



Identification of the Core Nutrition Impact Symptoms Cluster in Patients with Lung Cancer During Chemotherapy: A Symptom Network Analysis

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ARTICLE INFO

Key Words:

Lung cancer
Chemotherapy
Nutrition Impact Symptoms (NIS)
Symptom network
Network analysis

ABSTRACT

Objectives: Lung cancer patients undergoing chemotherapy are present in multiple Nutrition Impact Symptoms (NIS). There have been no studies utilizing symptom networks to identify core NIS in lung cancer patients undergoing chemotherapy, it is necessary to identify core symptoms for effective and precise symptom management. We aimed to construct a symptom network of NIS in lung cancer patients receiving chemotherapy, and explore the core Nutrition Impact Symptoms cluster.

Methods: A cross-sectional survey was conducted among 315 patients with lung cancer. The Patient-Generated Subjective Global Assessment-Short Form was used to assess the prevalence and severity of NIS. We constructed a symptom network and identified centrality indexes using R packages.

Results: Fatigue emerged as the most prevalent and severe symptom, affecting 87% of participants, with an intensity of 3.0 ± 1.3 . The network density was measured at 0.5. Strength centrality showed a stability coefficient of 0.7, with fatigue ($R_s = 0.73$), lack of appetite ($R_s = 1.02$), and nausea ($R_s = 0.70$) ranking as the top three symptoms. For betweenness centrality, the stability coefficient was 0.3, highlighting fatigue ($R_b = 12$), lack of appetite ($R_b = 34$), and emotional change ($R_b = 18$) as the primary symptoms.

Conclusions: This study identified a core symptom cluster consisting of fatigue, lack of appetite, and emotional change. These findings provide valuable insights for developing targeted symptom management strategies and interventions for this patient population in the future.

Implications for Nursing Practice: Nurses need to comprehensively consider the interaction of multidimensional symptoms to provide lung chemotherapy cancer with targeted symptom management strategies and intervention guidance to reduce the burden of symptoms and improve quality of life.

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Introduction

One of the most prevalent malignant tumors globally, lung cancer stands as a primary contributor to cancer-related fatalities, posing a grave danger to human well-being and imposing a significant socio-economic burden.^{1,2} In China, lung cancer dominates as the most prevalent form of malignancy, serving as the primary factor driving cancer incidence and mortality rates.³ The latest data on cancer morbidity and mortality in China show that lung cancer is the cancer with the highest morbidity and mortality.⁴ According to research projections, the number of lung cancer deaths in China is anticipated

to surge by 42.7% by the year 2030.⁵ Chemotherapy is a common treatment for lung cancer patients, and both the tumor itself and systemic treatment can affect the patient's nutrition.⁶ Malnutrition, as an independent determinant of reduced quality of life in lung cancer patients,⁷ can adversely affect various aspects, including physical capabilities, overall quality of life, successful completion of treatment regimens, healthcare expenditures, and ultimately, survival rates.⁸⁻¹⁰ Numerous studies have shown that lung cancer stands among the tumors that exhibit the highest prevalence of malnutrition,^{11,12} and most lung cancer patients have a high symptom burden before starting systemic antitumor treatment, increasing the risk of malnutrition.^{7,13} Among them, Nutrition Impact Symptoms are one of the independent risk factors for cancer related malnutrition.¹⁰

Nutrition Impact Symptoms (NIS) are defined as symptoms that may impact nutritional status and negatively increase the risk of malnutrition.¹⁴ NIS has been widely studied in patients with head and neck tumors. Several studies have shown that common symptoms of

Abbreviations: NIS, Nutritional Impact Symptom; PG-SGA SF, Patient-Generated Subjective Global Assessment-Short Form; IQR, interquartile range; M, mean; SD, standard deviation

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<https://doi.org/10.1016/j.soncn.2024.151794>

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Layperson Summary

What we investigated and why

Lung cancer patients undergoing chemotherapy are present in multiple Nutrition Impact Symptoms (NIS). There have been no studies utilizing symptom networks to identify core NIS in lung cancer patients undergoing chemotherapy, it is necessary to identify core symptoms for effective and precise symptom management. We aimed to construct a symptom network of NIS in lung cancer patients receiving chemotherapy, and explore the core Nutrition Impact Symptoms Cluster.

How we did our research

We conducted a cross-sectional survey of 315 patients with lung cancer undergoing chemotherapy. The Patient-Generated Subjective Global Assessment-Short Form (PG-SGA SF) was used to assess the prevalence and severity of NIS. We constructed a symptom network and identified centrality indexes using R packages.

