

Palliative care for patients with gastroesophageal cancer at all stages: a narrative review

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Background and Objective: Gastroesophageal junction (GEJ) cancer is a highly morbid disease with a poor prognosis. While uncommon in the United States, globally it is ranked as the sixth or seventh most common cancer depending on survey tool. GEJ cancer presents a unique and challenging symptom profile for patients at all disease stages, regardless of histology. Even patients with early stage disease experience debilitating cancer-related symptoms and treatment side effects. The heavy symptom burden associated with this disease includes dysphagia, nausea and vomiting, pain, anxiety, depression and malnutrition. These symptoms require a multidisciplinary approach involving local therapies including radiation and stent placement, systemic cancer-directed therapy, nutritional support, and supportive medical management. This review aims to examine the unique symptom burden experienced by patients with GEJ cancer and provide an updated overview of symptom management techniques.

Methods: A PubMed search was conducted using the terms “gastroesophageal junction cancer AND palliative care”. Articles published from 2008 to 2022 with a primary focus on supportive care for patients with GEJ cancers were reviewed.

Key Content and Findings: A total of 119 articles were identified and screened in our database search. Of these, 22 full text articles met inclusion criteria and were reviewed. Seventeen articles addressed technical interventions for the alleviation of dysphagia, 1 article focused on nutrition, 1 article described the impact of multidisciplinary tumor boards, 1 article presented the effect of home nurse visits, 1 article described the use of antiemetics, and 1 article was a narrative review of supportive care.

Conclusions: In this narrative review, we examine specific supportive care needs in the GEJ cancer population. While the predominant symptom addressed in the literature is dysphagia, patients with GEJ cancer carry a complex symptom burden from diagnosis, through cancer-directed therapy to end-of-life care. Early referral to specialty palliative care should be considered for all patients with GEJ cancer to foster symptom management and delivery of goal concordant care.

Keywords: Dysphagia; esophageal cancer; gastric cancer; palliative care; supportive care

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Introduction

Background

Gastric and esophageal cancer are the sixth and seventh most common cancers worldwide (1,2). Nearly half of all cases occur in east Asia, with approximately 47,000 new cases in the United States annually (3). The two most common histologies are adenocarcinoma and squamous cell carcinoma (SCC), with unique risk factors for each. Worldwide, SCC is the most common histologic subtype and is associated with tobacco and alcohol use. However, adenocarcinoma accounts for an increasing proportion of cases, especially in Western countries (2). Risk factors for gastroesophageal junction (GEJ) adenocarcinoma include high body mass index and Barrett esophagus (2). Because these risk factors are perceived as modifiable to some degree, the psychological impact of this cancer can be complex.

Treatment for GEJ cancer is selected based on stage and the patient's health status, and may include surgery, radiation, systemic therapy, nutritional support, and supportive care (4-8). Patients with resectable and metastatic GEJ cancer both have a heavy symptom burden. Localized esophageal cancer causes severe and uncomfortable symptoms. While curative-intent treatment can alleviate these symptoms, it also causes side effects. Systemic treatment confers adverse effects of fatigue, nausea, vomiting, and increased risk for infections. Radiation esophagitis results in dysphagia, odynophagia and dyspepsia, leading to difficulty maintaining adequate nutrition and tolerating oral medications. Esophagectomy is a surgery that requires a lengthy recovery and leads to significant lifestyle adaptations with long-term sequelae. Immunotherapy plays an increasing role as well (9,10), opening the door for additional toxicities.

