

The Evolving Multimodal Management Plan for Postoperative Ileus

P O I E N D U R I N G P R I M E R



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CME Information

Commercial Support Acknowledgment

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Target Audience

This activity is intended for colon/rectal surgeons, general surgeons, anesthesiologists, health-system pharmacists, medical/surgical nurses, and other health care professionals who manage postoperative ileus (POI).

Educational Activity Learning Objectives

- Upon completion of this activity, the participants should be able to:
- Describe the prevalence, pathophysiology, and defining criteria for postoperative ileus (POI)
- Distinguish evidence-based therapeutic options for the management of POI
- Describe how to implement a multimodal management plan in your institution for patients undergoing bowel resection procedures to improve time to bowel recovery

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Postoperative Ileus

Postoperative ileus (POI) is the temporary impairment of coordinated bowel motility that occurs for a variable period following surgery.^{1,2} POI is most commonly associated with abdominal surgeries, although it may be a consequence of other surgical procedures as well. This transient interruption that prevents effective transit of intestinal contents and/or tolerance of oral intake is considered a normal physiologic response to the stress and tissue injury associated with a surgical procedure and can be expected within the first few days following surgery. Differential recovery of the gastrointestinal (GI) tract occurs following surgery; the small intestine within the first 24 hours, followed by the stomach between 24 and 48 hours, and the colon between 48 and 72 hours.^{3,4} Depending on the duration and severity, POI may be associated with increased postoperative pain, increased nausea and vomiting, prolonged time to resumption of normal diet, delay in postoperative mobilization, increased risk of a variety of other complications, and prolonged hospitalization. The duration of POI is variable, but for many patients undergoing abdominal surgery, untreated POI can last beyond 5 days.⁵ Persistent POI or ileus with delayed onset may occur secondary to an intra-abdominal complication such as an anastomotic leak or abscess.

The etiology of POI is multifaceted. Neurogenic, hormonal, inflammatory, and pharmacologic components all contribute to the pathophysiology of POI.⁶ The systemic response to surgery includes sympathetic nervous system activation, an endocrine stress response, metabolic changes, and immune activation. Laparotomy and bowel manipulation result in sympathetic hyperactivity, which exerts a greater effect on the GI tract than parasympathetic input, contributing to decreased motility. Cytokines and other inflammatory mediators are elicited through the activation of pathways associated with the inflammatory response to surgical manipulation, and these factors also modulate GI motility. Local release of nitric oxide, vasoactive intestinal peptide, and substance P are also thought to contribute to the reduced motility following surgical procedures. Corticotropin-releasing hormone is another element of the stress response that



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contributes to POI. Exogenously-administered opioids, as well as endogenously-generated enkephalins and endorphins have significant direct effects on the GI tract that negatively impact motility. Risk factors for POI include the surgical site (higher incidence associated with abdominal surgeries), extent of bowel manipulation, operation duration, patient characteristics (such as the presence of preexisting GI disease), and opioid use.⁷ According to data from the Health Care Financing Administration for 1999 to 2000 from 150 US hospitals, 8.5% of abdominal surgeries had POI diagnostically coded in medical records.² The reported incidence of POI ranged from 4.1% for abdominal hysterectomy, to 19.2% for small bowel resection procedures. Chang et al evaluated records for 304 consecutive patients who underwent radical cystectomy from 1995 to 2000 and reported 18% with POI. POI was the most common minor complication following surgery for this patient population.⁸ In general, data from such analyses reflect only cases of POI coded in medical records; therefore, the true incidence of POI is likely to exceed these reports.

POI clearly presents an unfavorable burden on the patient, but it is also a burden on the health care system. The duration of hospitalization following abdominal surgery is contingent to a large extent on recovery of GI function. For patients with prolonged POI, longer hospitalization means additional demands on personnel, hospital beds, and associated resources. An economic analysis of POI associated with abdominal surgery reported by Goldstein et al used data from a 2002 national database.⁹ These investigators identified 8.5% (142,026) of the procedures with coded POI. The average length of stay for coded POI was 11.5 days compared with 5.5 days without coded POI, and the mean costs per hospital stay were \$18,877 and \$9,460, respectively. The projected cumulative annual costs for coded POI (total hospitalization and readmission costs) were \$1,464,167,173.



