

Patterns of Symptoms Following Surgery for Esophageal Cancer

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Symptom management in oncology nursing includes the multiple symptoms that patients face following diagnosis and treatment. Research on these groups of symptoms is a priority for oncology nurses, and the evaluation of symptom patterns and clusters in oncology is emerging as a focus of study (Barsevick, 2007; Doorenbos et al., 2008). Surgical outcomes traditionally have been evaluated by objective measures such as morbidity, mortality, and complication rates, but subjective measures, such as symptoms and quality of life, are important clinical outcomes of interest and can serve as additional measures of patient outcome. Patients diagnosed with esophageal cancer experience prolonged and severe symptoms because of their disease and the effects of multimodality treatment (Donohoe, McGillycuddy, & Reynolds, 2011). Nursing research on symptoms in patients with esophageal cancer is limited and a need exists to identify and understand the pattern of symptoms patients experience before, during, and after surgical treatment.

Background and Significance

An estimated 17,460 new cases of esophageal cancer were diagnosed in the United States in 2012, with an estimated 15,070 deaths (Siegel, Naishadham, & Jemal, 2012). Esophageal cancer is the eighth most common cancer worldwide, ranking sixth among all cancers in mortality (Ferlay et al., 2010). A combination of chemotherapy, radiation, and surgery has been recommended for treatment (Urschel, Vasan, & Blewett, 2002); this multimodality treatment can offer an improved chance for a cure but is associated with persistent symptoms and a significant negative impact on lifestyle and quality of life (Sweed, Schiech, Barsevick, Babb, & Goldberg, 2002).

Symptom research has focused on single symptoms such as pain or fatigue (Dodd, Miaskowski, & Lee, 2004; Miaskowski, Dodd, & Lee, 2004), but more recent ef-

Purpose/Objective: To explore patterns of symptoms before and after surgery for cancer of the esophagus.

Design: Longitudinal, descriptive study.

Setting: An urban comprehensive cancer center in the northeastern United States.

Sample: 218 patients with cancer of the esophagus undergoing esophagectomy.

Methods: Symptoms were assessed by self-report before surgery, at the first postoperative visit, and at 6 and 12 months postsurgery.

Main Research Variables: Symptoms and demographic and clinical variables, including stage, treatment, gender, and comorbidities.

Findings: Patients with esophageal cancer reported numerous symptoms before and after esophagectomy. Several patterns of symptoms were identified. General cancer symptoms (e.g., pain, cough, shortness of breath, weight loss) were reported as worse after surgery but recovered to baseline by one year. A second pattern of esophageal-specific symptoms (feeling full too quickly, feeling bloated, nausea, and diarrhea) worsened after surgery and did not recover to baseline by one year. Reflux was the only symptom that did not worsen after surgery but did worsen significantly during the first year of recovery.

Conclusions: Patients with esophageal cancer experienced multiple prolonged symptoms following surgical treatment for their disease. General cancer symptoms resolved by one year post-treatment, whereas esophageal-specific symptoms worsened after surgery and did not recover to baseline.

Implications for Nursing: Identification of symptom patterns preoperatively and during recovery can assist nurses in developing intervention protocols to minimize long-term complications for patients with esophageal cancer.

Knowledge Translation: Patients with esophageal cancer are at risk for multiple prolonged symptoms following surgery. Symptom assessment should occur often after surgery and include a broad range of symptoms.

forts have focused on groups of symptoms that occur together and are related to each other (Kim, McGuire, Tulman, & Barsevick, 2005). These groups of symptoms, termed *symptom clusters*, have been defined as groups

of two or more concurrent symptoms that are related to one another and independent of other symptom clusters (Kim et al., 2005). Investigating the occurrence of symptoms and their relation is an important goal for nursing (Barsevick, 2007).

The occurrence of multiple symptoms impacts recovery following treatment for esophageal cancer (Djarv, Lagergren, Blazeby, & Lagergren, 2008). Because of the poor prognosis and the effects of multimodality treatment, clinicians need to assess a variety of symptoms that may impact recovery as well as the pattern of occurrence of these symptoms. Djarv, Blazeby, and Lagergren (2009) investigated the predictors of postoperative quality of life following esophagectomy in a population-based study. They assessed 355 patients six months after surgery and found that 26%–47% of patients reported experiencing general cancer symptoms such as fatigue, pain, dyspnea, appetite loss, and diarrhea. When they assessed esophageal-specific symptoms, 22%–27% of patients reported problems with dysphagia, reflux, and cough, and 59% reported they had difficulty eating at six months after surgery.