Rationale and knowledge gap

The majority of GEJ cancers are metastatic at time of diagnosis and are treated with systemic therapy intended to prolong life and alleviate symptoms. Metastatic GEJ cancer has a poor prognosis; the median overall survival with best supportive care alone is approximately 3 months (11), but recent advances have improved survival rates to greater than one year in both HER2+ and HER2- disease (4-7). These advances have helped patients to live longer with all stages of disease, leading to longer term high symptom burden and need for supportive care. Dysphagia, nausea

and vomiting, pain, obstruction, and bleeding impact quality of life (QOL), but QOL is an underreported measure in randomized clinical trials (RCTs) of GEJ cancer therapies (12). Exploratory analysis of two phase III studies of ramucirumab +/- paclitaxel to treat metastatic GEJ cancer found fatigue, pain and appetite loss were the most common QOL concerns among 989 patients, and that these symptoms worsened with disease progression (13). Early specialty palliative care consultation, recommended for all patients with a new cancer diagnosis (14), should address the effects of GEJ cancer and its treatment at all stages of disease and include care coordination with interventionalists as appropriate. Palliative care support in this population can also address prognostic awareness, end-of-life planning, alleviation of caregiver burden, and the emotional toll of highly morbid disease and treatment sequelae (15). Advance care planning is covered separately in a dedicated review on the topic in this issue.

Objective

To describe predominating symptoms and relate high yield interventions in the palliation of GEJ cancer symptoms. We present this article in accordance with the Narrative Review reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1243/rc>).

Methods

Search strategy

A PubMed (pubmed.gov) search was conducted by the authors using the terms "gastroesophageal cancer AND palliative care". Additional search criteria were publication from 2008, the first year Hospice and Palliative Medicine certification was offered through the American Board of Internal Medicine (ABIM), through 2022. Abstracts were reviewed for eligibility. All screening was performed by a single reviewer. The search strategy is summarized in *Table 1*.

Inclusion and exclusion criteria

Articles in English with a primary focus on symptom management in patients with GEJ cancer were included. Articles that primarily addressed cancer-directed therapy with palliative intent, technical aspects of stent placement or stent characteristics were excluded as they were outside of the scope of this article. Articles were not excluded based

Table 1 The search strategy summary

Items	Specification
Date of search	August 1, 2022, March 1, 2023
Databases and other sources searched	PubMed
Search terms used	“Gastroesophageal cancer AND palliative care”
Timeframe	January 1, 2008 – December 31, 2022
Inclusion criteria	English language Primary focus on symptom management
Selection process	All screening was performed by the first author

on study design or outcomes.

Data analysis

Data charting was performed with collection of publication data and relevant content. A descriptive format was used to synthesize and report the results.

Results

A total of 119 articles were identified and screened in our database search. Of these, 22 full text articles met inclusion criteria and were reviewed (*Figure 1*). Seventeen articles addressed technical interventions for the alleviation of dysphagia, 1 article focused on nutrition, 1 article described the impact of multidisciplinary tumor boards, 1 article presented the effect of home nurse visits on dysphagia, 1 article described the use of antiemetics, and 1 article was a narrative review of supportive care (*Table 2*).

Narrative

Our literature search yielded 22 articles with an overarching focus on interventions to alleviate the symptom of dysphagia. While dysphagia is the most common symptom in patients with GEJ cancer, other symptoms have a profound impact on QOL. These symptoms include malnutrition, nausea, vomiting, pain, bleeding, anxiety, depression, caregiver burden and need for end-of-life planning. We present the findings of our search summarized in a narrative format about dysphagia. In the following sections, we broaden the discussion and draw on additional literature to include these other symptoms of GEJ cancer.

The results of our search illustrate ambiguity in the

meaning of the phrase “palliative care”. Most articles identified in our search addressed non-curative cancer-directed therapy with a goal of symptom control, also known as “palliative intent” therapy. Acknowledging that cancer-directed therapy may alleviate symptoms of GEJ cancer via tumor shrinkage, the focus of this review is on the discipline of palliative medicine, also known as supportive oncology. We present an overview of supportive care interventions meant to complement cancer-directed therapy in the alleviation of symptoms caused by GEJ cancer and its treatment.

