



The Chicago Consensus on Peritoneal Surface Malignancies: Palliative Care Considerations

Chicago Consensus Working Group

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ABSTRACT The Chicago Consensus Working Group provides multidisciplinary recommendations for palliative care specifically related to peritoneal surface malignancies. These guidelines are developed with input from leading experts including surgical oncologists, medical oncologists, gynecologic oncologists, pathologists, radiologists, palliative care physicians, and pharmacists. These guidelines recognize and address the emerging need for increased awareness in the appropriate management of peritoneal surface disease. They are not intended to replace the quest for higher levels of evidence.

THE CHICAGO CONSENSUS ON PERITONEAL SURFACE MALIGNANCIES: PALLIATIVE CARE CONSIDERATIONS

This article provides multidisciplinary recommendations for palliative management of peritoneal surface malignancies and constitutes 1 article in a series composed by the Chicago Consensus Working Group for the Management of Peritoneal Surface Malignancies.^{1–10} Information regarding formation of the Chicago Consensus Group and explanation of the working group's consensus methodology is discussed elsewhere.^{1,2}

The collaborators for the Chicago Consensus Working Group are listed in the acknowledgments.

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Principles of Management of Malignant Bowel Obstruction

Malignant bowel obstruction (MBO) is a frequent presentation of patients with peritoneal metastases and in a high percentage of these cases is the cause of death. Medical management of MBO has the potential to relieve clinical symptoms and resolve the underlying obstructive process. The goals of therapy include reducing pain, nausea, vomiting, and aspiration risk while potentially allowing the patient to regain oral nutrition support and ultimately allowing for a patient's transition to care in the home setting. Pharmacologic therapies include the use of antiemetics, antisecretory medications, and anti-inflammatory medications with the goal of reducing the intestinal obstruction.

The role of gastric antisecretory therapies, including histamine-2 receptor blockers (H₂RBs) and proton pump inhibitors (PPIs), has not been formally studied in the management of MBO. However, because of their ability to reduce gastric secretions, H₂RB and PPI therapies are recommended to reduce clinical symptoms and volume loss from nasogastric tube decompression. When used in a preoperative setting, both H₂RB and PPI therapies have demonstrated reductions in gastric fluid production.¹¹

Various anticholinergic therapies are used for symptomatic management of gastrointestinal symptoms, including abdominal pain and gastrointestinal secretions. Often used as a comparator in randomized studies, scopolamine (hyoscine butylbromide) has anticholinergic properties that can reduce gastrointestinal secretions.^{12,13} No formal studies on the use of dicyclomine or hyoscyamine as smooth muscle relaxants in the management of MBO exist.

The anti-inflammatory properties of corticosteroids reduce gastrointestinal wall and mesenteric edema in the setting of MBO; therefore, their use is an accepted standard practice in the management of MBO.¹⁴ A Cochrane review

analyzing the role of corticosteroids in the resolution of MBO in both advanced gynecologic and gastrointestinal cancers demonstrated a trend toward resolution of MBO without an impact on overall survival. The number needed to treat was 6 patients to resolve 1 MBO.¹⁵ Furthermore, an analysis of a national commercial health care database demonstrated increased odds of nasogastric tube removal within 4 days of insertion in patients with MBO when corticosteroids were used along with antisecretory therapy (octreotide), as compared with octreotide therapy alone.¹⁶

Octreotide is a synthetic peptide mimicking the natural effects of somatostatin, thereby reducing gastrointestinal secretions and gastrointestinal motility. In multiple studies, octreotide has been demonstrated to reduce vomiting episodes and gastrointestinal symptoms.^{17,18} In addition, quality-of-life scores have improved with the use of octreotide in nonrandomized clinical studies.^{19,20} When compared with anticholinergic therapies, octreotide has demonstrated benefits with respect to gastrointestinal secretions^{13,21} and vomiting.²² For individuals with an expected survival of greater than 4 weeks, a monthly intramuscular depot formulation of octreotide has demonstrated a reduction in gastrointestinal symptoms and vomiting.²³