A study assessing symptoms before and after surgery found that physical symptoms increased after surgery and that activity level, psychological distress, and swallowing problems decreased (Van Knippenberg et al., 1992). In another study, Sweed et al. (2002) evaluated symptoms and quality of life in 19 patients before esophageal surgery and at three and six months after surgery, with most patients also receiving neoadjuvant therapy (chemotherapy and/or radiation after surgical resection). A significant inverse relationship between symptom intensity and global quality of life was found. However, little average change in overall quality of life or functional status was found in the six-month study period. Symptoms such as hoarseness, acid reflux, stomach pain, and diarrhea increased following esophagectomy, with a corresponding decrease in quality of life (Sweed et al., 2002). Djarv et al. (2008) assessed the change in symptoms from six months to three years in such patients. They found that mean scores of dyspnea, insomnia, and constipation were worse at three years for a group of 87 patients who had undergone an esophagectomy than for an age- and sex-adjusted reference population. Esophageal-specific symptoms such as dysphagia, reflux, trouble swallowing, and dry mouth also worsened from six months to three years.

Patients with esophageal cancer in a study of long-term health-related quality of life following surgery also reported significant prolonged symptoms (Donohoe et al., 2011). When long-term survivors (\bar{X} time after surgery = 70.3 months) were compared to diagnosed but as yet untreated patients and unselected patients with cancer, significant increases in diarrhea,

swallowing dysfunction, reflux, and coughing were observed. Other symptoms such as nausea and vomiting, appetite loss, pain, and constipation decreased when compared with the control population. Viklund, Wengstrom, Rouvelas, Lindblad, and Lagergren (2006) assessed symptoms in a population-based study of 282 patients treated surgically. They identified dominant general and esophageal-specific symptoms six months following surgery. The most common general symptoms were fatigue, appetite loss, diarrhea, and dyspnea, and each was significantly worse compared with a reference population. Difficulty eating, cough, reflux, and esophageal pain were the most significant esophageal-specific symptoms identified six months following surgery.

The studies demonstrate that some symptoms can be significant and prolonged following surgery for cancer of the esophagus, whereas other symptoms improve. The relationship among symptoms for patients being treated for cancer of the esophagus continues to emerge, and a picture of the symptoms and symptom patterns experienced by these patients as they recover is unclear. Evaluating symptoms and understanding the pattern of recovery has become a growing area of interest and investigation. The purpose of the current study was to identify and describe the symptom pattern experienced by patients prior to and following surgical treatment for cancer of the esophagus. Past research has not always included a baseline assessment prior to surgery or long-term follow-up to assess the trajectory of symptoms following surgery. The current study builds on this past work to describe symptoms before surgery and throughout the first year following surgery.

Methods

Design and Sample

This longitudinal, descriptive study examined symptom patterns and quality of life before and after curative esophagectomy. All patients with esophageal cancer who were being considered for curative surgery were eligible to participate. Specific eligibility criteria for participation in this study included being diagnosed with esophageal cancer and expected to undergo a curative esophagectomy, aged at least 18 years, and able to speak and read English. Patients who received neoadjuvant chemoradiation, as well as those going directly to esophagectomy, were included. Patients completed a symptom assessment scale prior to curative esophagectomy and at three time points throughout the first year following this treatment. A total of 218 participants provided data used for the analysis. The institutional review board of Memorial Sloan-Kettering Cancer Center approved the study, which included written informed consent.

Variables and Instruments

The **Memorial Symptom Assessment Scale–Short Form (MSAS-SF)** (Chang, Hwang, Feuerman, & Kasimis, 2000), a well-validated instrument that uses a checklist format to assess symptoms, was used. The MSAS-SF is a self-report tool in which a patient rates symptom distress associated with 27 physical symptoms experienced in the previous seven days. Each symptom is scored as present (1) or absent (0). In addition, participants are asked for each symptom, “How much did it distress or bother you?” Responses to this question were “not at all,” “a little bit,” “somewhat,” “quite a bit,” and “very much.” Cronbach alpha coefficients for the MSAS-SF ranged from 0.76–0.87 (Chang et al., 2000). Usual time for completion is 3–5 minutes. The MSAS-SF included a section for additional items where a patient could write in symptoms. The section was used for two symptoms relevant to esophageal cancer surgery (reflux and feeling full too quickly). As the scale is a checklist and is not analyzed by subscales, the addition of these items did not affect reliability or validity of the instrument.

