



Editorial - Medical Second Opinions - The Clinic by Cleveland Clinic  
Second opinions from Cleveland Clinic's world-class expert physicians.

JUNE 20, 2023  
Cleveland, Ohio.  
IMPORTANT UPDATES

MARCO ANTONIO MEDINA ORTEGA

JHAN SEBASTIAN SAAVEDRA TORRES

## The Cleveland Clinic: Gastrointestinal symptoms in cancer patients with advanced disease.

*He's the best physician that knows the worthlessness of the most medicines.*<sup>1</sup>

— Benjamin Franklin (1706-1790) American statesman and scientist.

Gastrointestinal (GI) symptoms are prevalent, often persistent, and detrimental to patients' quality of life. Resulting from medication side effects or underlying disease, gastrointestinal (GI) symptoms are among the most common and unpleasant side effects experienced by advanced cancer patients. Gastrointestinal symptoms are reportedly common in advanced cancer, but a causal link is controversial and adequate population control data are lacking <sup>(1)</sup>. Nausea and vomiting are common symptoms, with a reported prevalence of 40–70%, in patients with advanced cancer <sup>(2)</sup>.

Gastrointestinal cancer is common, both in the United States and worldwide. Treatments are more effective when the cancer is detected at an early stage—which, unfortunately, can be a challenge <sup>(2)</sup>. Gastrointestinal (GI), and lung cancer patients, the incidence of severe patient-reported nausea was highest in breast cancer patients (17%, versus 14% and 4% in GI and lung cancer cohorts); GI patients reported more moderate to severe diarrhea (31%, versus 22% and 11% for breast and GI cancer cohorts); breast cancer patients reported more severe constipation (15%) and heartburn (11%) than did GI (7%, 5%) or lung (6%, 3%) cancer patients; and GI cancer patients experienced more moderate to severe decrease in appetite (36%) than did lung (30%) or breast (28%) cancer patients <sup>(3)</sup>.

Moreover, nausea and vomiting are significant causes of morbidity in this group of patients. In palliative care, the cornerstone of the management of nausea and vomiting is the use of pharmacological interventions, i.e. antiemetic drugs <sup>(1,2)</sup>. It should be noted that the successful management of nausea and vomiting necessitates a thorough assessment of the patient (taking a history, performing an examination and arranging appropriate investigations) <sup>(2)</sup>.

---

Physicians Marco A. Medina Ortega and Jhan S. Saavedra prepared this topic. Research Associates Medical Second Opinions - The Clinic by Cleveland Clinic provided assistance. - The Clinic by Cleveland Clinic cases are developed solely as the basis for class discussion. Cases are not intended to serve as endorsements, sources of primary data, or illustrations of effective or ineffective management.

Copyright © 2023 The Cleveland Clinic Foundation. All rights reserved. The information provided is for educational purposes only. Use of this website is subject to the website terms of use and privacy policy. This publication may not be digitized, photocopied, or otherwise reproduced, posted, or transmitted, without the permission of The Cleveland Clinic Foundation. 9500 Euclid Avenue, Cleveland, Ohio 44195 | 800.223.2273.

Gastrointestinal symptoms in advanced cancer patients: are non-specific weight loss, persistent abdominal pain, dysphagia, hematemesis, anorexia, nausea, early satiety, and dyspepsia. Patients presenting with a locally-advanced or metastatic disease usually present with significant abdominal pain, potential ascites, weight loss, fatigue, and have visceral metastasis on scans, and can have a gastric-outlet obstruction <sup>(4, 5)</sup>.

Palliative management of gastrointestinal symptoms in advanced cancer patients requires a multipronged approach that entails effective assessment, judicious use of latest evidence-based approaches, and monitoring that incorporates both clinical measures and patient-reported outcomes <sup>(6)</sup>.

New methodologies, insights, in Gastrointestinal symptoms in cancer patients with advanced disease. Current clinical guidelines now recommend that patients treated with moderate emetic risk chemotherapy regimens be preferentially treated with the 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonist, palonosetron, in combination with dexamethasone. A large randomized trial has also recently validated that single-dose fosaprepitant is equivalent to the standard 3-day, aprepitant regimen <sup>(6)</sup>.

Cancer patients with advanced life-limiting illness present a host of GI symptoms which may arise from medication side effects or the underlying disease. Potentially leading to serious metabolic disturbance, malnutrition, electrolyte disturbances, and other physiological repercussions, nausea and vomiting can also impair functionality and erode the patient's quality of life <sup>(7)</sup>.