What we have found

We have found that fatigue emerged as the most prevalent and severe Nutritional Impact Symptom, with lack of appetite identified as the core symptom. The core symptom cluster comprised fatigue, lack of appetite, and emotional change.

What it means

Nurses need to comprehensively consider the interaction of multidimensional symptoms to provide lung chemotherapy cancer with targeted symptom management strategies and intervention guidance to reduce the burden of symptoms and improve quality of life.

decision-making.^{22,23} The symptom network can not only construct symptom cluster but also identify core symptoms and focus on the interaction between symptoms at the micro level.²⁴

In the lung cancer population, it remains unclear which symptoms are core to NIS, and, to our knowledge, network analysis is rarely applied in NIS research. Therefore, this study had two primary objectives: first, to construct a comprehensive symptom network that captures the multidimensional NIS experiences of lung cancer patients undergoing chemotherapy; and second, to identify the core symptom cluster impacting nutrition during chemotherapy, providing valuable insights for clinicians and researchers to guide symptom management decisions.

Methods

Study Design

The cross-sectional survey for this study was conducted spanning from September 2023 to June 2024. Oncology head nurses and a nursing graduate student conducted a questionnaire survey after explaining the purpose of the study to patients and obtaining informed consent. The Ethics Committee of the First Affiliated Hospital of Jinzhou Medical University (KYL 202393) has approved this study, ensuring that it complies with all ethical standards and guidelines.

Study Population

The study sample consisted of lung cancer patients undergoing chemotherapy, who hospitalized in the oncology ward of the First Affiliated Hospital of Jinzhou Medical University. The participants were included in the study based on the following criteria: they had to be (1) over the age of 18, (2) diagnosed with lung cancer, (3) received chemotherapy and completed at least one course of treatment, and (4) willing to provide their consent for participation in the research. Exclusion criteria were: (1) Patients who could not understand and answer questions; (2) patients suffering from other serious life-threatening diseases.

Measures Tools

The questionnaire used in this study comprises two sections: general information and box 3 from the Patient-Generated Subjective Global Assessment-Short Form (PG-SGA SF).

General information includes six aspects: the patient's gender, age, educational level, cancer stage, comorbidity, and residence. This part of the information is collected from the medical record system.

Self-reported symptoms were collected using the PG-SGA SF. It is currently the most commonly used and practical NIS assessment tool both domestically and internationally.^{25,26} PG-SGA was developed by Ottery in 1994 on the basis of SGA for patients with malignant tumors.²⁷ PG-SGA SF is the patient self-assessment part of PG-SGA, which reflects about 80% to 90% of the score²⁸; It has been verified as an independent and effective nutritional screening tool for chemotherapy patients²⁵; Compared with the complete PG-SGA and other nutritional assessment tools, it has higher sensitivity and specificity.^{29,30} Studies showed the content validity of different versions of PG-SGA SF between 0.90 and 0.95,³¹⁻³⁵ which demonstrated significant reliability and sufficient exploratory properties to support its validity. The third box in the PG-SGA SF includes 14 nutrition impact symptom, namely pain, lack of appetite, diarrhea, vomiting, mouth sores, problems swallowing, nausea, dry mouth, strange taste, smell bother, feel full quickly, constipation, others, and fatigue. In this study, the severity of these 14 symptoms was graded using a Likert-style scale, with "1" to "5" representing "no symptom," "mild," "moderate," "severe," and "extremely severe," respectively. The total

NIS caused by chemoradiotherapy for head and neck cancer include dysphagia, dry mouth, altered taste, difficulty chewing, saliva problems, pain, and loss of appetite¹⁴⁻¹⁷; The common NIS in nasopharyngeal carcinoma patients contains pain, dry mouth, altered taste, sticky saliva, and loss of appetite.¹⁸ NIS has been less studied in lung cancer patients, but existing reports suggest a high incidence and symptom burden. It has been reported that 71% of lung cancer patients experience at least one NIS, and 42% of lung cancer patients experience different types of NIS.¹⁹ Previous reports show that loss of appetite, vomiting, dysphagia, dry mouth, and early satiety are the most common symptoms in patients with lung cancer chemotherapy.^{10,19} Promptly identifying and effectively managing these symptoms is paramount, as their interconnected and mutually reinforcing nature can intensify other symptoms, significantly diminishing an individual's quality of life, mental well-being, and the effectiveness of subsequent treatments.²⁰

