



# Advances in the Study of Symptom Clusters in Gastric Cancer Patients during the Perioperative Period

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DOI: 10.32629/aj.n.v4i1.1208

**Abstract:** This article provides a comprehensive review of the types of symptom clusters, assessment tools, and intervention methods for gastric cancer patients during the perioperative period. It suggests that future research should focus on the mechanisms and influencing factors of symptom clusters in gastric cancer patients during the perioperative period, in order to provide a basis for the development of scientifically sound and effective management measures.

**Keywords:** gastric cancer, perioperative period, symptom clusters

## 1. Introduction

According to the latest statistical data, in 2020, there were approximately 480,000 new cases (accounting for about 10.5%) and 370,000 deaths (accounting for about 12.4%) due to gastric cancer in China, posing a serious threat to human life and health[1]. At present, surgery remains the primary treatment option for gastric cancer. With the rapid development of Enhanced Recovery After Surgery (ERAS) concept, patients' average hospital stay has been shortened, bed turnover has accelerated, and studies have shown that gastric cancer patients often experience various concurrent symptoms during the perioperative period, such as fatigue, pain, nausea, vomiting, etc., due to the disease itself and related factors. These symptoms significantly impact patients' quality of life and functional status, and severe symptoms may even affect treatment progress and postoperative recovery. These concurrent symptoms often present as clusters, with synergy and intensification among them. When one symptom worsens, the severity of other symptoms also increases[2]. Compared to single symptoms, patients' burden is heavier. Therefore, managing symptoms as clusters can improve management efficiency, shorten patients' hospital stay, and reduce the medical burden. With the rapid development of ERAS, an increasing number of researchers have begun to focus on the characteristics of symptom clusters in gastric cancer patients during the perioperative period. Consequently, studies on symptom clusters in perioperative gastric cancer patients have gradually increased, ranging from cross-sectional studies to longitudinal studies, and from investigative studies to interventional studies. In recent years, some researchers have also begun to explore the identification of subgroups of symptoms within symptom clusters. However, due to differences in assessment tools and statistical methods used, the results obtained by different researchers vary greatly, making it difficult to provide clear guidance for clinical staff. To better understand the symptom management methods for gastric cancer patients during the perioperative period, this article reviews the types, assessment, and management methods of symptom clusters in perioperative gastric cancer patients, aiming to provide a basis for clinical nursing staff to better manage symptom clusters in gastric cancer patients during the perioperative period.

## 2. Overview

### 2.1 The concept of symptom clusters

The concept of symptom clusters was first proposed by Dodd[3] in 2001 and was defined as three or more interrelated symptoms that do not necessarily share a common etiology. In 2005, Kim et al. refined the concept of symptom clusters, defining them as consisting of two or more simultaneously occurring and interrelated symptoms, with the symptoms in the cluster being stable and relatively independent from other symptom clusters[4]. However, due to differences in measurement tools and statistical methods, there is still a lack of a unified and widely accepted concept of symptom clusters.

### 2.2 Number of symptoms in a symptom cluster

There is currently no consensus on the number of symptoms that make up a symptom cluster. Kim[4] and others defined symptom clusters as groups consisting of two or more interrelated symptoms. A systematic review of symptom clusters in patients with head and neck cancer showed that the number of symptom clusters in this population ranged from 2 to 5,

containing 2 to 11 symptoms[5]. However, due to differences in assessment and statistical methods, the composition of symptoms also varies. Even using the same assessment tool, the names and compositions of symptom clusters may not be the same.

## **2.3 Sentinel symptoms**

Sentinel symptoms are defined by researchers as symptoms that serve as indicators and markers within a symptom cluster and are the most common symptoms in the cluster[5, 6]. Research has shown that when sentinel symptoms are present, more than 50% of other symptoms may occur, but the absence of sentinel symptoms does not mean that other symptoms will not appear. Therefore, the relationship between sentinel symptoms and other symptoms within the symptom cluster is not yet clear. Moreover, research on sentinel symptoms is still in its infancy[6].