Dysphagia

Dysphagia, defined as difficulty or discomfort in swallowing, is categorized on the Mellow Scale or the Dysphagia Grading System into five severity levels: able to eat a normal meal, some solids, semisolids, liquids, or nothing at all (16-18). Decreased oral intake due to dysphagia results in unintentional weight loss and deconditioning, making definitive treatment of the underlying cancer riskier and more burdensome. Malnutrition is known to decrease survival and QOL (19). In addition to its impact on nutrition and treatment success, dysphagia also independently diminishes QOL by limiting a patient’s ability to enjoy favorite foods, share meals with loved ones, and partake in culturally significant customs and holidays. Patients with GEJ cancer value services and support for the physical, social and emotional implications of dysphagia (20). One of the emotional implications of dysphagia is fear of eating, which can lead to serious medical complications and avoidant behaviors. Dysphagia is treated with nutritional supplementation, procedures targeted at correcting mechanical obstruction, and treatment of the underlying

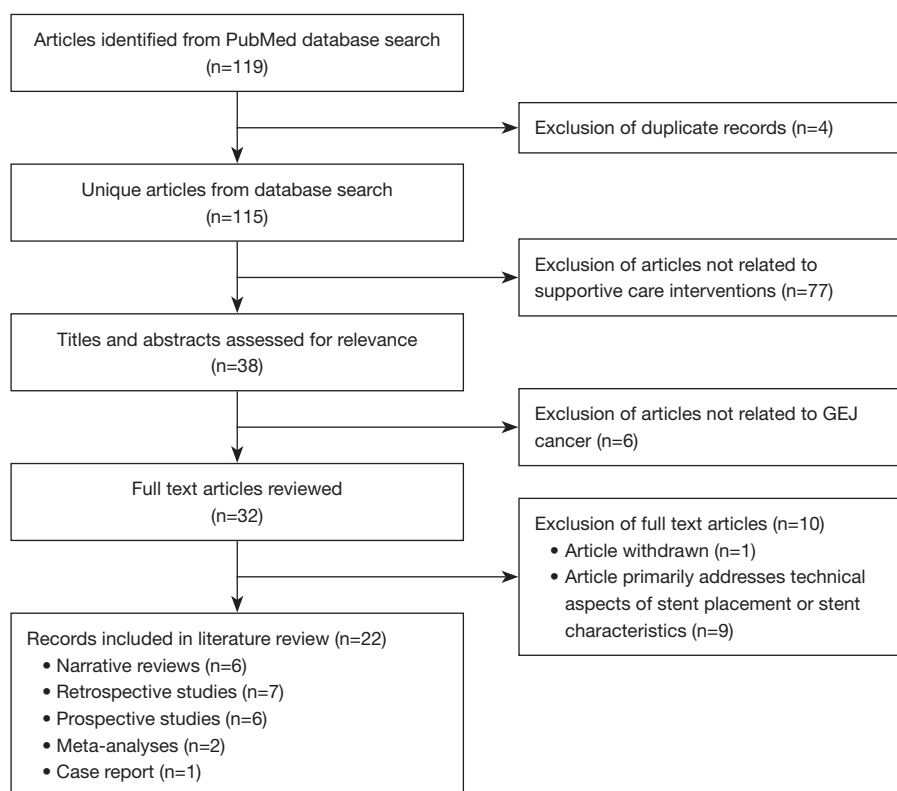


Figure 1 Flowchart of search results. GEJ, gastroesophageal junction.

tumor. Selection of palliative treatment should account for patient factors such as presence of bleeding or fistula, disease factors including location of the primary tumor, and treatment factors of safety and efficacy in order to provide an individualized approach (17,21).

Esophageal stenting, a procedure aimed at alleviating mechanical obstruction from GEJ tumor, has been recommended as first line palliative treatment for dysphagia (17). Esophageal stents work by keeping the lumen of the esophagus patent or by covering the site of anastomotic leak to prevent extravasation of luminal contents (22). A wide variety of stents is available, with differences in material, design and mode of employment (21) that can be valuable in different clinical situations (22). Self-expanding metal stents (SEMS) are the most commonly used (22-25).