Procedures

Participants completed the symptom assessment at several time points during their treatment and recovery: once prior to surgery (within two weeks of surgery), at their first postoperative visit (about 2–4 weeks after surgery), and at 6 and 12 months following surgery, with the first time point serving as a baseline. Patients who received neoadjuvant therapy completed the baseline assessment after completion of the therapy but prior to surgical resection. The time points were specifically chosen to assess changes in symptoms and quality of life from baseline through the first year of recovery. The majority of assessments were completed in person at the time of a clinical visit. In a few cases, assessments were mailed to participants who completed them and returned by mail or in person to the investigators.

Statistical Procedures

Descriptive statistics were used to initially analyze patient response to the MSAS-SF. Frequency of symptoms was assessed using McNemar χ^2 tests to compare proportions of respondents who reported being bothered by specific symptoms (“yes” or “no” responses) across specific time points. Responses were compared in the following time point pairs.

- Test point 1: Baseline to immediate postoperative for assessment of changes following surgery
- Test point 2: Immediately postoperative to 12 months postoperative for assessment of recovery
- Test point 3: Baseline to 12 months postoperative for confirmation of recovery or symptom worsening.

The six-month time point was not included in the McNemar test analysis reported here because no significant differences were noted in the proportion of respondents between that and the 12-month time point. Data were analyzed using SPSS®, version 19.

Results

Data from 218 participants were included in this analysis. In the four-year study period, 359 patients underwent a curative esophagectomy, and 308 patients (86%) were recruited for and consented to the study. Of these, 42 did not meet surgical eligibility criteria (for example, esophagectomy not completed because of metastatic disease that was found at the time of resection), 44 did not complete the assessment forms, and four withdrew from the study, leaving 218 participants. Demographics of these 218 participants are provided in Table 1. The mean age of participants was 62.5 years, with most being male. The majority of participants (83%) had adenocarcinoma and underwent an Ivor Lewis esophagectomy (92%). Patients who received preoperative chemotherapy and radiation completed this treatment, on average, 4–6 weeks prior to surgery.

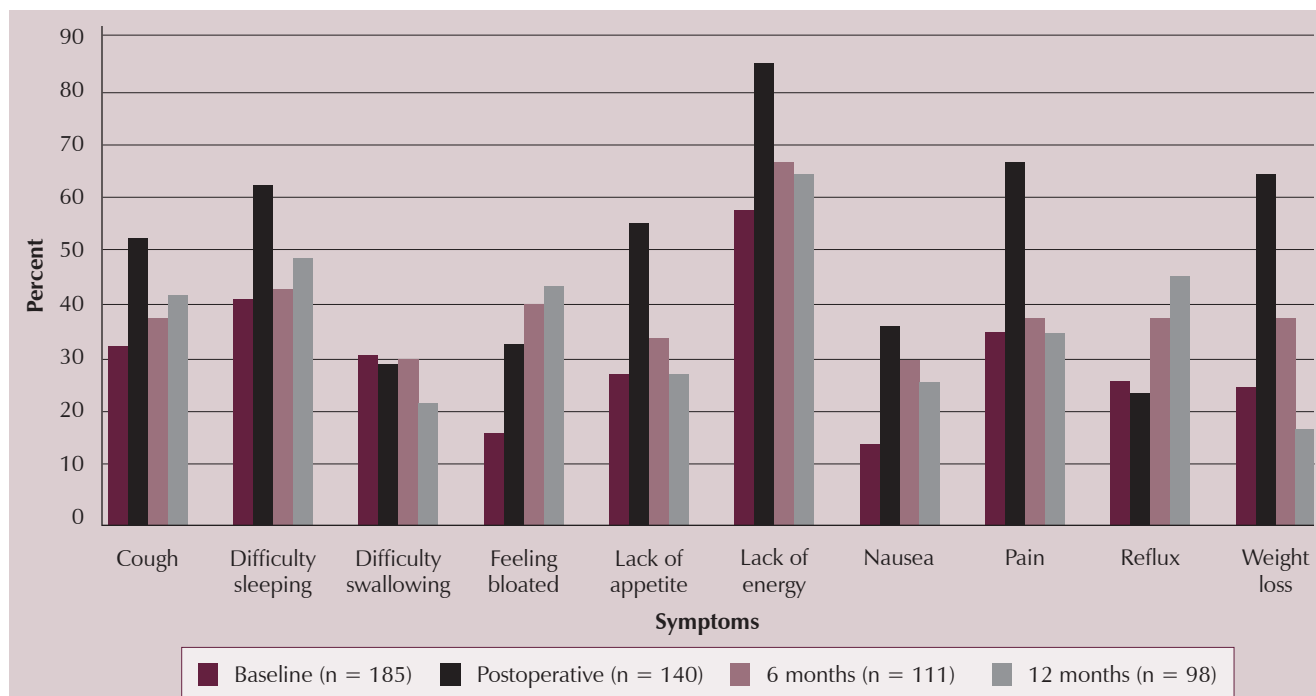
Symptom prevalence was assessed at the four time points (three are reported here: baseline, postsurgery, and at 12 months), and selected symptoms are noted in Figure 1. The most frequently reported symptoms