Network analysis postulates that symptoms are intricately interconnected and their manifestation is not solely contingent on the influence of a single variable, but rather on their complex interplay with each other.²¹ Leveraging the symptom network theory, we can generate a comprehensive symptom network representing multidimensional symptom experiences. This network yields clinically significant data, encompassing metrics like centrality and density indicators, which offer valuable insights. By analyzing the interaction between symptoms, we can help to understand the correlation strength, mechanism, and possible causal relationship between different symptoms, to provide support for individualized precise symptom management and promote the formulation of clinical

score for symptom severity ranged from 0 to 56 points. The symptoms evaluated by this scale were those that had occurred within the past 2 weeks. It is important to note that the “others” category in the PG-SGA SF includes three symptoms: dental problems, anxiety, and depression. In this study, anxiety and depression were selected from this category, grouped under “emotional changes,” and measured according to the grading assignment described above. The scale demonstrated a Cronbach’s α coefficient of 0.70 and a split-half reliability of 0.77, indicating acceptable internal consistency.^{36,37}

Sample Size Calculation

The sample size required for symptom network analysis was calculated based on the number of symptoms and the associated parameters. Base on the formula $[N + N(N - 1)/2]$ estimates the associated parameters,³⁸ where N is the number of nodes, that is, the number of symptoms involved. The tool used in this study involves a total of 14 symptoms, and the associated parameters obtained by bringing n equal to 14 into the formula is 105 cases. To ensure the reliability of the model, the sample size is determined by multiplying the number of associated parameters by a factor ranging from 3 to 5.³⁹ In this study, three times the associated parameters are used as the final sample size, that is, 105 times 3 is equal to 315.

This study employs data processing methods as outlined by scholars such as Kim⁴⁰ and Gaorong,⁴¹ the construction of the symptom network involved excluding uncommon symptoms with an incidence rate below 10%, resulting in a total of nine symptoms for network analysis. Applying nine symptoms to the formula, the minimum number of correlations required was determined to be 45. Additionally, accounting for five times this minimum correlation requirement and a 20% dropout rate, the theoretical sample size for this study was calculated to be 270 cases [ie, $45 \times 5 + (45 \times 5 \times 20\%) = 270$].

Data Analysis

Statistical analysis, including descriptive statistics and linear regression, was performed using IBM SPSS 23.0 software. The significance level was set at a two-tailed $\alpha = 0.05$, with $P < .05$ indicating statistical significance. General information and symptom data were characterized using frequencies and percentages. In addition to the mean and standard deviation for age, total symptom scores, and severity ratings, median values, and interquartile ranges were also utilized for description.

A concurrent symptom network graph, comprising nine symptoms, was developed using the qgraph package in R software (version 4.3.3). The spring layout method was employed to create an undirected association network, where nodes with higher connectivity are positioned at the network’s center and the distance between nodes is minimized.²⁴ Each node in this network symbolizes a symptom, while the line connecting two nodes signifies the edge of the network. The thickness of the edge indicates the strength of the correlation between the two symptoms.^{38,39}

The centrality index of network structure serves as a pivotal method for assessing the significance of nodes within a network, providing an indicator to discern core symptoms from a mechanistic standpoint.²⁴ Our analysis of centrality is conducted from three distinct perspectives: strength, closeness, and betweenness. Strength is an index that gauges the importance of nodes in a network, quantifying the direct connection degree of a node with its counterparts. The greater the value, the more important the symptom is to other symptoms.³⁹ Closeness measures the indirect connection degree of a node with other nodes, while The betweenness centrality measure quantifies the significance of a node in the average path connecting two other nodes.⁴²

Furthermore, this study employed the bootnet package in R software, with nBoots set to 1000 and nCores set to 8, to calculate

the accuracy and stability of the network. The coefficient should ideally exceed 0.5, but a minimum threshold of 0.25 is also acceptable.^{24,39,42-44}

Results

Participant Characteristics

The demographic characteristics of the participants are presented in Table 1. A total of 315 participants were enrolled in this study, with an average age of 64.2 years. The majority of the participants were male (67.6%), had an educational level of junior high school and below (73.3%), and resided in urban areas (62.9%). Comorbidities were present in 28.6% of the participants, with hypertension being the most prevalent (17.1%), followed by diabetes (7.6%). Approximately 87.6% of the participants were in the late stage of lung cancer (III + IV).

Prevalence and Severity of Nutrition Impact Symptoms (NIS)

Table 2 presents the prevalence and severity of NIS among participants. The four most prevalent and severe NIS were, respectively, fatigue (87.0%, 3.0 ± 1.3), nausea (52.7%, 2.2 ± 1.2), vomiting (47.3%, 1.9 ± 1.1), and lack of appetite (46.3%, 1.8 ± 1.0).