SEMS are safe and effective at alleviating dysphagia, as demonstrated in a 2014 Cochrane database review of 53 RCTs including 3,684 patients with esophageal cancer (16). SEMS are successfully placed in 95% of cases and result in improvement of dysphagia in 90% of cases (22). QOL scores significantly improved after stenting in a prospective

study of 33 patients with inoperable esophageal cancer who underwent SEMS placement (26). Outcomes have been shown similar in patients with first line SEMS and SEMS placed after cancer-directed therapy (27). Pain and inflammation, which are common in patients with GEJ cancer, can make safe and effective stenting more challenging (28). Side effects of stenting include gastroesophageal reflux (45%), chest pain (36–60%), foreign body sensation (25%), hiccup (1–2%), bleeding (1–2%), and stent migration (4–31%) (22,24,25,29,30). Reflux symptoms can be managed with standard anti-reflux therapy such as PPI and head of bed elevation; SEMS designed with antireflux properties are not more effective than conventional stents in relieving reflux symptoms (31).

When successful, stent placement provides more immediate relief from dysphagia as compared with chemoradiation (30,32), but benefits can be short-lived (33), lasting around 8 weeks (26). Dysphagia recurred in 12.4% of patients in a retrospective study of 442 patients who underwent esophageal stent placement (30). One prospective study of 87 patients with esophageal cancer receiving SEMS found the average re-intervention rate

Table 2 Articles included in literature review

Article title	Year of publication	Journal specialty	Supportive care domain
Endoscopic evaluation and treatment of esophageal cancer	2009	Gastroenterology	Dysphagia
Palliative stenting for relief of dysphagia in patients with inoperable esophageal cancer: impact on quality of life	2009	Gastroenterology	Dysphagia
Intraluminal brachytherapy in the management of squamous carcinoma of the esophagus	2009	Gastroenterology	Dysphagia
Complications of metallic stent placement in malignant esophageal stricture and their management	2010	Surgery	Dysphagia
Clinical outcomes of using a conservative approach of late esophageal stent placement in palliation of malignant dysphagia	2010	Gastroenterology	Dysphagia
The use of self-expanding stents in esophageal and gastroesophageal junction cancer palliation: a meta-analysis and meta-regression analysis of outcomes	2010	Gastroenterology	Dysphagia
Acceptable results after self-expanding metallic stent treatment for dysphagia in non-resectable oesophageal cancer	2012	Medicine	Dysphagia
Low morbidity after palliation of obstructing gastro-oesophageal adenocarcinoma to restore swallowing function	2012	Medicine	Dysphagia
Ten-year experience of esophageal self-expanding metal stent insertion at a single institution	2013	Gastroenterology	Dysphagia
Intraluminal high-dose-rate brachytherapy for palliation of dysphagia in cancer of the esophagus: initial experience at a single UK center	2013	Gastroenterology	Dysphagia
Interventions for dysphagia in oesophageal cancer	2014	Cochrane Database of Systematic Reviews	Dysphagia
Chemotherapy versus self-expanding metal stent as primary treatment of severe dysphagia from unresectable oesophageal or gastro-oesophageal junction cancer	2014	Gastroenterology	Dysphagia
Esophageal stents: when and how	2016	Gastroenterology	Dysphagia
Endoscopic management of esophageal strictures	2017	Gastroenterology	Dysphagia
Comparison of endoscopic laser therapy and self expanding metal stents for palliation in patients with non-resectable oesophageal carcinoma	2017	Surgery	Dysphagia
Radioactive self-expanding stents for palliative management of unresectable esophageal cancer: a systematic review and meta-analysis	2017	Gastroenterology	Dysphagia
Stenting in Palliation of Unresectable Esophageal Cancer	2018	Surgery	Dysphagia
Palliative care for patients with esophageal cancer: a narrative review	2020	Translational medicine	Multifactorial
Impact of multidisciplinary tumor board discussion on palliation of patients with esophageal or gastro-esophageal junction cancer: a population-based study	2020	Oncology	Interteam communication
The role of home visits by a nurse to improve palliation in patients treated with self-expandable metallic stents due to incurable esophageal cancer	2020	Gastroenterology	Dysphagia
Nutritional Support Indications in Gastroesophageal Cancer Patients: From Perioperative to Palliative Systemic Therapy. A Comprehensive Review of the Last Decade	2021	Nutrition	Nutrition
Use of long term aprepitant as a treatment for refractory nausea following oesophageal stent insertion - a case report	2022	Palliative care	Nausea