Management of POI

Numerous strategies to limit the extent of POI have been applied to the management of patients at risk for the development of POI (Table 1).²

Table 1: Management Options to Minimize Postoperative Ileus² (Adapted)

Management Option	Benefit
Patient education and optimization	Reduce preoperative anxiety, enhance postoperative recovery
Limited nasogastric tube use	Allows resumption of oral intake
Early oral/enteral/sham feeding	Gastrocolic reflex, stimulation of GI hormones Counteracts catabolism Improves immune function Hastens wound healing
Laxatives	Help to induce bowel movement
Early ambulation	Helps to prevent post-op complications such as thrombosis, atelectasis, pneumonia
Laparoscopic surgery	Reduced manipulation and trauma of the bowel leads to less sympathetic activation and inflammation, reduced pain and associated opioid use, earlier ambulation, reduced need for nasogastric tube, earlier resumption of diet
Epidural anesthesia/analgesia	Synergistically block inhibitory sympathetic reflexes; epidural analgesia reduces systemic opioid requirement thus minimizing opioid-related adverse effects
Opioid-sparing analgesia	Minimizing the use of opioids reduces associated GI effects; anti-inflammatory effects of NSAIDs
Peripheral opioid antagonism	Reverse GI effects of opioids without compromising postoperative analgesia

Nonpharmacologic options include the use of nasogastric (NG) tubes, early feeding, early ambulation, and laparoscopic surgical techniques. Pharmacologic options investigated for the management of POI include epidural anesthesia/analgesia, nonsteroidal anti-inflammatory drugs (NSAIDs), prokinetic agents, and peripherally selective μ -opioid receptor antagonists. The routine use of NG tubes for gastric decompression following abdominal surgery has been challenged by evidence suggesting that NG tubes do *not* hasten the return of bowel function, increase patient comfort, or reduce hospital stay. A meta-analysis by Nelson et al of 33 studies and 5240 patients indicated that patients without routine NG tube use had significantly earlier



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return of bowel function, a significant reduction in pulmonary complications, and a shorter length of hospital stay compared with patients using NG tubes.¹⁰ Anastomotic leak was not different between the 2 groups. Removal of an NG tube also eliminates a barrier to enteral nutrition. Early feeding can stimulate GI motility through the gastrocolic reflex and the stimulation of GI hormones. Kehlet and Holte presented data from 7 studies comparing early feeding vs traditional feeding on the duration of POI.¹¹ Significant but modest reduction of ileus was reported in 3 of the 7 studies. More recently, several meta-analyses of early vs later enteral feeding following GI or gynecologic surgeries reported slightly reduced length of stay with early feeding and supported the safety of early nutrition in these patient populations.^{12,13,14} Importantly, there was no benefit demonstrated by restricting postoperative oral nutrition. Gum chewing (a form of sham feeding) has also been evaluated as a means to stimulate GI motility and reduce the duration of POI. A recent systematic review identified 9 clinical trials with 437 patients in which sugarless gum chewing was compared with standard care following elective intestinal resections.¹⁵ Each of the reported outcome measures was significantly reduced in patients who chewed gum compared with traditional care, including time to bowel movement. Further investigation is required to determine the true efficacy of gum chewing for POI; however, for those individuals who are not at risk of choking due to swallowing difficulties, this inexpensive intervention may be beneficial. Routine postsurgical ambulation has been advocated to minimize a variety of complications (including POI) and is clearly beneficial for the prevention of lower extremity thromboembolism. However, early ambulation alone has not been demonstrated to reduce the duration of POI.^{16,17}