Analysis of Symptom Network and Node Indicators

Fig. 1 illustrates the NIS symptom network during chemotherapy for lung cancer patients. The density of this symptom network is calculated to be 0.5. Analyze the correlation between symptoms based on the thickness of the edges within the symptom network model, strong correlations are observed between symptom groups S14 (fatigue) and S2 (lack of appetite) ($r = 0.4$), S7 (nausea) and S4 (vomiting) ($r = 0.5$), S2 (lack of appetite) and S13 (emotional change) ($r = 0.3$). Conversely, a significant negative correlation is noted

TABLE 1
Characteristics of Participants ($n = 315$)

Characteristics	Values
Age ^b	64.2 \pm 7.25 (59-70)
Sex ^a	
Male	213 (67.6)
Female	102 (32.4)
Education levels ^a	
Primary school or below	114 (36.2)
Junior middle school	117 (37.1)
Senior middle school	75 (23.8)
University or above	9 (2.9)
Cancer stage ^a	
I	33 (10.5)
II	6 (1.9)
III	96 (30.5)
IV	165 (52.4)
Not clear	15 (4.7)
Comorbidities ^a	
Hypertension	54 (17.1)
Diabetes	24 (7.6)
Cardiovascular disease	3 (1.0)
Otherwise	9 (2.9)
No comorbidities	225 (71.4)
Residences ^a	
Rural	117 (37.1)
Urban	198 (62.9)

IQR, interquartile range; M, mean; SD, standard deviation.

^a Values given are n (%).

^b Values given are mean \pm SD and IQR.

TABLE 2
Symptom Incidence and Severity of the Nine Included Symptoms ($n = 315$)

Symptom	Incidence n (%)	Severity score $M \pm SD$ (IQR)
Fatigue	274 (87.0)	3.0 ± 1.3 (2-4)
Nausea	166 (52.7)	2.2 ± 1.2 (1-3)
Vomiting	149 (47.3)	1.9 ± 1.1 (1-3)
Lack of appetite	146 (46.3)	1.8 ± 1.0 (1-2)
Dry mouth	93 (29.5)	1.5 ± 0.8 (1-2)
Pain	88 (27.9)	1.4 ± 0.7 (1-2)
Emotional change ^a	67 (21.3)	1.4 ± 0.7 (1-1)
Constipation	60 (19.1)	1.4 ± 0.8 (1-1)
Feel full quickly	33 (10.5)	1.2 ± 0.5 (1-1)

IQR, interquartile range; M, mean; SD, standard deviation.

^a Emotional change: Anxiety or Depression.

between symptom group S2 (lack of appetite) and S12 (constipation) ($r = -0.2$).

Three metrics were utilized to assess the centrality of the network: strength, betweenness, and closeness. The findings are depicted in Fig. 2. Based on the strength metric, the most prominent symptoms were fatigue ($R_s = 0.73$), nausea ($R_s = 0.70$), and lack of appetite ($R_s = 1.02$). According to the betweenness metric, the primary symptoms were fatigue ($R_b = 12$), lack of appetite ($R_b = 34$), and emotional change ($R_b = 18$). The symptoms that ranked highest based on the closeness metric mirrored those of the betweenness metric: fatigue ($R_c = 0.013$), lack of appetite ($R_c = 0.014$), and emotional change ($R_c = 0.012$). Notably, lack of appetite ($R_s = 1.02$, $R_b = 34$, $R_c = 0.014$) scored the highest across three centrality measures, establishing itself as the core NIS for patients undergoing chemotherapy for lung cancer.

Accuracy Verification of Symptom Network Analysis Results

Accuracy Testing of Nodes and Edges

The graph presented in Fig. 3 showcases the analysis outcomes regarding the weight values of edges within the symptom network. The extensive range of CI values among certain edge weights, results in diminished estimation precision, particularly for edges with lower weights. However, the edge weights for edges S14 (fatigue) and S2 (lack of appetite), S7 (nausea) and S4 (vomiting), S2 (lack of appetite), and S13 (emotional change) were reliable.

The stability test for the three centrality indicators is depicted in Fig. 4. The strength centrality exhibits a stability coefficient of 0.7, while that of betweenness stands at 0.3. These values suggest that

the outcomes derived from both strength and betweenness centralities are robustly stable. The stability coefficient of closeness is 0.2, which is less than 0.25, suggesting that closeness is unstable.

Difference Test of Nodes and Edges

The results of the Edge Weight Difference Test are illustrated in Fig. 5. The findings suggest notable disparities among the three most potent edge weights: S14 (fatigue) and S2 (lack of appetite), S7 (nausea) and S4 (vomiting), and S2 (lack of appetite) and S12 (constipation). These differences are distinct from other edge weights within the network.