## **2.4 Core symptoms**

There is currently limited research on core symptoms. Some scholars believe that after exploratory factor analysis, symptoms with high correlation and stability over time and across populations within the symptom cluster can be considered core symptoms, such as nausea and vomiting, which are present in all reported gastrointestinal symptom clusters and remain stable over time[4, 7]. Investigating the core symptoms of symptom clusters can help identify symptom clusters, explore and develop symptom management interventions centered around core symptoms, and minimize patients' symptom burden[8].

## **2.5 Assessment Tools for Symptom Clusters**

Currently, the assessment tools for symptom clusters in cancer patients mainly consist of single symptom assessment scales, such as the Brief Pain Inventory (BPI) [9], and multiple symptom assessment scales. The latter can evaluate multiple symptoms simultaneously and are most commonly used in symptom cluster research.

### **2.5.1 M.D. Anderson Symptom Inventory Gastrointestinal Cancer Module (MDASI-GI)**

This specific multi-symptom assessment scale was developed by the University of Texas MD Anderson Cancer Center for patients with gastrointestinal cancer and is widely used in the field of symptom assessment for gastrointestinal cancer patients [10]. The Chinese version of MDASI-GI consists of two parts. The first part includes 13 general cancer symptoms and 5 gastric cancer-specific symptoms, which are used to assess the severity of the cancer. The second part evaluates the impact of the aforementioned 18 symptoms on 6 daily life activities. The scale uses a 0-10 numeric rating system, where 0 points indicate "no symptoms" and 10 points indicate "the most severe imaginable" in the first part; higher scores indicate a higher severity of symptoms. In the second part, 0 points indicate "no interference" and 10 points indicate "complete interference"; higher scores indicate a more significant interference of symptoms with daily life activities. The Cronbach's  $\alpha$  coefficients of the scale are 0.842 and 0.859, indicating good reliability and validity [11]. The scale items are concise and clear, making it convenient for clinical use. However, the scale contains relatively few items, which may lead to the omission of certain symptoms during the survey process.

### **2.5.2 Memorial Symptom Assessment Scale (MSAS) [12]**

This scale is a multidimensional disease symptom assessment scale that evaluates the patient's self-perceived symptoms in the past week. It includes three subscales: Physical Symptom Subscale Score (PHYS), Psychological Symptom Subscale Score (PSYCH), and Global Distress Index (GDI), with a total of 32 items. Among them, 24 items assess the frequency, severity, and distress of the patient's symptoms, while the remaining 8 items measure the severity and distress of the symptoms. The occurrence is reflected by "yes/no", and both frequency and severity are assessed using a 4-point Likert scale. A score of 1 represents "very little" and "mild," while a score of 4 represents "almost always" and "very severe." Distress is measured using a 5-point Likert scale, with scores ranging from 0 to 4, representing "none to very much." If a symptom is not present, the score is 0; the score for each symptom is the average of the severity and distress scores. The higher the score, the more severe and distressing the symptoms. MSAS can also calculate the Global Distress Index, which is the sum of the occurrence scores of sadness, anxiety, anger, and tension, and the distress scores of anorexia, fatigue, pain, drowsiness, constipation, and dry mouth. The Chinese version of the scale has a Cronbach's alpha coefficient of 0.79-0.87, indicating good consistency [13].

### **2.5.3 Edmonton Symptom Assessment Scale (ESAS)**

This scale was developed by Canadian researcher Bruera[14] in 1991 and is mainly used to assess symptoms in patients with advanced or palliative cancer treatment. The scale primarily evaluates nine common cancer patient symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath. In addition, there is an optional symptom, which is any symptom other than the listed nine. Among them, depression, anxiety, and well-being are psychological symptoms, while the other six are physical symptoms. The scale uses Likert scoring, with 0 to 10 representing "no symptoms to the most severe imaginable level," and higher scores indicating more severe symptoms. Some researchers

categorize symptoms as mild, moderate, or severe. Scores of 1 to 3 are considered mild, 4 to 6 are moderate, and 7 to 10 are severe [15]. Canadian researcher Hannon [15] added "constipation" and "sleep" items in 2015, creating the ESAS-CS scale, with an internal consistency reliability of greater than 0.8. Chinese researcher Dong [16] translated the scale into Chinese in 2014, with an internal consistency reliability of 0.7.

