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Postprint: Scoping Review of Symptom Clusters in Gastric Cancer Patients During Chemotherapy

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Abstract

Background: Symptom clusters refer to two or more symptoms that occur simultaneously and influence each other. Currently, chemotherapy-related symptom clusters reported among gastric cancer patients vary considerably across studies, exhibiting heterogeneity that poses challenges for management and intervention.

Objective: To conduct a scoping review of studies on symptom clusters in gastric cancer patients during chemotherapy to identify the types, composition, and current research status of symptom clusters, thereby providing a reference for future research.

Methods: Using the PRISMA extension checklist for scoping reviews as the methodological framework, we systematically searched PubMed, Web of Science, Medline, CINAHL, CNKI, Wanfang Data Knowledge Service Platform, VIP, and Chinese Biomedical Literature Database for relevant studies on symptom clusters in gastric cancer patients during chemotherapy from database inception to May 24, 2023. Information from included studies was extracted and analyzed.

Results: Twelve articles were included. Research methods for symptom clusters comprised symptom assessment methods and extraction analysis of symptom clusters. Gastric cancer patients experienced 20 types of symptom clusters during chemotherapy. Prior to chemotherapy, illness symptom cluster, emotional symptom cluster, gastrointestinal symptom cluster, gastric cancer-specific symptom cluster, and nervous system-related symptom cluster could appear. After the first chemotherapy session, limb-related symptom cluster, body image alteration symptom cluster, and energy deficiency symptom cluster also emerged. After the third chemotherapy session, the types and composition of symptom clusters became most complex. After the sixth chemotherapy session, chemotherapy-related symptom cluster appeared.

Conclusion: Gastric cancer patients experience multiple symptom clusters during chemotherapy that evolve dynamically with treatment progression. Future

research should explore gastric cancer-specific symptom assessment tools and incorporate advanced analytical techniques such as symptom network analysis to accurately identify symptom clusters early and develop precision symptom management protocols.

Full Text

Symptom Clusters in Gastric Cancer Patients Receiving Chemotherapy: A Scoping Review

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Abstract

Background

Symptom clusters refer to two or more symptoms occurring simultaneously and influencing each other. Currently, symptom clusters identified in gastric cancer patients receiving chemotherapy vary across studies, exhibiting considerable heterogeneity that hinders effective management and intervention.

Objective

To conduct a scoping review of studies on symptom clusters in gastric cancer patients during chemotherapy to identify the types, composition, and current research status of symptom clusters, thereby providing a reference for future research.

Methods

Following the PRISMA extension for scoping reviews (PRISMA-ScR) as the methodological framework, we systematically searched PubMed, Web of Science, Medline, CINAHL, CNKI, Wanfang Data, VIP, and SinoMed databases for relevant studies from inception to May 24, 2023. Information from included studies was extracted and analyzed.

Results

Twelve articles were included. Research methods encompassed symptom assessment approaches and analytical techniques for extracting symptom clusters. Gastric cancer patients experienced 20 distinct symptom clusters during chemotherapy. Before chemotherapy, disease-related, emotional, gastrointestinal, gastric cancer-specific, and nervous system-related symptom clusters could

already be present. After the first chemotherapy cycle, limb-related, body image alteration, and energy deficiency symptom clusters emerged. Following the third chemotherapy cycle, the types and composition of symptom clusters became most complex. After the sixth chemotherapy cycle, chemotherapy-related symptom clusters appeared.

Conclusion

Gastric cancer patients experience multiple symptom clusters during chemotherapy that change dynamically with treatment progression. Future research should explore gastric cancer-specific symptom assessment tools and incorporate advanced analytical techniques such as symptom network analysis to accurately identify symptom clusters early and develop precise symptom management protocols.

Keywords: gastric cancer; chemotherapy; symptom clusters; nursing care; scoping review

1 Materials and Methods

This study employed the PRISMA extension for scoping reviews (PRISMA-ScR), adapted by Andrea et al. in 2016, as its methodological framework.

1.1 Research Questions

This scoping review aimed to investigate symptom cluster research in gastric cancer patients receiving chemotherapy, specifically addressing: (1) What assessment and analytical methods can be used to identify and determine symptom clusters? (2) What symptom clusters exist during chemotherapy, and what are the characteristics of their constituent symptoms? (3) Do symptom clusters change dynamically with treatment progression?

1.2 Inclusion and Exclusion Criteria

Inclusion criteria followed the PCC principle: (1) **Population:** gastric cancer patients aged ≥ 18 years; (2) **Concept:** studies involving symptom clusters in gastric cancer patients receiving chemotherapy; (3) **Context:** patients receiving chemotherapy in outpatient or inpatient settings. Exclusion criteria were: (1) non-Chinese or non-English literature; (2) duplicate publications or unavailable full texts; (3) reviews, guidelines, conference papers, and opinion pieces.