was 2.8 per patient (34). Another prospective study of 312 patients found that among patients receiving SEMs, re-intervention was necessary in 5% (35). Stents may be removed electively after 4 to 6 weeks to reduce the risk of fistula formation (22). Alternatively, SEMs serve as a tool to optimize nutrition before surgery, and can be removed at the time of esophagectomy after neoadjuvant chemoradiation (23).

Balloon dilation, thermal ablation or argon plasma coagulation (APC), cryotherapy, chemical ablation, and laser or photodynamic therapy (PDT) are other options to improve the patency of the lumen of the esophagus (16,29,36). Dilation does not provide long term relief from dysphagia in patients with compressive or obstructive symptoms from GEJ tumors (29). SEMs have been shown to be more effective (22) and to require fewer repeat interventions than laser ablation (37). Further, PDT carries risk of significant side effects including sunburn and photosensitivity (29). Endoscopic injection with alcohol and other chemical sclerosants has been associated with pain (16), normal tissue damage and perforations (29). These techniques have generally fallen out of favor compared to SEMs (29).

Radiation is another effective technique for the treatment of dysphagia. Palliative radiation can relieve dysphagia and improve QOL (38,39). Radiotherapy is typically recommended for patients with a life expectancy of more than three months who have not responded to other palliative approaches (17). Radiation is an effective treatment for dysphagia and confers fewer severe adverse effects than combined chemoradiation (40). In a Dutch retrospective study of 948 patients with esophageal or GEJ cancer, patients who were discussed at multidisciplinary tumor boards before receiving first line therapy were more likely to be referred for radiation (41).

Intraluminal brachytherapy (ILBT) and external beam radiation therapy (EBRT) are both acceptable types of radiation that can be used for dysphagia palliation. EBRT has been shown to increase mean body weight, decrease dysphagia and odynophagia, and improve QOL (42-44). In head-to-head comparisons, EBRT resulted in less nausea, vomiting, pain and appetite loss than ILBT, though both techniques resulted in decreased functional status (45). However, in one study, palliative EBRT given concurrently with SEMs offered no additional QOL benefit to SEMs in isolation (46,47). The meta analysis referenced above found 2 RCTs comparing ILBT versus SEMs; although ILBT was slower to ameliorate dysphagia, it resulted

in overall higher QOL (16). ILBT was associated with significant improvements in QOL in regard to feelings, sleeping, eating and social life in a prospective study of 30 patients (48). Though safe and effective (49), ILBT is not always readily available and often can be performed only at certain radiation centers (21). Radioactive stents may be a cost effective modality to combine SEMs with ILBT (50). Localized procedures for palliation of dysphagia should be selected depending on center expertise.

Malnutrition

Proper nutritional assessment is essential to identify malnutrition, generate a plan for intervention, and maintain adequate performance status for cancer-directed therapy (19). In patients who can tolerate oral liquids, nutritional support is offered via high calorie shakes and dietary modifications including soft textures and increased liquid intake (51). Temporary pre-operative jejunostomy or percutaneous endoscopic gastrostomy (PEG) tube may be offered if the patient continues to lose weight despite these interventions. Total parenteral nutrition (TPN) is typically not indicated due to high risk of infectious complications, but may be considered as a short-term bridge until enteral access is re-established after definitive surgery. Notably, these interventions do not address the underlying cause for dysphagia. A patient's values surrounding nutrition should be established prior to offering enteral nutrition tube or TPN. These modalities carry serious emotional weight in bypassing the human experience of oral intake, and may contribute to anxiety and depression. Even patients who choose a feeding tube or TPN with full clarity and understanding have a significant decrease in the connections surrounding food, family meals and celebrations, and the pleasure of eating and drinking.