Fig. 6 shows the results of the strength difference test of bootstrapped nodes. The node S2, with the highest intensity, representing lack of appetite, showed significant differences from more than half of the other nodes ($DT_s = 1.0$). Additionally, the node S14, representing fatigue, also demonstrated differences from over half of the nodes ($DT_s = 0.7$).

Discussion

Fatigue is a subjective feeling of fatigue and exhaustion.⁴⁵ This study confirms that fatigue is not only the most common but also the most severe NIS in these patients, aligning with findings from numerous previous studies.^{24,45-47} Furthermore, within the network model developed for this study, fatigue occupies a central position. This suggests that it is the most critical core symptom among lung cancer patients receiving chemotherapy. This conclusion is consistent with a network analysis of symptom stability across heterogeneous cancer groups, including lung cancer.⁴⁵ The high centrality of fatigue may be attributed to the direct or indirect toxicity resulting from both the cancer itself and its treatment.^{45,48} Research indicates that this centrality diminishes as the number of chemotherapy cycles increases, particularly after the fourth cycle.⁴⁵ However, since this study employed a cross-sectional survey design, no changes were observed in this regard. This observation warrants further investigation in future research endeavors.

Although lack of appetite did not rank among the top three symptoms in incidence and severity, it exhibited the highest intensity centrality indicators within the symptom network, highlighting its notable importance. While nausea and vomiting are more prevalent than lack of appetite, prophylactic medication is routinely administered before and after chemotherapy to alleviate these symptoms, underscoring the critical need for effective management of lack of appetite. Furthermore, the network analysis results in this study reveal that lack of appetite has the highest betweenness centrality, indicating a significant bridging effect on key symptoms such as fatigue and emotional changes. Consequently, it serves as a bridging symptom within the NIS network model for patients undergoing chemotherapy for lung cancer, warranting prioritization in intervention strategies. The research posits that bridging symptoms permeate the symptom network, with various symptoms and symptom clusters potentially spreading through bridge symptom.⁴⁹

Emotional change as a psychological symptom, this study mainly refers to anxiety and depression symptoms, its incidence and severity are relatively low, but the central indicators are relatively high, especially the intermediate indicators are second only to lack of appetite, which has a positive impact on physiological symptoms such as lack of appetite, fatigue, nausea, and vomiting, which are included in the core symptom cluster. A number of studies have shown that anxiety and depression are positively correlated with malnutrition in cancer patients.⁵⁰⁻⁵³ In the correlation analysis of nutrition-related symptoms, different scholars have proposed that nausea and vomiting in cancer patients are positively correlated with anxiety⁵⁴; Anxiety is also associated with taste changes in cancer patients⁵⁵; Anxiety and appetite also has a certain correlation, loss of appetite in cancer patients experienced more anxiety⁵⁶; Depression is closely related to

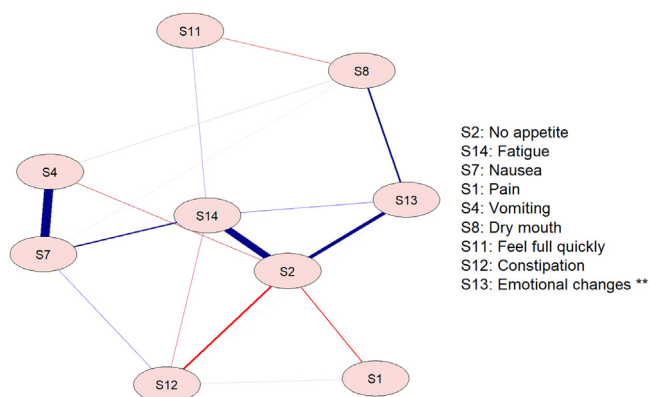


FIG 1. Symptom network of digestive cancer patients. Emotional change*: Anxiety or Depression.