Surgical stress is a primary contributor to POI; therefore, strategies that minimize surgical trauma and bowel manipulation should theoretically reduce the duration or extent of POI. A meta-analysis of 25 studies (3526 patients) of colorectal surgery demonstrated earlier passage of flatus (−1 day), earlier bowel movement (−0.9 days), a significant reduction in postoperative pain as assessed by visual analog scale (first postoperative day), and shortened hospital length of stay (−1.5 days) associated with laparoscopic compared with open surgery.¹⁸ Limitations associated with laparoscopic surgery include the specialized training required for performing



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such surgeries, operative time may be longer for laparoscopic procedures, and not all procedures are amenable to the laparoscopic approach. Implementation of fast-track, multimodal surgical protocols may also minimize some of the previously demonstrated differences between open and laparoscopic surgeries.¹⁹

Intraoperative inhaled or intravenous (IV) anesthetics can temporarily inhibit GI motility. The adjunctive use of epidural anesthesia with general anesthesia may help to minimize these GI effects by blocking inhibitory sympathetic reflexes, preventing the release of afferent pain neurotransmitters, and increasing splanchnic blood flow. Patient-controlled analgesia (PCA) with IV opioids is very effective for the control of postoperative pain, but has direct inhibitory effects on GI motility. Opioids decrease gastric motility, inhibit small and large intestinal propulsion, and have other GI effects that contribute to the abdominal discomfort associated with POI. Numerous studies have demonstrated a reduction in the duration of POI with thoracic epidural analgesia in the postoperative period compared with systemic opioids.²⁰ Intravenous lidocaine has also been utilized for postoperative analgesia. Marret et al have reported an analysis of 8 randomized, controlled trials in which IV lidocaine or placebo was used for control of postoperative pain in patients undergoing abdominal surgery.²¹ In addition to reducing opioid consumption, compared with controls, perioperative/postoperative IV lidocaine was associated with reduced incidence of nausea and vomiting, reduced duration of POI, reduced postoperative pain, and reduced length of hospital stay. The postoperative use of NSAIDs is another strategy to reduce postoperative opioid consumption for patients at risk for the development of POI. A recent randomized, prospective, double-blind study of morphine PCA with or without ketorolac in 102 patients who underwent elective colorectal resections demonstrated an 18.3% reduction in total morphine consumption, earlier passage of flatus, and earlier bowel movement in patients receiving the morphine/ketorolac combination.²²

Prokinetic agents such as metoclopramide and erythromycin have been investigated in several placebo-controlled clinical trials of patients undergoing abdominal surgeries; however, a beneficial effect on the duration of POI has not been demonstrated.^{23,24} Two recent randomized



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studies have evaluated bisacodyl for accelerating GI recovery following elective colorectal surgeries. In a small study (N = 20 patients), use of bisacodyl suppositories on the third postoperative day resulted in significantly earlier defecations relative to placebo controls; however, the trend for a shorter length of hospital stay did not reach significance.²⁵ In a prospective, randomized study of 200 elective colorectal resection patients, oral bisacodyl treatment (started 1 day prior to surgery, and twice daily through postoperative day 3) resulted in significantly earlier defecation by 1 day compared with controls but no difference in tolerance of solid food or hospital length of stay.²⁶ Additional clinical trials are needed to further evaluate the utility of stimulant laxatives for POI.

The GI effects of opioids include inhibition of enteric nerve activity, inhibition of propulsive motor activity, inhibition of secretory activity, and alterations in immune cell function.²⁷ These effects are mediated primarily by opioid binding to μ receptors in the GI tract. Methylnaltrexone (MNTX) and alvimopan are agents that antagonize opioid binding at μ receptors but do not cross the blood-brain barrier; therefore, they do not compromise the analgesic effects of opioids. The efficacy and safety of MNTX for POI was evaluated in a phase 2 study of 65 patients undergoing segmental colectomy.²⁸ Patients were randomized to treatment with MNTX (0.3 mg/kg IV) or placebo within 90 minutes of the end of surgery and then every 6 hours for a maximum of 7 days. Patients treated with MNTX had significantly earlier time to tolerance of full liquids, first bowel movement, and discharge eligibility compared with placebo-treated patients (Table 2).²⁸