Nausea and vomiting

Nausea and vomiting are common symptoms in patients with GEJ cancer and have numerous causes. Patients may experience nausea due to mechanical obstruction, esophageal dysmotility, side effects of chemotherapy, radiation, opioid pain medications, and anxiety. At best, nausea and vomiting are uncomfortable and lead to decreased QOL, limiting a patient's ability to enjoy favorite pastimes. At worst, these symptoms can be severe and result in serious dehydration, treatment delays and complications, and inability to participate in basic activities of daily life.

Table 3 Anti-emetics available for at home use in patients who are unable to swallow solids

Drug name	Route of administration available at home	Class of drug	Advantages	Disadvantages
Dexamethasone	Oral solution	Steroid	Increases appetite and energy	Hyperglycemia, hypertension, long term use results in mineralocorticoid effects
Dronabinol	Oral solution	Synthetic THC cannabinoid	Increases appetite	Hyperemesis syndrome
Granisetron	Transdermal	Serotonin antagonist	Effective for chemotherapy-induced nausea/vomiting	QT prolongation, constipation, out of pocket expense
Haloperidol	Oral solution	Dopamine antagonist	Effective for medication-induced nausea/vomiting, can be administered rectally (off-label)	Dystonia, sedation, QT prolongation
Lorazepam	Oral solution	Benzodiazepine	Effective anxiolytic	Sedation
Medical marijuana	Oral solution, inhaled	Cannabinoid	May promote anxiolysis	Federally unsupported, dosages not well defined, no standardization of products, hyperemesis syndrome
Metoclopramide	Oral solution, oral disintegrating tablet	Dopamine antagonist	Promotes peristalsis	QT prolongation, extrapyramidal effects, sedation
Olanzapine	Oral disintegrating tablet	Second generation antipsychotic	Ease of administration	Extrapyramidal effects, sedation
Ondansetron	Oral solution, oral disintegrating tablet	Serotonin antagonist	Effective for chemotherapy or radiation-induced nausea/vomiting	QT prolongation, constipation, out of pocket expense
Phenergan	Rectal suppository	Antihistamine	Per rectum administration bypasses any oral administration	PR route should be avoided in neutropenia, sedation
Prochlorperazine	Rectal suppository	Dopamine antagonist	Per rectum administration bypasses any oral administration	PR route should be avoided in neutropenia, dystonia, sedation, QT prolongation
Scopolamine	Transdermal	Anticholinergic	Transdermal administration bypasses any oral administration	Not approved for nausea/vomiting outside of motion sickness or post-operative symptoms

THC, tetrahydrocannabinol; PR, per rectum.

Nausea affects nutrition as well, which is particularly important in the neoadjuvant setting because malnutrition can jeopardize a patient's ability to receive chemotherapy. The mainstay of treatment for nausea is medication, but it may include invasive procedures as outlined above for dysphagia, and non-pharmacologic interventions, including adjustments to eating patterns and schedules, breathing techniques and acupuncture.