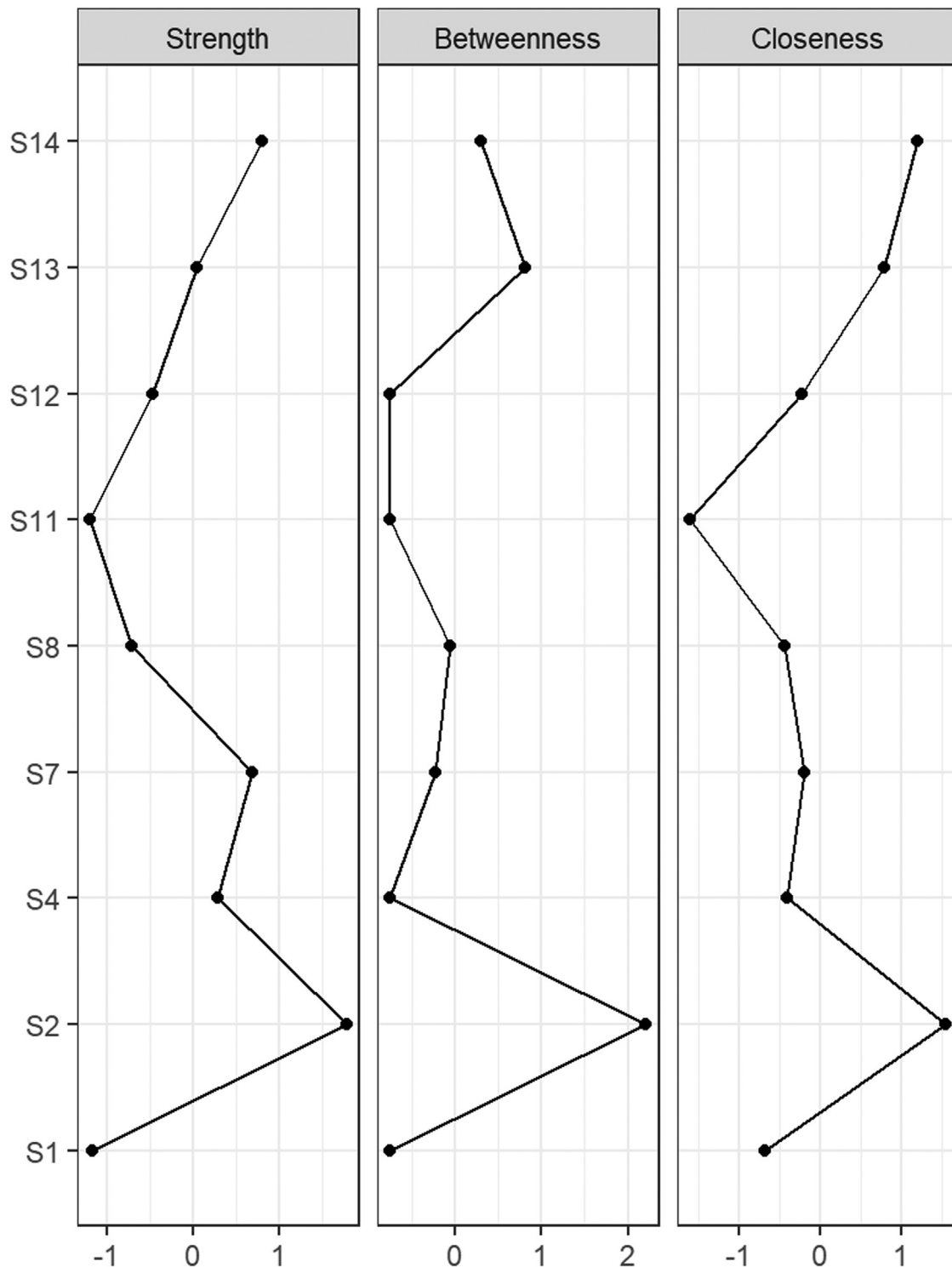


FIG 2. Centrality indicators of symptoms' network nodes. Centrality indices are shown as standardized z-scores.

all fatigue dimensions except mental fatigue.⁵⁷ In addition, patients' quality of life has been found to be inversely impacted by the severity of their psychological symptom cluster, according to studies, highlighting a negative correlation between the two factors,⁵⁸ and managing this group of psychological symptoms can positively impact the quality of life for cancer patients.³⁹

The core symptom cluster in this research, which includes both physiological and psychological symptoms, is composed of fatigue, lack of appetite, and emotional change. This study's network model reveals that these symptoms exert the most significant influence on

the patient's symptom network, thus identifying them as the core NIS group during lung cancer chemotherapy. Fatigue serve as core and sentinel symptom during lung cancer chemotherapy^{59,60}; the potential benefits of alleviating sentinel symptoms, which can lead to a reduction in the severity of the overall symptom cluster, diminished reliance on medical resources, and an enhancement in the quality of life among lung cancer patients.⁶¹ Lack of appetite serve as mediating symptom, by meticulously intervening in mediating symptoms, their function as mediators within the symptom network can be diminished, thereby mitigating the severity of other symptoms.³⁹