Table 2: Methylnaltrexone for POI²⁸

Endpoint	Methylnaltrexone (0.3 mg/kg IV) (N = 33)	Placebo (N = 32)	P-value*
Full liquids	70 ± 9	100 ± 19	0.05
1st BM	97 ± 6	120 ± 10	0.01
GI recovery	124 ± 9	151 ± 16	0.06
Discharge eligible	119 ± 7	149 ± 17	0.03
Actual discharge	140 ± 6	165 ± 16	0.09



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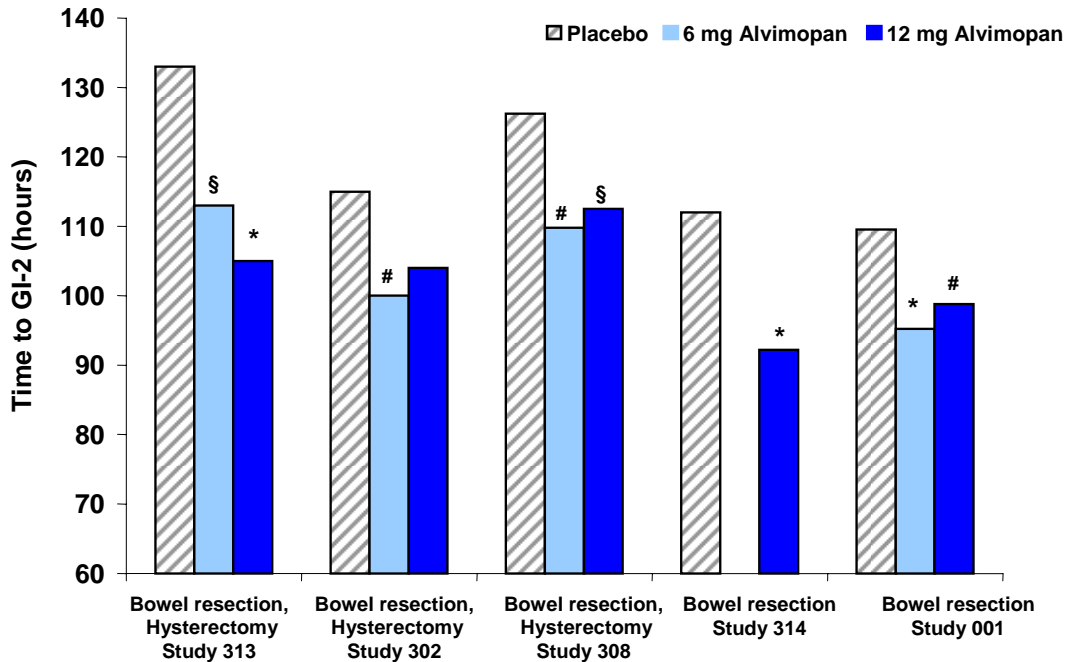
Values represent mean time in hours \pm standard error; *1-sided

Phase 3 trials of MNTX for POI in patients undergoing segmental colectomy or ventral hernia repair did not demonstrate an advantage for the treatment group.²⁹⁻³⁴ In studies of opioid-induced constipation, adverse events associated with MNTX treatment (subcutaneous administration 0.15 mg/kg) included abdominal pain, flatulence, and nausea.³⁵ MNTX was approved in 2008 by the FDA for opioid-induced constipation to help restore bowel function in patients with late-stage, advanced illness who are receiving opioids on a continuous basis to help alleviate their pain.³⁶

