460 (0.169, 1.252)	0.129
Radical surgery (compared to no)	1.830 (1.054, 3.178)	0.032	**0.308 (0.165, 0.576)**	**< 0.001**
Chinese herbal therapy (compared to no)	**1.907 (1.172, 3.102)**	**0.009**	**3.027 (1.671, 5.485)**	**< 0.001**
CD-RISC	**0.972 (0.961, 0.983)**	**< 0.001**	0.987 (0.971, 1.003)	0.108
SSSR	0.998 (0.985, 1.012)	0.822	**0.963(0.944, 0.982)**	**< 0.001**

Significant values are in [bold]. Model fitness: Nagelkerke $R^2 = 0.216$, $\chi^2 = 139.178$, $P < 0.001$.
CD-RISC, Connor and Davidson's Resilience Scale; CI, confidence interval; OR, odds ratio; SSRS, Social Support Rating Scale.

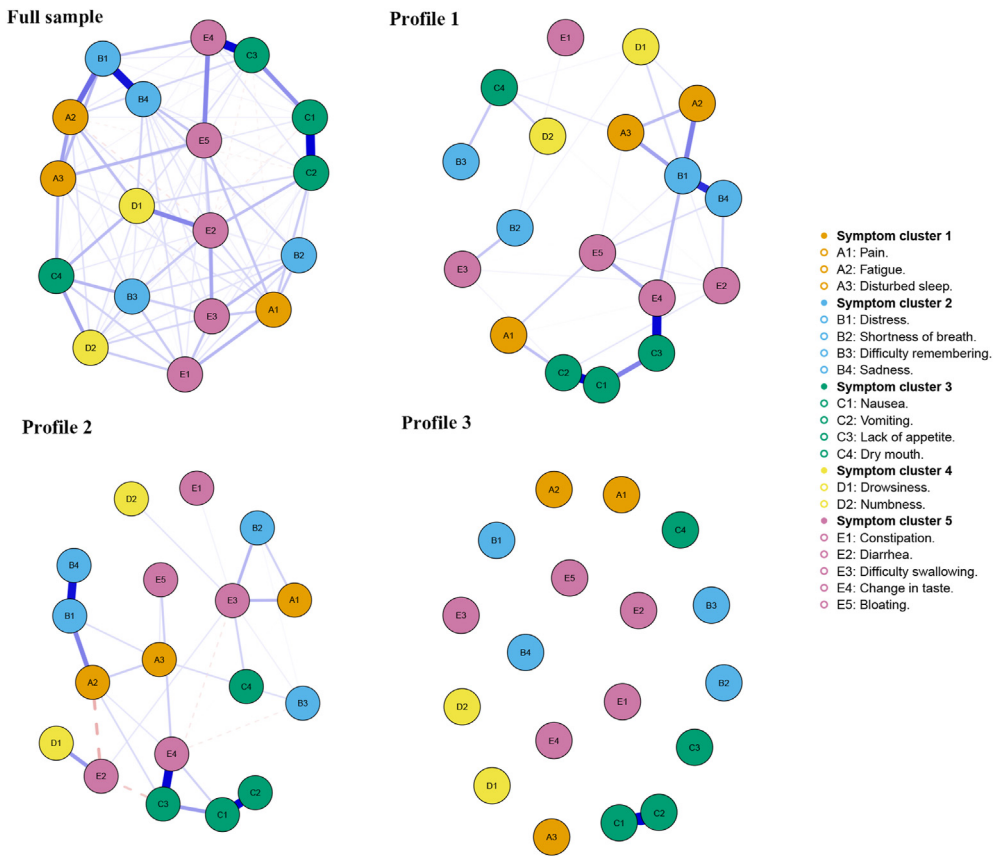

Fig. 2. Symptom network in the full sample and three subgroups.

the correlation coefficients of strength in the symptom networks were all greater than 0.5, which means that the strength can be used as the dominant indicator among the three indicators. In the full sample network (Fig. 2a), sadness had the highest strength centrality index (rs = 1.490). In subgroup 1 (Fig. 2b), distress had the highest strength centrality index (rs = 2.012). In subgroup 2 (Fig. 2c), lack of appetite had the highest strength centrality index (rs = 1.780). In subgroup 3 (Fig. 2d), fatigue had the highest strength centrality index (rs = 1.482).