Diarrhea also compromises quality of life, and may interfere with adherence to treatment schedules. Diarrhea is a common side effect of certain chemotherapeutic regimens; symptom prevalence ranges from 50-80% depending on the medication <sup>(5,6)</sup>. Among heterogeneous cancer patients, the prevalence of moderate to severe diarrhea has been reported at 14% <sup>(7)</sup>.

Diarrhea is an unpleasant but common side effect in people receiving treatment for cancer. It may also be caused by the cancer itself. Sometimes diarrhea can be a sign of something more serious <sup>(8)</sup>.

Chemotherapy-related diarrhea (CRD) is most commonly described with fluoropyrimidines (particularly fluorouracil [FU] and capecitabine) and irinotecan. Diarrhea is the dose-limiting and major toxicity of regimens containing a fluoropyrimidine with irinotecan <sup>(8)</sup>.

Chemotherapy can cause constipation. This means not having a bowel movement often enough or having difficult bowel movements <sup>(8)</sup>. Other medicines, such as pain medication, can also cause constipation <sup>(6)</sup>. Constipation, a common symptom among elderly patients in general, afflicts 50-87% of terminally ill cancer patients <sup>(9)</sup>.

The treatment of constipation in palliative care is based on inadequate experimental evidence, such that there are insufficient randomized controlled trial data. Recommendations for laxative use can be related to efficacy. Particularly in patients with advanced-stage tumor disease this must be undertaken with careful consideration of their physical activity and dietary needs <sup>(10)</sup>.

Recent findings in the literature include an updated version of the Rome criteria and related information on the functional gastrointestinal disorders, as well as information on opioid antagonists. Knowledge of the role of definitions, causes of constipation and the pathophysiology of opioid-induced constipation must be given a high priority in the treatment of patients receiving opioids <sup>(11)</sup>.

---

The information provided on <http://www.clevelandclinic.org/> is designed to support, not replace, the relationship that exists between patient/site visitor and his/her physician, nor is intended to replace the medical advice of your doctor or healthcare provider. Please consult your healthcare provider for advice about a specific medical condition.

In the United States, approximately 500,000 patients die of cancer annually. Opioid pain medications are used in the terminal phase of care for more than 50% of these patients (11). When laxative regimens have failed, methylnaltrexone may be indicated for the relief of opioid-induced constipation (OIC) in patients with advanced illness receiving palliative care. The present, cost-benefit analysis (CBA) provides pharmacoeconomic evidence for the adoption of methylnaltrexone for treating OIC in terminally ill cancer patients (12).

New medications, such as skin patch delivery of granisetron for nausea or methylnaltrexone for constipation, show promise in both the management of symptoms and as preventive agents. The integration of complementary and alternative therapies, such as relaxation techniques, ginger, and electroacupuncture may also assist with symptom relief (5,6).

---

## The most common types of gastrointestinal cancers are as follows:

- Esophageal cancer
- Gastric (stomach) cancer
- Colorectal cancer
- Pancreatic cancer
- Liver cancer

Other types are much less common, including neuroendocrine tumors, gastrointestinal stromal tumors, and anal cancer.

Generally speaking, gastrointestinal cancers are more likely to develop in men, and the risk increases with age. Studies have linked these cancers to cigarette smoking, alcohol consumption and unhealthy diets.

Cleveland, Ohio.  
IMPORTANT UPDATES

### Author's Notes:

- The good news is that healthy lifestyle changes can help reduce the risk for GI cancer. - says. Marco A. Medina Ortega MD. (Medical Surgery)
- Routine collection of patient-reported data on these symptoms can support good clinical care for advanced cancer patients while also helping to build an evidence base to support clinicians in managing these cancer-related symptoms. - says. Jhan S. Saavedra T MD. (Physician Family Medicine)
- “We often consider the risk of colorectal cancer to increase with age,” says. Marco A. Medina Ortega MD. (Medical Surgery) “but recently, the incidence in patients under 50 is rapidly increasing. For this reason, the American Cancer Society recently recommended that routine colorectal cancer screening should start at age 45. It is important to catch colorectal cancers early, because if we do, they are highly curable.”
- Routine colorectal screening also markedly reduces the risk of colon cancer by finding and removing polyps before they have the chance to become cancerous. - says. Marco A. Medina Ortega MD. (Medical Surgery)
- A palliative care specialist will take the following issues into account for each patient: Physical. Common physical symptoms that can be addressed include pain, fatigue, loss of appetite, nausea, vomiting, shortness of breath, and insomnia. - says Dr. Jhan S. Saavedra T MD. (Physician Family Medicine)