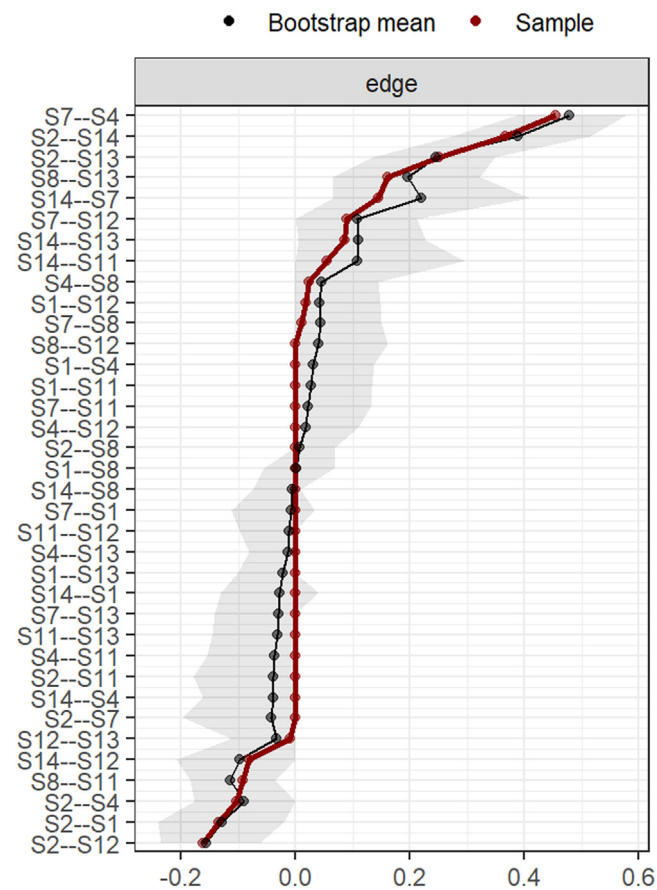


FIG 3. Bootstrap analysis results of the edge weight.

Emotional change serves as another mediating symptom, which affects a variety of physical symptoms, and quality of life. Future research could focus on symptom management interventions targeting this core symptom cluster, this ultimately facilitates the

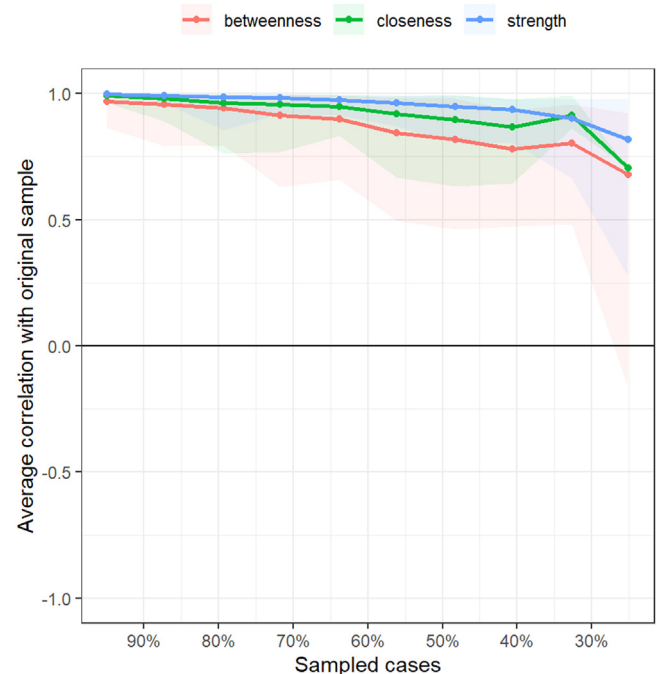


FIG 4. Related stability coefficient of strength, betweenness, and closeness indicators.

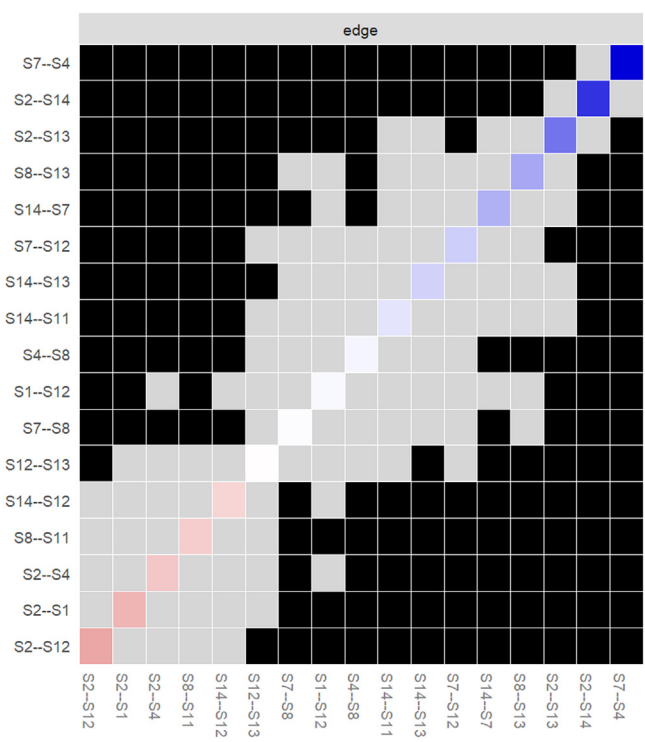


FIG 5. Bootstrap difference test of edge weight.

achievement of effective intervention in the NIS of lung cancer chemotherapy patients, enhancing nutritional state, treatment compliance and quality of life.