Discussion

Full sample

Building on previous work on symptom clusters, this study used the LPA to identify three latent profiles and construct a symptom network of gastric cancer patients undergoing CTX. In the full sample of this study, fatigue and lack of appetite showed high occurrence and severity in single symptoms, with only minor differences in values, followed by a change in taste. Pain—fatigue—disturbed sleep showed the highest mean severity among symptom clusters, which is not unexpected in patients receiving cancer toxicology.[4,5,26] However, the associations between pain, fatigue, and disturbed sleep in our study were not as strong as the associations between nausea—vomiting, sadness—distress, and lack of appetite—change in taste. No matter how the other symptom relationships change, these three sets of symptom associations were always closely related in the networks of the full sample, Profile 1, and Profile 2.

Profile 1: Low class

More than half of the patients in this study were classified in the *low* class, and the overall symptom severity of patients in this group was lower than that in the other two subgroups. The centrality index of the network analysis showed the highest intensity of distress as their core symptom. Shim et al.[27] previously researched the psychological and somatic symptoms of gastric cancer patients and built symptom networks at three time periods before and after surgery, discovering that distress and sadness were the most central symptoms in the three networks. Consistently, sadness—distress had a strong link in all samples of the present study, and sadness played a central role in the symptom networks of the overall samples, which may have contributed to the large proportion of patients in the *low* class. In our study sample, resilience levels were lower in all the three subgroups of patients than those found in the general community population in the study by Han et al. (67.30 ± 16.89).[28] Fortunately, our social support levels were all higher than those of the general population of similar ages (37.91 ± 6.12)[22] and colorectal cancer CTX patients in Liu et al. (39.11 ± 3.96).[29] Patients in the *low* class were more resilient and had more social support than the other two subgroups did, which provides them with enough positive resources to cope with the disease burden.[30,31] Therefore, patients in this group have a good performance status that does not affect their daily lives, despite the presence of multiple symptoms. However, it was found that the deterioration in the quality of life is more of an indirect effect of cancer through emotional distress such as anxiety, depression, and somatization.[32]

Profile 2: Moderate class

Profile 2 shows the *moderate* class, where patients in this subgroup reported symptom severity between the *low* class and *all high* class, with fatigue and lack of appetite being the two most severe symptoms in this subgroup. Unlike in Profile 1, lack of appetite is a core symptom in this symptom network. Rha et al.[33] found that the presence of lack of appetite in symptom clusters coincided with cyclic use of chemotherapeutic agents and was strongly associated with change in taste in the symptom network, which is consistent with the present study. Lack of appetite