**First author: Marco A. Medina Ortega MD.** (Medical Surgery)

Disclaimers: None

Competing interests: None

Complete Funding Declaration: No relevant funding to report

The publisher's final edited version of this article is available at: Unicauca-Temas-reflexion

## REFERENCES

1. Abernethy, A. P., Wheeler, J. L., & Zafar, S. Y. (2010). Management of gastrointestinal symptoms in advanced cancer patients: the rapid learning cancer clinic model. *Current opinion in supportive and palliative care*, 4(1), 36–45. <https://doi.org/10.1097/SPC.0b013e32833575fd>
2. Bruera E, Sweeney C (2002) Chronic nausea and vomiting. In: Berger AM, Portenoy RK, Weissman DE (eds) *Principles and practice of palliative care and supportive oncology*, 2nd edn. Lippincott Williams & Wilkins, Philadelphia, pp 222–232
3. Clemens, K. E., & Klaschik, E. (2008). Management of constipation in palliative care patients. *Current opinion in supportive and palliative care*, 2(1), 22–27. <https://doi.org/10.1097/SPC.0b013e3282f53146>
4. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*. 2011 Mar-Apr;61(2):69-90.
5. Tan IB, Ivanova T, Lim KH, Ong CW, Deng N, Lee J, Tan SH, Wu J, Lee MH, Ooi CH, Rha SY, Wong WK, Boussioutas A, Yeoh KG, So J, Yong WP, Tsuburaya A, Grabsch H, Toh HC, Rozen S, Cheong JH, Noh SH, Wan WK, Ajani JA, Lee JS, Tellez MS, Tan P. Intrinsic subtypes of gastric cancer, based on gene expression pattern, predict survival and respond differently to chemotherapy. *Gastroenterology*. 2011 Aug;141(2):476-85, 485.e1-11.
6. Rangwala, Fatimaa; Zafar, S. Yousefa; Abernethy, Amy P.a,b. Gastrointestinal symptoms in cancer patients with advanced disease: new methodologies, insights, and a proposed approach. *Current Opinion in Supportive and Palliative Care* 6(1):p 69-76, March 2012. | DOI: 10.1097/SPC.0b013e32834f689d
7. Stephenson, J., & Davies, A. (2006). An assessment of aetiology-based guidelines for the management of nausea and vomiting in patients with advanced cancer. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 14(4), 348–353. <https://doi.org/10.1007/s00520-005-0897-1>
8. Vehreschild, M. J., Meissner, A. M., Cornely, O. A., Maschmeyer, G., Neumann, S., von Lilienfeld-Toal, M., Karthaus, M., Wattad, M., Staib, P., Hellmich, M., Christ, H., & Vehreschild, J. J. (2011). Clinically defined chemotherapy-associated bowel syndrome predicts severe complications and death in cancer patients. *Haematologica*, 96(12), 1855–1860. <https://doi.org/10.3324/haematol.2011.049627>
9. Choi YS, Billings JA. Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. *Journal of Pain & Symptom Management*. 2002
10. Clemens, K. E., & Klaschik, E. (2008). Management of constipation in palliative care patients. *Current opinion in supportive and palliative care*, 2(1), 22–27. <https://doi.org/10.1097/SPC.0b013e3282f53146>
11. Iskedjian, M., Iyer, S., Librach, S. L., Wang, M., Farah, B., & Berbari, J. (2011). Methylnaltrexone in the treatment of opioid-induced constipation in cancer patients receiving palliative care: willingness-to-pay and cost-benefit analysis. *Journal of pain and symptom management*, 41(1), 104–115. <https://doi.org/10.1016/j.jpainsymman.2010.04.012>
12. Youn Seon Choi, MD, PhD., Opioid Antagonists: A Review of Their Role in Palliative Care, Focusing on Use in Opioid-Related Constipation- REVIEW ARTICLE- VOLUME 24, ISSUE 1, P71-90, JULY 2002, DOI: [https://doi.org/10.1016/S0885-3924\(02\)00424-4](https://doi.org/10.1016/S0885-3924(02)00424-4)