1.3 Literature Search Strategy

We searched PubMed, Web of Science, Medline, CINAHL, CNKI, Wanfang Data, VIP, and SinoMed databases for studies on symptom clusters in gastric cancer patients during chemotherapy from inception to May 24, 2023. English

search terms included “Stomach Neoplasms/Neoplasm, Stomach/Stomach Neoplasm/Neoplasms, Stomach/Gastric Neoplasms/Gastric Neoplasm/Neoplasm, Gastric/Neoplasms, Gastric/Cancer of Stomach/Stomach Cancers/Gastric Cancer/Cancer, Gastric/Cancers, Gastric/Gastric Cancers/Stomach Cancer/Cancer, Stomach/Cancers, Stomach/Cancer of the Stomach/Gastric Cancer, Familial Diffuse” and “Syndrome/Syndromes/Symptom Cluster/Cluster, Symptom/Clusters, Symptom/Symptom Clusters.” Chinese search terms were “胃肿瘤/胃恶性肿瘤/胃癌” and “症状群/症候群/症状集.” We combined subject headings with free-text terms and employed snowball searching when necessary. The PubMed search strategy is detailed in .

1.4 Literature Screening and Data Extraction

Retrieved literature was managed using EndNote X9. After removing duplicates, two researchers (the first and third authors) independently screened titles and abstracts, then reviewed full texts according to the inclusion criteria. Disagreements were resolved through discussion with a third researcher (the corresponding author). Data were independently extracted using a standardized form, including first author, study type, sample size, treatment stage, chemotherapy regimen, assessment and analysis methods, and symptom cluster types, then compiled into tables for further analysis.

2 Results

2.1 Literature Screening Results

The initial search yielded 13,080 articles. After importing into EndNote X9 and removing duplicates (n=5,719), 7,361 articles remained. Title and abstract screening excluded 7,315 articles, leaving 53 for full-text review. After excluding 41 articles (2 unavailable full texts, 31 with irrelevant content, 8 duplicates), 12 articles were ultimately included [9,11,15-24]. The screening process is illustrated in [Figure 1: see original paper].

2.2 Characteristics of Included Studies

Among the 12 included studies, 9 were in Chinese [16-24] and 3 in English [9,11,15]. Six were cross-sectional studies [11,15-16,19,21,23], five were longitudinal studies [17-18,20,22,24], and one was a qualitative study [9]. Detailed characteristics are presented in .

2.3 Assessment and Analysis Methods for Symptom Clusters

2.3.1 Symptom Assessment Methods Eleven quantitative studies used four different assessment tools: the MD Anderson Symptom Inventory (MDASI) and its Chinese version, the MD Anderson Symptom Inventory-Gastrointestinal Cancer module (MDASI-GI), the Memorial Symptom

Assessment Scale (MSAS), and self-developed symptom questionnaires. MDASI-GI was most frequently used (n=5) [11,18,21-22,24]. One qualitative study [9] employed semi-structured interviews to understand patients' authentic symptom experiences.

2.3.2 Symptom Cluster Extraction Methods Eleven studies used quantitative methods, primarily exploratory factor analysis, principal component analysis, and correspondence analysis. Exploratory factor analysis was most common (n=6) [11,15,18-20,22]. Only seven studies specified inclusion criteria for symptoms, such as incidence $\geq 20\%$ or Cronbach's $\alpha > 0.8$, with incidence $\geq 20\%$ being most frequently applied (n=6) [11,15-16,20,22,24]. The 12 included studies identified 1-6 symptom clusters each.

2.4 Types and Characteristics of Symptom Clusters

The 12 studies identified 20 distinct symptom clusters involving both physical and psychological dimensions. Primary symptoms included pain, fatigue, sleep disturbance, dry mouth, appetite loss, nausea, vomiting, dysphagia, early satiety, nervousness, anxiety, and irritability. Due to varying analytical methods and naming conventions across studies, the symptom clusters differed considerably. The most common were gastrointestinal symptom clusters (n=9) [11,16-20,22-24], followed by gastric cancer-specific symptom clusters (n=6) [11,18,20,22-24] and nervous system-related symptom clusters (n=6) [11,15,17,20,22,24]. In this review, nausea, vomiting, and dysphagia consistently co-occurred within gastrointestinal symptom clusters, indicating stable composition [11,16-20,22-24]. Most gastric cancer-specific clusters included dysphagia, early satiety, and appetite changes, though other symptoms varied significantly over time, suggesting instability.