Table 1. Patient and Tumor Characteristics (N = 218)

Characteristic	n	%
Gender		
Male	184	84
Female	34	16
Age (years)^a		
Younger than 60	75	34
60–74	116	53
75 or older	27	12
Comorbidity		
No	145	67
Yes, at least one	73	34
Stage		
0–I	95	43
II	81	37
III	41	19
IV	1	< 1
Surgery type		
Ivor Lewis	200	92
Other	18	8
Treatment		
Surgery only	71	32
Neoadjuvant treatment and surgery	147	67
Complications		
No	179	82
Yes, at least one	39	18

^a Mean age is 62.5 years; range is 22–82.

Note. Because of rounding, not all percentages total 100.



Note. Participants could select more than one symptom.

Figure 1. Selected Symptom Prevalence (N = 218)

at baseline were lack of energy, difficulty sleeping, difficulty concentrating, pain, and cough, whereas the most bothersome symptoms at baseline were problems with sexual activity or interest, swelling, weight change, not looking like self, and change in the taste of food. Postsurgery, the most frequent symptoms were lack of energy, pain, feeling full too quickly, weight change, and sleep disturbances; and the most bothersome symptoms were lack of energy, sleep disturbance, problems with sexual activity or interest, change in the taste of food, and weight change. At one year, lack of energy, feeling full too quickly, drowsiness, difficulty sleeping, and reflux were the most frequently noted symptoms, whereas problems with sexual activity or interest, lack of energy, cough, feeling full too quickly, and reflux were the most bothersome symptoms.

Variables were selected for additional frequency analysis if at least 25% of respondents reported the symptom as bothersome in at least one of the four time points. Variables excluded from analysis include changes in skin, numbness or tingling in the hands or feet, problems with urination, vomiting, sweats, mouth sores, itching, dizziness, and swelling. For most symptoms, the proportion of participants who reported each symptom was larger postoperatively and then lessened at months 6 and 12 postoperatively to levels similar to preoperative.

In McNemar χ^2 testing, symptoms followed one of four patterns: (a) symptom worsened after surgery from baseline, then recovered to baseline at one year;

(b) symptom worsened after surgery from baseline, and did not recover by one year; (c) symptom did not change from baseline to postoperative, but worsened in one year; or (d) no change in symptom severity.

Symptom patterns were developed using the following guidelines.

- Pattern 1: A statistically significant increase ($p < 0.05$) in the proportion of patients reporting the symptom from test point 1 to test point 2, followed by an insignificant McNemar χ^2 test from test point 1 to test point 3, indicating a failure to reject the null hypothesis of no change in proportion
- Pattern 2: A statistically significant increase in the proportion of patients reporting the symptom from test point 1 to test point 2, and a statistically significant increase in the proportion of patients reporting the symptom from test point 1 to test point 3
- Pattern 3: An insignificant McNemar χ^2 test from test point 1 to test point 2, with a statistically significant increase in the proportion of patients reporting the symptom from test point 2 to test point 3
- Pattern 4: Insignificant McNemar χ^2 tests between proportions at all test points.