If medical therapies fail to relieve the clinical symptoms or allow for successful removal of a nasogastric tube, placement of a decompressive gastrostomy tube allows for independent management of gastrointestinal secretions and potentially a resumption of recreational oral intake of liquids or soft foods.^{24,25} A decompressive gastrostomy tube can be placed by using endoscopic, radiologic, or surgical techniques with an acceptable risk profile.²⁶ Studies of decompressive gastrostomy tubes have demonstrated benefits with respect to gastrointestinal symptoms,^{27,28} vomiting episodes,²⁹ and quality of life.³⁰ Although no improvement in overall survival has been demonstrated with decompressive gastrostomy tubes, earlier placement can allow for improved palliation of clinical symptoms.³¹ In the setting of ascites, decompressive gastrostomy tubes can be safely placed following paracentesis or placement of an intraperitoneal drainage catheter, albeit with a higher risk of complications, including leakage and peritonitis.³²

Surgical Management

The initial management of patients presenting with MBO should include medical management to palliate symptoms (nasogastric tube decompression, intravenous fluid resuscitation, antiemetics, and antisecretory medications) and evaluation as to whether surgical or procedural intervention is a viable option. To help determine the level of obstruction, disease burden, and evidence of perforation, a computed tomography (CT) scan of the abdomen and

pelvis should be obtained. In the absence of peritonitis, perforation, or closed-loop obstruction, the patient can be admitted with serial abdominal examinations and continued medical management of the MBO with the hope that it will resolve.

If the obstruction persists and the patient is deemed a suitable surgical candidate, preparation should be made for an operation. When considering surgery, the patient's functional status, primary tumor biology, nutritional status, advanced health directive, and available therapeutic options must all be assessed.

For patients who are surgical candidates, options include resection of the obstructing segment, bowel resection or ostomy for acute perforation, surgical bypass, surgically placed gastrostomy tube, or complete cytoreductive surgery with or without intraperitoneal chemotherapy. It is important to note that indications for an emergency operation in patients with disseminated cancer carries a high incidence of associated morbidity and mortality, with high rates of 30-day mortality and discharge to an institution.^{33,34} This needs to be considered and clearly communicated to patients and their family members when deciding whether to operate in this situation. Early involvement of palliative care providers can be instrumental in providing education and support for patients and their family members during this process.³⁵

Principles of Nutrition Support in MBO Malnutrition is increasingly recognized in the setting of cancer and increases in incidence with metastatic disease.³⁶ Malnutrition is associated with a number of adverse outcomes, including longer hospital stays, postoperative complications, and a reduction in overall survival.^{37,38} After a patient develops MBO, medical therapies are initiated with the aim of reducing clinical symptoms and promoting independent oral intake. Should a patient fail to achieve adequate oral or enteral caloric intake, the decision to proceed with parenteral nutrition (PN) support can be considered.

In the absence of randomized clinical trials in MBO, PN has been evaluated as a means of reversing cancer cachexia and nutritional deficits. However, the potential benefits of improved caloric intake have to be balanced with the risks of PN, including central line infections/thrombosis, electrolyte abnormalities, and concerns about increased tumor growth.^{39,40}

Regarding PN in the management of MBO, retrospective studies provide divergent results with respect to overall survival.^{41–44} However, survival greater than 1 year has been reported in up to 10% of individuals.⁴⁵ Among individuals receiving PN support, a Karnofsky score of greater than 50 has been associated with improved survival,^{46–49} as was receipt of new chemotherapy^{50,51} and radiographic

response to chemotherapy.⁵¹ However, a meta-analysis of survival and quality of life in patients with MBO receiving home PN demonstrated the high associated costs of PN therapy.⁵² A formal Cochrane review for the use of home PN in individuals with inoperable MBO found that the benefits of PN are uncertain. Among 13 observational studies, mean survival ranged from 3 to 1278 days, and adverse effects of therapy occurred in 12% of patients.⁵³

Parenteral nutrition can be considered when the risk of death from starvation or malnutrition is higher than the risk from disease progression. As recommended by the European Society for Clinical Nutrition and Metabolism, PN should be offered if expected survival with tumor progression is longer than 2 to 3 months.⁵⁴ This recommendation is based on the knowledge that micronutrient starvation often results in death within 2 months among healthy individuals and that the mean survival in MBO without nutritional support is approximately 48 days.^{54,55} Additionally, improvements in quality of life have been demonstrated in individuals receiving PN who survived longer than 3 months.⁴⁷

Synthesizing the above studies, we propose the use of PN in select patients with MBO. Factors predicting improved outcomes and survival include the availability of chemotherapeutic options, sufficient functional status (Karnofsky score > 50 or Eastern Cooperative Oncology Group score < 2), and expected survival with tumor progression of greater than 2 to 3 months.