Alvimopan has been studied for the treatment of POI in multiple phase 3 studies and was approved by the FDA in 2008 to accelerate the restoration of normal bowel function in adult patients who have undergone partial large or small bowel resection surgery.^{5,37-41} Patients were randomized to treatment with alvimopan (6 or 12 mg) or placebo, with the first dose given preoperatively between 5 hours and 30 minutes prior to surgery, and postoperatively twice a day up to 7 days or until hospital discharge. All patients were managed with a standardized multimodal accelerated care pathway that included early ambulation, early oral feeding, and postoperative removal of NG tubes. Patients in the North American alvimopan studies were scheduled for postoperative analgesia with opioid-based PCA (epidurals and NSAIDs were excluded). Study 001 (conducted in Europe and New Zealand) differed with respect to postoperative analgesia; opioid-based IV PCA was not required and nonopioid analgesia was allowed. In study 001, less than half of the patients received PCA morphine, and with the use of NSAIDs and other nonopioid analgesics, the total morphine doses were less than half reported in the US studies. Endpoints for the phase 3 studies included indices of GI recovery (GI-2, GI-3), time to discharge order written (DOW), and safety. GI-3 is the later time of first tolerated solid food and the time for first flatus or bowel movement; GI-2 is the later time of first tolerated solid food and the time to first bowel movement. Figure 1 presents GI recovery results from 5 alvimopan studies.^{5,37-40} Studies 313, 302, and 308 included both bowel resection and hysterectomy patients, whereas data from studies 314 and 001 are for bowel resection patients only.



Figure 1: Alvimopan Phase 3 Studies: GI Recovery



* $P < 0.001$; # $P < 0.01$; § $P < 0.02$; Studies 313, 302, 308 include bowel resection and hysterectomy; studies 314, 001 bowel resection only; all studies conducted in North America except 001, which was conducted in Europe and New Zealand. GI-2: later time of first tolerated solid food and time for first bowel movement

Treatment with alvimopan (both 6- and 12-mg doses) resulted in a reduction in time to GI-2 compared with placebo. Pooled retrospective analysis of bowel resection patients only from these phase 3 alvimopan studies (studies 313, 302, 308, 314, and 001) demonstrated a significant reduction in GI recovery for alvimopan (12-mg dose for this analysis) compared with placebo (Table 3).⁴²

Table 3: Alvimopan Bowel Resection Pooled Analysis⁴²

Endpoint	Placebo Recovery (hours, 95% CI)	Alvimopan 12 mg Recovery (hours, 95% CI)	Difference in Recovery (hours)	Hazard Ratio, P value
GI-2	117.9 (114.2, 121.5)	100.9 (98.0, 103.7)	17	1.44, $P < 0.001$
GI-3	105.2 (101.8, 108.6)	92.5 (89.8, 95.2)	12	1.32, $P < 0.001$



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Data from 5 randomized, double-blind phase 3 studies (313, 302, 308, 314, and 001). Of the modified intent-to-treat population for the 5 trials (N = 2949), 1877 patients underwent bowel resection and were treated with either alvimopan 12 mg or placebo; the first dose was given preoperatively between 5 hours and 30 minutes prior to surgery, and postoperatively BID up to 7 days or until hospital discharge. All patients were managed with a standardized multimodal accelerated care pathway that included early ambulation, early oral feeding, and postoperative removal of NG tubes. The mean patient age was 61.4 ± 14.0 years. One hundred thirty-six patients (7.2%) underwent small bowel resection, and 1741 (92.8%) underwent large bowel resection. The overall mean duration of surgery was 2.2 ± 1.1 hours.

GI-3: later time of first tolerated solid food and time for first flatus or bowel movement; GI-2: later time of first tolerated solid food and time for first bowel movement. Hazard ratio > 1.0 favors alvimopan vs placebo.

Pooled retrospective analysis of bowel resection patients (studies 302, 308, 313) by Delaney et al demonstrated a significant reduction in readiness for hospital discharge and time to discharge order written for alvimopan compared with placebo ($P < 0.001$ for both endpoints, both 6- and 12-mg doses of alvimopan).⁴³ Time to DOW was ≥ 16 hours earlier for patients treated with alvimopan (both doses) compared with placebo.