Symptoms in the first pattern included pain, lack of energy, cough, shortness of breath, difficulty sleeping, dry mouth, change in the taste of food, weight loss, and not looking like self. Symptoms in the second pattern were feeling full too quickly, bloated, drowsiness, nausea, and diarrhea. Reflux was the only symptom

that did not worsen from baseline to postoperative but did worsen from postoperative to one year. Symptoms that did not significantly change in the study period were difficulty swallowing, difficulty concentrating, and problems with sexual activity or interest. Table 2 reports p values for the McNemar test for each scenario.

Discussion

The current study identified four patterns of symptoms in a group of patients treated surgically for cancer of the esophagus. The authors found that patients have persistent symptoms during the course of their recovery. This finding was similar to studies that found patients with esophageal cancer, who were at least one year post-treatment, reported more symptoms than the general population and had higher scores on reports of single symptoms (Donohoe et al., 2011). In that study, the most significant symptom was difficulty swallowing, which was reported in 30% of patients and was highly correlated with impaired global quality of life (Spearman's rho = 0.508, p < 0.001). In the authors' sample, difficulty swallowing remained prevalent with 29% of patients reporting it prior to surgery, 28% at six months, and 21% reporting it one year after surgery. Other studies also have found prevalent general and esophageal-specific symptoms reported after surgery. In Sweden, a nationwide observation study found that, at six months postsurgery, 26%–47% of patients reported the general cancer symptoms of fatigue, pain, dyspnea, appetite loss, and diarrhea (Djarv et al., 2009). Patients also reported the esophageal-specific symptoms of dysphagia, reflux, and cough (22%–27%), and eating difficulties (59%) (Djarv et al., 2009).

The first pattern included pain, difficulty sleeping, cough, dyspnea, lack of energy, change in appetite, and weight loss, and was most likely the result of surgery or multimodality treatment. These symptoms were worse immediately after surgery but recovered to baseline by one year.

A second pattern included drowsiness, feeling bloated, nausea, diarrhea, and feeling full. Each of these symptoms worsened after surgery and did not recover to baseline at one year. The second pattern included symptoms more specific to esophageal cancer and esophageal surgery. The surgical procedure for an esophagectomy along with the anatomic changes that result from it may have led to these symptoms. The most common location for an esophageal tumor is the lower third of the esophagus, and 60% of patients with a tumor in this location undergo a transthoracic

esophagectomy (Altorki, 2008). This procedure involves removal of part of the esophagus and possibly part of the stomach, depending on the location of the tumor. The surgical margins are then reconnected to form a much smaller stomach located higher in the patients' chest. Because of the smaller stomach volume following surgery, patients must eat smaller meals more often during the day. Following meals, patients may experience cramping, diarrhea, lightheadedness, and palpitations, referred to as dumping syndrome (Orringer, 2008). This occurs in about 20%–50% of patients undergoing an esophagectomy, and is overcome by dietary modifications such as eating small meals, avoidance of fluids and high-carbohydrate foods, avoidance of milk products, and the occasional use of antidiarrheal medications (Battafarano & Patterson, 2008; Engstad & Schipper, 2009). The patients in the current study did report worsening diarrhea and bloating after surgery that improved in the first year but did not return to baseline. Dumping syndrome also impacts patients' day-to-day lives. In the authors' clinical experience, patients who have dumping syndrome often are afraid to eat away from home for fear of symptoms occurring while they are out. How long the syndrome can affect patients is unclear, and future research should focus on its duration and impact.

In addition to the dietary changes as a result of the surgery, patients also often have to adjust their sleep

Table 2. McNemar Test P Value for Symptom Patterns

Symptom Pattern	Baseline Postoperative	One Year Postoperative	Baseline One Year
Worsens postoperative but recovers to baseline at one year			
Appetite change	< 0.001	< 0.001	1
Change in food taste	< 0.001	0.002	0.523
Cough	< 0.001	0.327	0.281
Difficulty sleeping	< 0.001	0.006	0.307
Dry mouth	< 0.001	0.009	0.064
Lack of energy	< 0.001	0.004	0.064
Not looking like self	0.007	0.002	1
Pain	< 0.001	< 0.001	0.743
Shortness of breath	< 0.001	0.007	0.21
Weight loss	< 0.001	< 0.001	0.265
Worsens postoperative and does not recover by one year			
Bloated	< 0.001	0.238	0.002
Diarrhea	< 0.001	1	< 0.001
Drowsiness	< 0.001	1	0.003
Feeling full quickly	< 0.001	0.523	< 0.001
Nausea	< 0.001	0.115	0.001
No change postoperative but worsens in one year			
Reflux	0.868	0.013	0.028
No change in one year			
Difficulty concentrating	0.441	0.169	0.728
Difficulty swallowing	0.302	0.481	0.86
Sexual issues	0.392	0.727	0.064