2.5 Changes in Symptom Clusters Across Chemotherapy Stages

2.5.1 Pre-Chemotherapy Symptom Clusters Before chemotherapy, gastric cancer patients exhibited 3-5 symptom clusters, including disease-related, emotional, gastrointestinal, gastric cancer-specific, and nervous system-related clusters, which persisted throughout treatment [17,18,24]. Emotional symptom clusters were most severe; in Hu's study [18], the emotional cluster comprised five symptoms, each with incidence $> 70\%$ and higher severity than other concurrent symptoms. Hou et al. [17] found gastrointestinal clusters had higher incidence than other clusters at all stages, with the pre-chemotherapy cluster consisting of nausea, vomiting, dysphagia, and oral ulcers. Xia's study [24] showed the pre-chemotherapy gastrointestinal cluster comprised dry mouth, appetite loss, nausea, and vomiting, while Hu [18] identified it as dry mouth, constipation, diarrhea, appetite changes, and early satiety. All three studies confirmed gastrointestinal clusters were most severe before chemotherapy, primarily manifesting as nausea, vomiting, and dry mouth, and persisted through all treatment stages.

2.5.2 Symptom Clusters After the First Chemotherapy Cycle Following the first chemotherapy cycle, the number of symptom clusters increased to 4-5, with new clusters emerging alongside gastrointestinal clusters, including limb-related, body image alteration, and energy deficiency clusters [16,18,20,22,24]. Chen et al. [16] found patients developed limb-related clusters characterized by hand/foot numbness, tingling, and arm/leg swelling. Weight loss, dysphagia, appetite loss, vomiting, and pain contributed to energy deficiency clusters. Hair loss and feeling “not looking like oneself” led to body image alteration clusters. All 12 studies indicated disease-related and gastrointestinal clusters worsened after the first cycle and remained persistent.

2.5.3 Symptom Clusters After the Third Chemotherapy Cycle After the third chemotherapy cycle, the number of symptom clusters continued to increase, with most patients experiencing 4-6 clusters, including physical, psychological, and epithelium-related clusters [17-18,20,22]. Su’s study [20] revealed psychological clusters manifested as distress, sleep difficulty, anxiety, and depression, while epithelium-related clusters comprised bleeding, venous injection site pain, diarrhea, hair loss, and oral mucositis. Existing disease-related, emotional, gastrointestinal, and gastric cancer-specific clusters persisted and intensified. The third chemotherapy cycle represented the most complex stage for symptom cluster types and composition, with gastrointestinal clusters being most severe, characterized by concurrent nausea, vomiting, appetite loss, heartburn, acid reflux, taste changes, and oral/throat dryness, creating substantial symptom burden.

2.5.4 Symptom Clusters After the Sixth Chemotherapy Cycle By the sixth chemotherapy cycle, gastric cancer patients continued to experience 4-6 symptom clusters, with chemotherapy-related clusters newly emerging. Hu’s study [18] showed chemotherapy-related clusters appeared after the fifth cycle, comprising numbness and drowsiness, and persisted after the sixth cycle. Hou et al. [17] found physical symptom clusters worsened due to altered gastrointestinal microenvironment from chemotherapy drugs, causing abdominal and anal pain. Thus, physical clusters at this stage included not only hair loss and skin changes but also pain.

3 Discussion

3.1 Diverse Identification Methods Highlight Need for Gastric Cancer-Specific Assessment Tools

Symptom cluster assessment and extraction methods varied considerably across studies. The 12 included studies employed four different assessment tools, three of which were commonly used multi-symptom scales (MSAS, MDASI, and MDASI-GI). While widely applied and well-established, these scales lack

assessment of chemotherapy-specific symptoms for gastric cancer patients. Two studies [20,23] used self-developed questionnaires, which offer scientific rigor, operability, and practicality for more accurate assessment but require further validation of reliability, validity, and representativeness for application in this specific population. Since each tool has distinct emphases and requirements regarding assessment objects, timing, and frequency, simple application or combination may fail to capture the unique symptom experiences of this population during specific periods, potentially compromising study outcomes and hindering development of effective symptom management protocols [25]. Future research should explore gastric cancer-specific symptom cluster assessment tools, clarify optimal assessment timing, and develop scientifically robust, representative, and operable instruments to accurately identify symptom clusters and facilitate management and intervention.