Treatment with alvimopan was also associated with a reduction in overall POI morbidity in bowel resection patients compared with controls.^{39,43} Postoperative NG tube insertion and early postoperative bowel obstruction or POI as serious adverse events were significantly reduced in patients treated with alvimopan (both doses) compared with placebo.⁴³ The proportion of patients requiring hospital readmission for POI was reduced for the alvimopan treatment groups compared with placebo (8.0% for placebo; 3.3% for alvimopan 6 mg; 3.1% for alvimopan 12 mg).⁴³

The worldwide alvimopan safety POI population includes 1650 patients treated with alvimopan from 9 placebo-controlled clinical trials.⁴⁴ This patient population ranged from 19 to 97 years old, was 32% male, 83% Caucasian, and 999/1650 (61%) underwent bowel resection surgeries. Treatment-emergent adverse events that were reported with a greater frequency in patients treated with alvimopan include anemia, constipation, dyspepsia, flatulence, and hypokalemia.



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Further investigation is required to evaluate the efficacy of alvimopan in patients who receive epidurals or NSAIDs for postoperative analgesia.

Alvimopan has also been studied in patients taking opioids for chronic noncancer pain. A 12-month study in which patients were treated with either alvimopan (0.5 mg) or placebo twice daily reported an imbalance in the number of reports of myocardial infarction in patients treated with alvimopan (1.3%) compared with placebo (0).⁴⁵ Following thorough evaluation of these safety data, the FDA concluded that the serious cardiovascular adverse events occurred in patients at high risk for cardiovascular disease; that myocardial infarction did not appear to be linked to the duration of dosing; this serious adverse event was not observed in other alvimopan studies (including POI studies in bowel resection patients treated with 12 mg twice daily for up to 7 days); and a causal relationship was not been established between alvimopan and myocardial infarction. In keeping with a risk-management program, alvimopan is only available to hospitals that enroll in the Entereg Access Support and Education (E.A.S.E.TM) program.⁴⁴ The following is required of participating hospitals: a) limit use of alvimopan to short term, inpatient use; b) patients will not receive more than 15 doses of alvimopan; c) alvimopan will not be dispensed to patients following hospital discharge; and d) the hospital will not transfer alvimopan to unregistered hospitals.

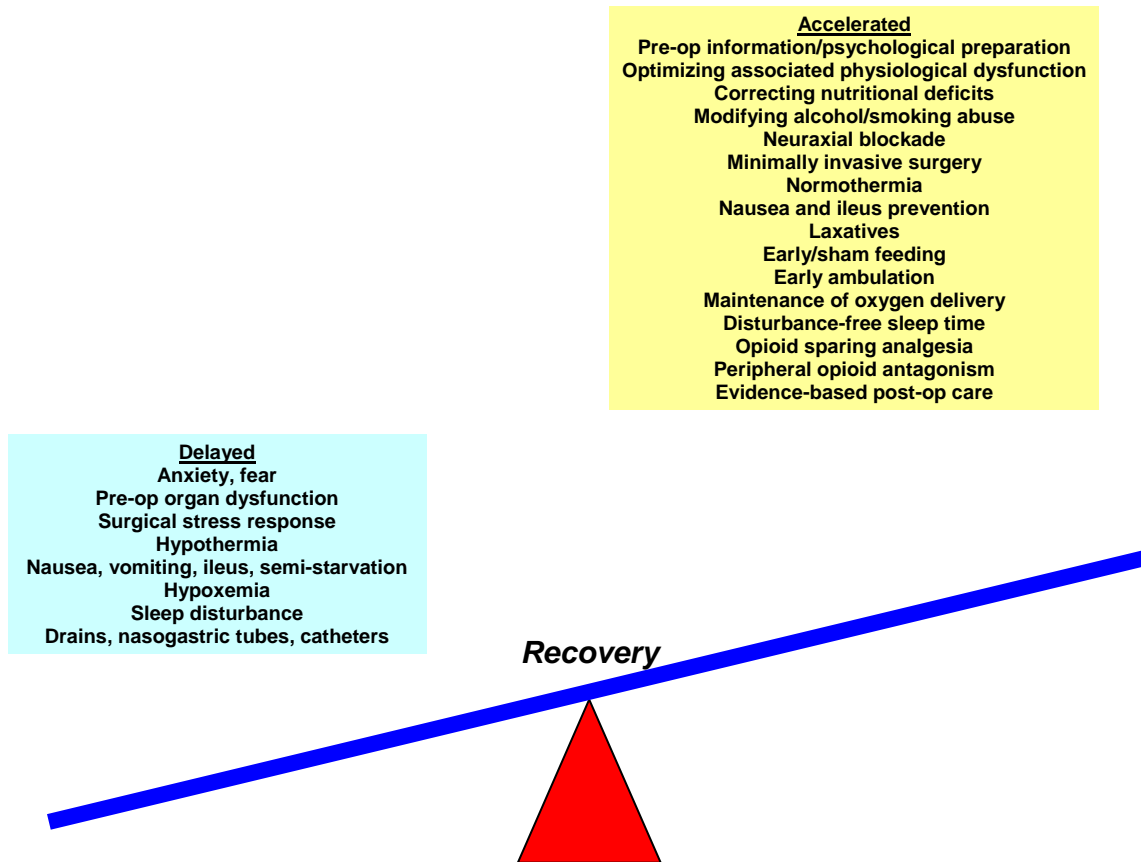
Multimodal Perioperative Management of POI