A variety of anti-emetics are available for IV administration, and some patients with severe nausea and vomiting may require frequent visits to an infusion center for symptom control and hydration. Many anti-emetics are

available in oral formulations that can be self-administered at home, offering patients a chance to reassert control over their symptom burden. For patients with limited enteral access due to dysphagia or mechanical obstruction, at-home options include transdermal application, inhalable substances, sublingual administration of oral solution or oral dissolvable tablet (ODT), rectal suppositories, and PEG tube administration if PEG tube is in place. *Table 3* provides an overview of anti-emetic medication options available in the United States for patients who are unable to swallow. Of note, some of these options may be unaffordable or difficult to access depending on insurance

coverage and local availability. Formulations available in other countries include the cannabinoid oral spray nabiximols and transdermal ondansetron. In addition to the agents listed in *Table 3*, oral aprepitant was described in an Australian case report as a safe and effective long term anti-emetic in a patient who developed nausea following SEMS placement (52).

Some data support acupuncture as an effective treatment for cancer-related nausea and vomiting. In a meta-analysis of 3 systematic reviews involving 36 RCTs, many trials were assessed to have a moderate or high overall risk of bias (53). One RCT with a low risk of bias showed acupuncture was more effective than medication in controlling chemotherapy-induced nausea and vomiting (53).

Pain

Patients with GEJ cancer often experience pain at the site of the primary tumor, presenting as dysphagia or odynophagia as discussed above. Somatic pain may also occur at distant metastatic sites especially with bone and visceral involvement, surgical sites including PEG tube insertion site, and sites of increased pressure in the context of weight loss and deconditioning. Neuropathic pain should be considered as well, especially following invasive procedures with risk of nerve injury and in patients with chemotherapy-induced peripheral neuropathy. Dyspepsia may also present as pain, with burning as the presenting symptom of unchecked acid reflux in the absence of proper closure of the lower esophageal sphincter. Analgesia is typically indicated as an adjuvant to treatment of the underlying cause for pain.

Choice of analgesic typically follows the same selection process as that for other disease states. *Table 4* lists commonly used at-home pain medications for patients with GEJ cancer who are unable to reliably swallow. Sublingual and transdermal administration should be considered where indicated. In addition, antacids should be considered including proton pump inhibitors, H₂ blockers, and cytoprotectants.

Mood

Patients with GEJ cancer express states of hope for the future alternating with despair and shock (20). Our literature search did not return any articles specifically focused on mood in patients facing GEJ cancer. Specialty palliative care physicians assess mood using validated tools, employ

pharmacologic and non-pharmacologic techniques as part of patient-centered supportive oncologic care, and coordinate close contact with members of the interdisciplinary care team, including chaplains, social workers, psychologists, therapists, psychiatrists, and integrative therapy. Paying special attention to the psychological wellbeing of the caregiver is also an important part of what palliative care teams do, as the burden of being a caregiver can range from overwhelming to devastating.

End-of-life planning

Metastatic GEJ cancer confers a poor prognosis on the order of one year or less. Even resectable disease has a high likelihood of recurrence and carries risk for a limited life span. GEJ tumors can cause sudden life-threatening events including perforation, obstruction, fistula and bleeding. Anticipatory guidance can help patients and caregivers prepare for these potential complications. Code status and advanced care planning should be addressed early in the disease course. Specialty palliative care consultation plays an important role in fostering prognostic awareness, advance care planning, and transition to comfort-focused care in this vulnerable patient population (15).

Prognostic awareness entails aligning the patient's understanding of their prognosis with provider assessment. While not specific to GEJ cancer, data show that patients with advanced malignancy often falsely believe the intent of their treatment is curative. In the CanCORS study, 69% of patients with advanced lung cancer and 81% of patients with advanced colorectal cancer thought their palliative-intent chemotherapy could cure them of their cancer (54). This illustrates a breakdown in crucial communication between patients and their oncology providers. Using specialized training in complex care conversations, palliative care providers can assess patients' prognostic awareness and provide additional support in clear and direct communication of treatment goals and prognosis.

Good prognostic awareness is an important step to ensuring the delivery of goal concordant care, or treatment that aligns with the patient's values in the face of life-limiting disease. Advance care planning promotes this type of treatment, though a full discussion of advance care planning is outside the scope of this narrative review and is covered separately in a dedicated review on the topic in this issue. Early introduction of hospice as a viable option for aggressive symptom-focused management is an important way to empower patients to achieve goal concordant care.