Strengths and Limitations

The primary strength of this study lies in its focus on the Nutrition Impact Symptoms (NIS) for patients undergoing

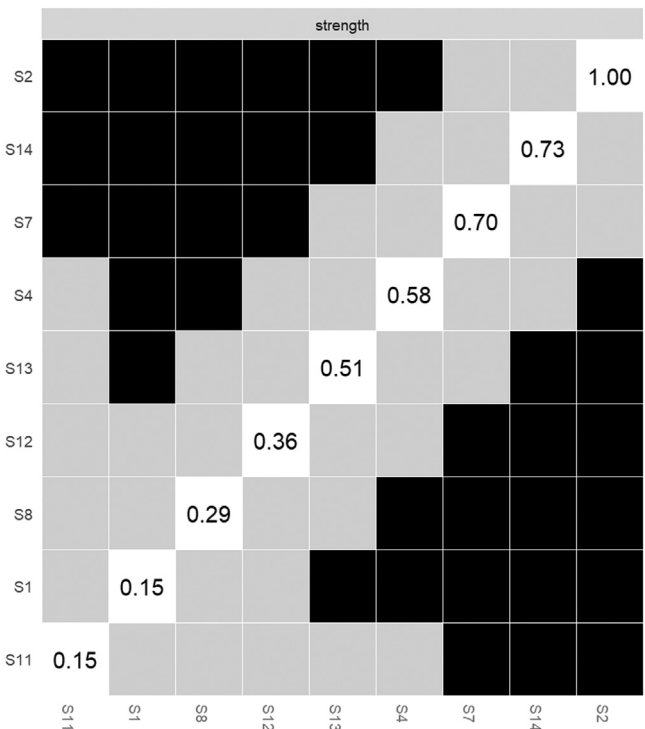


FIG 6. Bootstrap difference test of node strength.

chemotherapy for lung cancer, the data used are homogeneous, and utilizing Network Analysis, researchers aim to pinpoint core symptoms and symptom clusters, furnishing a theoretical foundation that underpins the precise symptom-targeted interventions of future. However, the cross-sectional design of this study restricts the generalizability of the findings, and it cannot elucidate the causal relationship between symptoms. Additionally, the number of participants in this study is relatively small, and the participants are confined to Liaoning Province in China, which further limits the generalizability of the research. Finally, the majority of the participants in this study are elderly patients, which may limit the applicability of the findings.

Conclusion

This study applied Network Analysis to construct a symptom network model for Nutrition Impact Symptoms (NIS) in 315 lung cancer patients undergoing chemotherapy. Fatigue was identified as the most prevalent and severe NIS, with lack of appetite emerging as the core symptom. The core symptom cluster consisted of fatigue, lack of appetite, and emotional changes. These findings provide critical intervention targets for clinical staff to enhance nutritional symptom management, enabling more precise symptom control and intervention for patients receiving chemotherapy for lung cancer, while also offering valuable insights for preventing cancer-related malnutrition. Given the limitations of this study, future research should emphasize longitudinal, dynamic studies of symptom networks to clarify evolving trends and the underlying mechanisms driving symptom interactions.

Implications for Nursing Practice

In nursing practice, we emphasize the importance of early symptom identification and targeted interventions to improve patient outcomes. Based on the results of this study, nurses can comprehensively consider the interactions among multidimensional symptoms to develop personalized interventions that more effectively manage NIS in lung cancer patients undergoing chemotherapy. This approach aims to reduce symptom burden and enhance patients' quality of life.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

CRedit authorship contribution statement

Dan-Dan Zheng: Writing – original draft, Visualization, Software, Conceptualization. **Ting Jin:** Investigation. **Dan Li:** Writing – review & editing. **Kang-Ning Bao:** Data curation. **Rui-Hua Jin:** Supervision, Methodology.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors would like to express our sincere gratitude to the Second Ward of Oncology Department at the First Affiliated Hospital of Jinzhou Medical University for their invaluable support throughout the research process. We are also deeply thankful to all the patient participants who have contributed to this study.

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