#### **2.5.4 Others**

In order to better assess the unique symptoms of different types of cancer, researchers have added specific items to the multi-symptom assessment scales, creating specific scales. For example, the previously mentioned MDASI-GI is a scale where researchers added a gastrointestinal tumor-specific module to the Anderson Symptom Assessment Scale. These types of scales are mainly used to evaluate cancer symptoms of a specific disease.

### **3. Types of symptom clusters in perioperative gastric cancer patients**

Due to differences in sample size, research subject characteristics, research time points, symptom assessment tools, and statistical methods, different researchers have identified different numbers and classifications of symptom clusters in perioperative gastric cancer patients. The naming of symptom clusters also varies. Here, we summarize several common types:

#### **3.1 Gastrointestinal Symptom Cluster**

The gastrointestinal symptom cluster is common in perioperative gastric cancer patients. The pathogenic mechanism may be related to gastrointestinal mucosal damage, abnormal release of inflammatory mediators, and neurotransmitters [17]. Ma Tong [18] and others investigated the dynamic changes of symptom clusters in 130 patients scheduled for gastric cancer surgery at three time points (T1 — one day before surgery; T2 — three days after surgery; T3 — 7 days after surgery). They found that the gastrointestinal symptom cluster mainly included abdominal distension, nausea, loss of appetite, dry mouth, changes in taste, and difficulty swallowing. At T1, the gastrointestinal symptom cluster included abdominal distension, nausea, and loss of appetite, while at T2 and T3, it included dry mouth and changes in taste. Wang Lina [19] and others divided the investigation time points into early postoperative period (T1, 2-3 days after surgery), eating period (T2, 6-7 days after surgery), and home recovery period (T3, 21-28 days after surgery). They found that postoperative gastrointestinal symptom clusters mainly included nausea, loss of appetite, vomiting, diarrhea, changes in taste, and abdominal distension. Other researchers divided the investigation time points into the first day after admission (T1), the second to fourth days after surgery (T2), and one month after surgery (T3), revealing that the gastrointestinal symptom cluster included nausea, vomiting, changes in taste, constipation, loss of appetite, and abdominal distension, among five other symptoms [20]. The gastrointestinal symptom cluster changes over time, mainly due to patients' early postoperative fasting or minimal liquid diet, which results in less gastrointestinal stimulation. As the patient's diet becomes more complex later, they need to constantly change and adapt to their eating habits, increasing the chance of gastrointestinal symptoms during this period, especially diarrhea, constipation, nausea, vomiting, and other core symptoms. Although the gastrointestinal symptom cluster is a recognized cluster, there is currently no universally accepted method for extracting and rotating symptom cluster factors, and different researchers have explored different compositions of symptom clusters [21].

#### **3.2 Energy Deficiency Symptom Cluster**

Energy deficiency symptom cluster is a common symptom cluster in cancer patients. Several studies have confirmed its occurrence is related to the mediation of pro-inflammatory cytokines [22, 23]. Some researchers have also pointed out that this symptom cluster may be related to preoperative intestinal preparation, the consumption during surgery, and postoperative fasting and water restriction [24]. Due to different research methods or tools used, different researchers have different symptom classifications within this symptom cluster. Using MDASI-GI as an assessment tool, Wang Lina [19] and others categorized drowsiness, fatigue, shortness of breath, forgetfulness, dry mouth, constipation, and difficulty swallowing as part of this symptom cluster; Ma Tong [18] and others' research included drowsiness, fatigue, constipation, and decreased appetite in the energy deficiency symptom cluster. In Liu Hongxia [20] and others' research, the energy deficiency symptom cluster included fatigue, drowsiness, and dry mouth. In longitudinal studies of symptom clusters in postoperative chemotherapy patients with gastric cancer, similar results were found, and drowsiness and fatigue were considered core symptoms [25, 26]. After surgery, patients have less food and water intake, reduced saliva secretion in the mouth, and some postoperative medications have side effects such as dry mouth. Various factors cause dry lips in patients, and symptoms such as fatigue and drowsiness reduce their activity levels and food and water intake, further aggravating dry mouth symptoms. The symptoms interact with each other, causing adverse effects on the patient's postoperative recovery.