Table 4 Analgesics available for at home use in patients who are unable to swallow solids

Drug name	Route of administration available at home	Class of drug	Advantages	Disadvantages
Acetaminophen	Oral solution, rectal suppository	Centrally acting non-opioid	Non sedating	Dosage limited in patients with liver dysfunction
Buprenorphine	Transdermal, buccal, sublingual	Partial opioid agonist-antagonist	May be used in patients otherwise intolerant of opioids, may be used in renal dysfunction	Sedation, constipation
Dexamethasone	Oral solution	Steroid	Helpful for bony metastasis pain	Hyperglycemia, hypertension, long term use results in mineralocorticoid effects
Fentanyl	Transdermal, oral transmucosal, intranasal	Opioid	Ease of administration	Sedation, constipation
Hydromorphone	Oral solution, intranasal	Opioid	May be used in renal dysfunction	Sedation, constipation; intranasal formulation not widely available
Ibuprofen	Oral solution	NSAID	Non sedating	Thrombocytopenia, gastritis, risk for GI bleeding, contraindicated in renal dysfunction
Lidocaine	Transdermal, topical	Local anesthetic	Non sedating	Low penetration, effective mainly for musculoskeletal pain
Methadone	Oral solution	Opioid	Rapid absorption from the upper GI tract	Sedation, constipation
Morphine (immediate release)	Oral solution	Opioid	Short action of onset	Sedation, constipation, contraindicated in renal dysfunction
Morphine (extended release) Kadian	Capsule	Opioid	Capsule can be opened and contents swallowed or flushed through PEG tube	Sedation, constipation
Oxycodone (extended release) (Xtampza)	Capsule	Opioid	Capsule can be opened and contents “sprinkled” into pureed food or thickened liquids or flushed through PEG tube	Sedation, constipation, contraindicated in renal dysfunction
Oxycodone (immediate release)	Oral solution	Opioid	Short action of onset	Sedation, constipation, contraindicated in renal dysfunction

NSAID, nonsteroidal anti-inflammatory drug; GI, gastrointestinal; PEG, percutaneous endoscopic gastrostomy.

Caregiver burden

Though all types of cancer impact a patient's loved ones, GEJ cancer imposes unique burdens on the patient's family and friends. The cultural and psychological distress of watching a cachectic loved one unable to eat can be very distressing for a primary caregiver. Caregivers may request PEG tube, TPN, or other means of artificial nutrition in the face of disease progression and functional decline. They

may feel powerless at home to nourish their loved one, or overwhelmed by recommendations for frequent high calorie meals with specific texture restrictions. Caregivers also express distress over the changing relationship with their loved one (20). The comprehensive specialty palliative care team includes social work and chaplain support for caregivers to address these experiences. A randomized trial of 80 patients treated with SEMS for inoperable esophageal

or GEJ cancer found improved QOL among patients who received home visits from a specialty nurse; the authors conclude that increased interactions with a nurse are helpful to both patient and family in the recovery period after stent placement (55). Additionally, enhanced social support was shown in one study to improve spiritual well-being of patients with esophageal cancer (56).

Conclusions

Patients with GEJ cancer experience unique, severe symptoms as a result of their natural disease progression and from treatment side effects. Our literature search returned articles mainly focused on technical interventions to alleviate dysphagia, but this is just one of a constellation of symptoms. This review has significant limitations in that it used narrow search terms in a single database. The phrase “palliative care” likely does not capture additional relevant literature in the fields of interventional radiology, psychiatry, nutrition and others. More research is needed to provide insight to specific QOL needs in this population. Early referral to specialty palliative care should be considered for all patients with GEJ cancer to foster symptom management and delivery of goal concordant care. Acknowledging that specialty palliative care is a scarce resource both in the United States and internationally, efforts are needed to improve palliative care access for this population.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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