environment as a result of anatomic changes from surgery. During a transthoracic esophagectomy for a lower esophageal tumor, the lower esophageal sphincter is removed with the gastroesophageal junction and upper third of the stomach (Altorki, 2008). The lower esophageal sphincter normally prevents food and stomach acid from backing up into the esophagus or trachea (Liebermann-Meffert, 2008). Without this protective mechanism, patients are at risk for reflux, delayed gastric emptying, feeling full or bloated, and aspiration. If sleeping flat, stomach contents or gastric acid could rise into the esophagus and trachea and lead to aspiration. Reflux is common after esophageal surgery, and often patients who experience reflux must sleep with the head of the bed elevated (Fell & Ximenes-Netto, 2008). The current study identified that reflux was the only symptom that continued to worsen over the first year following an esophagectomy. Nurses should assess patients for sleep problems. More research is needed on the appropriate management of reflux.

Limitations

The current study included patients seen at an urban comprehensive cancer center that treats a large number of patients with cancer of the esophagus. As a result, the findings may not be applicable to patients treated at other locations and facilities. Future research should include patients from diverse treatment settings. Findings from this study are limited by missing data, which was excluded from analysis during the course of the study. That is to say, although the study did include a large number of patients, patients who had progressive disease were not included in follow-up assessments and not all patients completed every assessment. How this missing data could have impacted the findings is unknown. A minor limitation is the addition of items to the original version of the MSAS. The two items (reflux and feeling full too quickly) are symptoms that are specific to this patient population. The MSAS was used as a symptom checklist, and the authors did not analyze subscales; therefore, the addition of two items would not have significant impact on the reliability and validity of the scale. The original instrument includes space for participants to write in additional symptoms.

Implications for Nursing

This study adds to a growing knowledge base with which to view the long-term effects of surgery for esophageal cancer. Treatment can lead to prolonged symptoms that impact recovery, and symptom assessment should be part of routine care for survivors of esophageal cancer. Symptom assessment should cover a range of symptoms, both general and cancer-specific. In addition, symptom management should begin early

in the treatment process. As patients are being prepared for surgery, preoperative education should include the potential symptoms and side effects that can be expected during and after surgery. The addition of this information to the standard preoperative education will better prepare patients for what they can expect postoperatively.

Several patterns of symptoms were identified in this study. One pattern of symptoms worsened following surgery and then recovered to baseline by one year, whereas a second pattern worsened immediately post-surgery and improved, but not to baseline, by one year. One symptom, reflux, continued to worsen throughout the first year following surgery. Nurses should be alert to the persistence of reflux. Being knowledgeable of the symptom pattern of these patients over time is important as these symptoms may change and persist during recovery.

Future research should focus on the development of nursing interventions to assist patients in their recovery from curative esophagectomy. An example of a nurse-led follow-up program for patients with esophageal or gastric cardia cancer in the Netherlands was reported by Verschuur et al. (2009). In that study, home visits were conducted at six weeks and 3, 6, 9, and 12 months following curative esophagectomy. Follow-up focused on treatment issues, potential problems after surgery, and medical-legal issues. The nurse-led follow-up had a small but statistically nonsignificant positive effect on quality of life and patient satisfaction. These findings are similar to previous studies that found a positive impact from nurse-led follow-up on symptoms and patient satisfaction and costs (Faithful, Corner, Meyer, Huddart, & Dearnaley, 2001; Moore et al., 2002). Because of the prolonged nature of symptoms and the worsening of reflux following surgery, a nurse-led intervention should be investigated in this population.

Nurses play a pivotal role in symptom assessment and management and often are the primary healthcare professional to address patients' symptoms. The first step in preventing or treating symptoms is to be knowledgeable about occurrence. Knowing what to expect when patients are recovering from esophageal surgery will aid nurses in caring for these patients. Focusing on treating and assessing symptoms as a group also will help nurses have an increased awareness of symptoms and make more accurate and timely identification. Interventions should be investigated that target these symptoms with a goal of enhancing patient outcomes.

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