### 3.3 Psychological Symptom Cluster

Also known as emotional symptom cluster, psychological symptom cluster is a common symptom cluster among cancer patients. It may be related to patients' fear of cancer and recurrence, concerns about surgery and prognosis, and physical discomfort caused by treatment [27]. Research has shown that psychological symptom clusters can promote the production of other physical symptoms in cancer patients by affecting the release of inflammatory cytokines [28]. Various studies have shown that psychological symptom clusters stably exist in different stages after surgery for gastric cancer patients. Different studies have reported different single symptoms or group compositions for the psychological symptom cluster. For example, some studies include sadness, distress, and sleep disturbances [18]; others include pain, sleep disturbances, distress, and sadness [19]. Some studies also show a positive correlation between anxiety, depression, and gastrointestinal diseases [29].

### 3.4 Surgery-related Symptom Cluster

Liu Hongxia [20] investigated the symptoms of 210 patients undergoing radical gastrectomy at three time points: the first day after admission (T1), 2-4 days after surgery (T2), and one month after surgery (T3). The results showed that the surgery-related symptom cluster only appeared at T2, including dysphagia, shortness of breath, and abdominal distention. Zhu Yu [21] and others used the Memory Symptom Assessment Scale to investigate the symptom clusters of gastrointestinal tumor patients within one week after surgery, concluding that the surgery-related symptom cluster included difficulty in urination, itching, and oral ulcers, which may be related to surgery, anesthetic drugs, and stress. Although different researchers have different results, the surgery-related symptom clusters are all related to surgery-related factors such as preoperative eating, intraoperative tracheal intubation stimulation, anesthetic drugs, and postoperative pain.

### 3.5 Others

Different researchers use different symptom assessment scales, and the methods of naming and classifying symptom clusters are also different. Other symptom clusters include gastrointestinal symptom cluster, fatigue-related symptom cluster, emotion-appetite-related symptom cluster, disease behavior symptom cluster, affective/cognitive symptom cluster, and confusion symptom cluster [20, 21, 30].

## 4. Intervention Methods for Perioperative Symptom Clusters in Gastric Cancer

Currently, there are few intervention methods for perioperative symptom clusters in gastric cancer patients, and they are still limited to small-scale studies by a few researchers. Zou Suduan [31] used auricular acupressure for patients after gastric cancer radical surgery, and the results showed that the severity of abdominal distention, nausea, vomiting, and hiccups in the intervention group was lower than that in the control group. Some researchers [32] explored the improvement of postoperative symptom clusters in gastric cancer patients with the combination of hand acupoint massage and sham feeding (chewing gum). The results showed that this method can effectively alleviate the severity of illness-emotional symptom clusters, surgery-related symptom clusters, and gastrointestinal symptom clusters in patients after gastric cancer surgery, and the combined method is better than sham feeding alone. The effectiveness of other interventions, such as foot reflexology and music therapy, has also been verified [33]. However, the mechanism of symptom cluster formation in gastric cancer patients during the perioperative period is still unclear, making it difficult to form systematic intervention measures. Current research focuses on the investigation of symptom clusters, with fewer related interventional studies and no systematic approach. Therefore, it is suggested that future researchers conduct mechanism studies on perioperative symptom clusters in gastric cancer patients, develop symptom screening tools suitable for Chinese patients, and provide a reference basis for effective management measures.

## 5. Conclusion

At present, research on symptom clusters in gastric cancer patients is mainly focused on chemotherapy patients or survival period patients, with fewer studies on perioperative patients. Most studies are either cross-sectional at a certain time point after surgery or longitudinal surveys at multiple time points. There are fewer studies on the mechanism and influencing factors of symptom cluster occurrence, and the symptom screening and assessment tools used by different researchers also vary. Therefore, it is difficult to form a systematic symptom cluster management method. In the future, it is recommended that researchers conduct more related studies to provide a basis for the development of scientific and effective management measures, reduce the incidence and severity of perioperative symptoms in gastric cancer patients, improve patient outcomes, and enhance their quality of life.

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