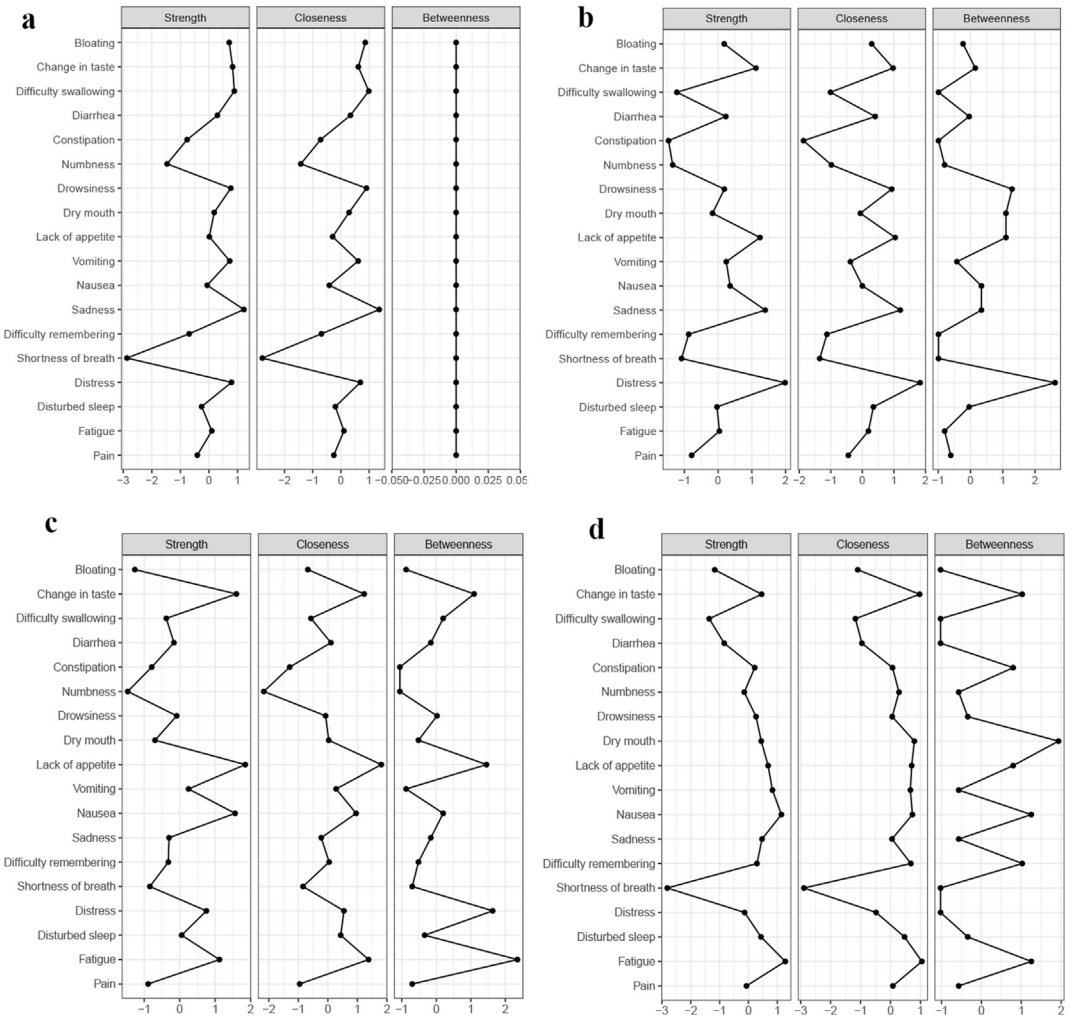

Fig. 3. Centrality indices of the networks of the full sample and three subgroups.

predicts poor patient survival and causes significant distress to both patients and family members.[34,35] Thus, nutritional interventions such as dietary counseling to alleviate lack of appetite should be an important part of symptom management in the *moderate* class.[36] Compared to the *lower* class, patients in the *moderate* class and *all high* class were more likely to receive CTX in combination with TCM. The active ingredients of TCM, including flavonoids, alkaloids, terpenoids, etc., can not only enhance the body's immune function, and induce apoptosis of the tumor cells, but also reverse the multidrug resistance.[37–39] Therefore, treating physicians prefer CTX in combination with Chinese herbal medicine to improve the efficacy and reduce the adverse effects in patients with heavy symptom loads. Furthermore, we discovered that the resilience in the *moderate* class was not as great as that in the *low* class. Studies[40,41] have demonstrated that individuals with high resilience can improve their health outcomes through cognitive behavioral therapy.[42,43] Increasing resilience offers patients more confidence in self-management of symptoms, which could be a crucial step in smoothing the transition to the *low* class.