3.2 Multiple Symptom Cluster Types Require Standardized Nomenclature and Classification

The 12 studies identified 20 distinct symptom clusters, yet naming conventions lacked standardization. Current approaches include: (1) naming by symptom category (e.g., gastrointestinal, emotional clusters); or (2) naming by high-loading symptoms (e.g., dysphagia-abdominal pain-vomiting cluster, pain-constipation-diarrhea cluster) [26]. For example, Hu [18] identified a disease-related cluster comprising pain, fatigue, and sleep disturbance, while Si et al. [19] defined a fatigue-related cluster including weakness, pain, shortness of breath, and drowsiness. Additionally, symptoms within the same cluster varied across studies; Hou et al. [17] included nausea, vomiting, dysphagia, and oral ulcers in gastrointestinal clusters, whereas Hu [18] included dry mouth, constipation, diarrhea, appetite changes, and early satiety. Future research should identify core symptoms within each cluster and elucidate their mechanisms to standardize nomenclature and classification, enabling scientific and effective symptom management.

3.3 Relationship Between Chemotherapy Regimens and Symptom Clusters Requires Further Investigation

Systemic chemotherapy is the most common postoperative treatment for gastric cancer, effectively prolonging survival while causing adverse effects like nausea, vomiting, and appetite loss. Different regimens produce distinct toxicities, resulting in varying symptom cluster manifestations and severity. Zhang et al. [27] found chemotherapy regimen was a significant factor affecting symptom cluster severity in 180 patients with digestive tract cancers undergoing chemotherapy. Feng et al. [28] similarly demonstrated that regimen type influenced symptom cluster severity, with different toxicities causing different neurotoxic symptom clusters. Wang [22] found regimens affected gastrointestinal, gastric cancer-specific, and nervous system-related clusters, particularly during mid-to-late chemotherapy stages, with combined drug use significantly increasing adverse

reactions. Patients receiving platinum-based and paclitaxel regimens experienced more severe nervous system-related clusters, consistent with these drugs' peripheral neuropathy effects [29]. Despite this, only 7 of 12 included studies detailed chemotherapy regimens, and only Wang [22] briefly discussed regimen effects on specific clusters. The relationship between different chemotherapy regimens and symptom clusters remains unclear, warranting future research using rigorous designs like randomized controlled trials to explore these relationships and identify influencing factors for developing practical symptom management protocols.

3.4 Dynamic Changes in Symptom Clusters Across Chemotherapy Stages Require Stage-Specific Management

Five longitudinal studies demonstrated that symptom clusters in gastric cancer patients are not static but change dynamically with chemotherapy progression, necessitating stage-specific management priorities: (1) **Pre-chemotherapy**: Emotional clusters are most severe and should be prioritized. Patients lacking disease and treatment knowledge often experience anxiety and depression. Nurses should provide personalized psychological care based on patient characteristics to alleviate negative emotions and facilitate treatment [30]. Chen et al. [31] showed poor psychological status increases symptom distress severity, highlighting the importance of pre-chemotherapy psychological intervention. (2) **Early chemotherapy (cycles 1-2)**: Gastrointestinal clusters are most common and severe. Nausea and vomiting, as core and persistent symptoms, cause significant fluid and electrolyte loss, potentially disrupting treatment [32]. Healthcare providers should optimize antiemetic therapy and incorporate non-pharmacological interventions such as relaxation training, music therapy, and traditional Chinese medicine [33-35]. (3) **Mid-to-late chemotherapy (cycles 3-6)**: Disease-related clusters become prominent. Prolonged treatment and cumulative toxicity intensify pain, fatigue, and weight loss. Comprehensive nursing care addressing cognition, behavior, and self-management should be implemented to enhance patient knowledge, train adverse reaction management, and improve self-care capacity and quality of life [36].

4 Conclusion

Gastric cancer patients experience multiple symptom clusters with varying constituent symptoms that change dynamically across chemotherapy stages, requiring clinicians to tailor symptom management to each stage's characteristics. Current heterogeneity in assessment tools and lack of standardized nomenclature and classification contribute to inconsistent symptom cluster identification. Future research should develop gastric cancer-specific, operable, representative, and comprehensive symptom cluster identification tools. Additionally, the relationship between different chemotherapy regimens and symptom clusters requires clarification through investigation of influencing factors, enabling

construction of more precise symptom management protocols and advancing symptom management toward scientific, precise, and innovative directions.

Author Contributions: HUANG Yulin conducted literature search and screening, extracted and analyzed data, and drafted the manuscript; WANG Haoyun contributed to topic selection, conceptualization, design, and manuscript revision; LI Yanmei participated in literature search and screening, data extraction, and figure/table preparation; XIAO Xueying was responsible for quality control and final approval of the manuscript.

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Note: Figure translations are in progress. See original paper for figures.

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