Management of Malignancy-Related Ascites

Portal hypertension related to liver cirrhosis is the most common cause of ascites in the United States. However, in approximately 10% of patients presenting with ascites, the underlying diagnosis is related to cancer, and in some patients ascites is the only manifestation of neoplastic disease. Ascites is commonly caused by ovarian, endometrial, breast, esophageal, gastric, colorectal, lung, pancreatic, hepatobiliary, and primary peritoneal carcinomatosis.⁵⁶ In most cases its pathophysiology is related to peritoneal metastasis resulting in blockage of the draining lymphatic channels and increased capillary permeability. However, it can also be caused by large liver metastasis causing portal hypertension with or without peritoneal disease, or chylous ascites related to lymphoproliferative disorders.

Patients with suspected malignancy-related ascites should undergo a thorough history and physical examination; any previous oncologic disease and/or risk factors should be recorded, and specific signs and symptoms regarding a primary tumor should be investigated. Other conditions that can cause ascites, such as liver cirrhosis or infectious diseases like peritoneal tuberculosis, must be

ruled out. In patients with no known history of cancer, initial tests should include at minimum diagnostic abdominal paracentesis with cytology, esophagogastroduodenoscopy, colonoscopy, contrast-enhanced CT/MRI of the abdomen and pelvis, and pelvic ultrasound (female patients). If no tumor is identified, diagnostic laparoscopy with biopsy and tumor burden assessment (peritoneal cancer index [PCI] score) is encouraged. Together with diagnostic studies, performance and nutritional status must be assessed and advanced directives and goals of care should be discussed. It is recommended that palliative care physicians, medical and surgical oncologists, and other specialists in cancer care (nutritional support specialists, physical therapists, psychologists, etc) be involved early in the management of malignancy-related ascites because of its indication of advanced disease.

The cornerstone of treatment planning for these patients is primary tumor biology because this will define patient prognosis and survival rate. Patients presenting with a favorable tumor biology (appendiceal or ovarian cancer) and good overall status will benefit from more advanced therapeutic modalities, including chemotherapy, cytoreduction surgery, and/or intraperitoneal chemotherapy. On the other hand, patients with aggressive disease (pancreatic or gastric cancer) and poor performance status will probably be treated with palliative chemotherapy, best supportive care, or enrollment in a clinical trial. One supportive measure is the use of diuretics, which should be administered with caution because they may cause systemic blood volume depletion, electrolyte abnormalities, and renal dysfunction.⁵⁷ No randomized trials have evaluated the effectiveness of diuretics for malignancy-related ascites, but their value appears to be more consistent in patients with ascites and portal hypertension (from liver metastasis). Another method to palliate malignancy-related ascites is paracentesis, which is effective in relieving symptoms. The drawbacks are that it requires repeated treatments, leads to recurrent hospitalizations, depletes the patient of protein and electrolytes, and has a risk of peritonitis. The use of peritoneovenous shunts has been described to reduce the need of repeated paracentesis in patients receiving palliative care. Candidates for this procedure have to be selected carefully because mortality and high morbidity have been reported.⁵⁶ In general, the use of peritoneovenous shunts is discouraged in patients with malignancy-related ascites.

Laparoscopic intraperitoneal chemotherapy can offer a palliative pathway for improving ascites. No prospective clinical trials have addressed this method, but a variety of small series have demonstrated its benefit for some patients.^{58,59} Intraperitoneal chemotherapy has been shown to reduce malignant ascites and improve related symptoms, improving quality of life in patients who are not candidates

for extensive cytoreduction. This technique is also minimally invasive, resulting in reduced postoperative stays for patients.⁶⁰ Intraperitoneal chemotherapy regimens differed depending on tumor biology, prior treatments, and toxicity of the intraperitoneal chemotherapy agent.

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