Profile 3: All high class

Profile 3 is the *all high* class. The study found that patients reported high levels of symptom severity, particularly with change in taste. Patients in all high-symptom groups were more likely to receive radical surgery, have low levels of education, and have limited social support. Radical surgical treatment can cause surgery-related pain and result in various gastrointestinal symptoms, including nausea, vomiting, and bloating.[44,45] Patients with lower levels of literacy may struggle to follow symptom management recommendations provided by their care providers. Strong social support has been shown to have a positive impact on cancer prognosis as it enables patients feel emotionally supported during treatment.[46] Fatigue was identified as a core symptom in the symptom network of Profile 3. In an analysis of symptom data from 249 heterogeneous cancer patients, fatigue has the highest strength value in a dynamic symptom network.[33] In a comprehensive longitudinal study on the epidemiology of insomnia in cancer patients, Trudel-Fitzgerald et al.[47] discovered that fatigue serves as a significant predictor for subsequent development of depression, insomnia, and pain. A systematic evaluation[48] demonstrated that the provision of self-management support, comprising at least one in-person session delivered by a healthcare professional following cancer treatment, exhibited the most favorable outcomes in terms of fatigue and behavioral improvements. Furthermore, they underscored the pivotal role played by nurses, as the largest workforce within cancer care, in delivering self-management support for cancer-related fatigue.

Implications for nursing practice and research

Our study identified 3 potential profiles of 677 gastric cancer CTX patients from 4 tertiary hospitals in eastern China. We collect additional group-specific knowledge through symptom networks that form in accordance with various levels of symptom severity. The core symptoms of the symptom networks of the 3 subgroups were varied, and we discovered that distress, lack of appetite, and fatigue were the core

symptoms of the three subgroups, with different potential influencing factors and management measures. Our findings suggest that symptom management in patients undergoing CTX for gastric cancer ought to focus on incorporating psychoemotional as well as gastrointestinal symptoms. It is very important to pay attention to psychological counseling and avoid the aggravation of psychological problems inducing other somatic symptoms. Healthcare providers have the potential to be enabled to develop more individualized and targeted symptom management techniques with assistance of pertinent data on the demographic, disease characteristics, and psychological profiles of the various subgroups.

Limitations

Despite the strengths of our study, such as the large sample size of gastric cancer CTX patients and locally verified symptom subgroups, there are certain drawbacks to consider. Firstly, because of the imbalance in numbers between subgroups, the Profile 3 symptom network may have meaningful symptom associations that are not shown. Secondly, we were unable to establish potential causative links between variables due to the cross-sectional design, and the three latent profiles and symptom networks may have changed dynamically over time. Furthermore, differences in survey instruments may overlook the value of some symptoms (eg, difficulty concentrating and hair loss). We should take into account not only the most prevalent and severe symptoms across the entire sample but also the possibility that distinct population groups may exhibit highly diverse symptom patterns.[49] Future research could use alternative symptom lists in diverse circumstances to illustrate the generalizability of our findings, and objective indicators are also required to investigate the underlying mechanism.

Conclusions

This study provides a comprehensive account of differences in symptom networks in subgroups of patients undergoing CTX for gastric cancer, which have different influencing factors, and identifies core symptoms that are potentially of greater value and can be targets for intervention.

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CRediT authorship contribution statement

Peibei Duan: Conceptualization, Methodology, Data curation, Formal analysis, Writing. **Xun Li**: Methodology, Writing—Original draft preparation, Data curation. **Yanling Zou**: Formal analysis, Writing—Original draft preparation, Data curation. **Ziyan Zhang**: Conceptualization, Methodology, Data collection. **Yi Li**: Data collection, Writing—Original and Revised draft preparation. **Xiaoqing Wang**: Data collection, Writing—Revised draft preparation. **Lihua Yang**: Data collection, Methodology. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability statement

The data are not publicly available due to their containing information that could compromise the privacy of research participants.

Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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Ethics statement

The study was approved by the Affiliated Hospital of Nanjing University of Chinese Medicine's Institutional Review Board (IRB No. 2021NL-089-03). All participants provided written informed consent.

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