Numerous factors can contribute to either delayed or accelerated recovery following elective surgery (Figure 2).⁴⁶



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Figure 2: Factors That Impact Recovery Following Abdominal Surgery⁴⁶ (Adapted)



With the multifactorial etiology of POI, a multimodal (fast-track) approach incorporating several individual evidence-based management strategies applied simultaneously can help to accelerate recovery and reduce the duration and morbidity of POI. The goals of a multimodal approach for patients at risk for the development of POI are to enhance the recovery of bowel function, reduce POI-related morbidity, improve patient outcomes, and reduce the length of hospital stay.

Surgeons, nurses, pharmacists, anesthesiologists, and support personnel can participate in the proactive prevention and treatment of POI. Working together as an interdisciplinary team is integral to the successful implementation of a multimodal approach for patients undergoing bowel resection procedures. The leader of such a process may be a surgeon or a team (such as a surgeon and an anesthesiologist), but every member of the interdisciplinary team is vital. Prior to the initiation of a program for a specific procedure, team meetings must be organized to educate all participants on the importance of the multimodal approach and provide training as needed.



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Protocols, care plans, and standard order sheets should be developed for specific procedures. Preoperative components of a multimodal approach may include patient education; stabilization of coexisting diseases; optimization of patient comfort (minimize anxiety); ensuring optimal hydration/electrolytes; and prophylactic therapy for nausea, ileus, pain, etc. Intraoperative efforts to minimize the surgical stress response may include laparoscopic surgery (if indicated), the use of local or regional anesthesia, and multimodal analgesia. Postoperative multimodal components that facilitate recovery include prompt removal of NG tubes, early oral/enteral/sham feeding, opioid-sparing analgesia, peripheral opioid antagonism where appropriate, and early ambulation. With many individuals involved in the care of patients as they progress from preop to the operating room to the postanesthesia care unit to the floors, it is essential to have continuity and a systematic transfer of information. An example of postoperative orders for abdominal surgery patients from an institution with a standardized, multimodal approach is included in Table 4.⁴⁷

Table 4: Example of Standard Postoperative Orders for Abdominal Surgery Patients – A Multimodal Approach

GENERAL CARE:

- CBC on POD #1, POD #3, and every 2nd day thereafter while on prophylactic heparin, unless otherwise indicated
- BMP on POD #1, and POD #3, unless otherwise indicated. Every 2nd day thereafter unless specifically indicated
- Heparin 5000 IU sc tid, pneumatic antiembolism stockings
- Prophylactic antibiotics are not routinely continued after surgery, except for specific therapeutic indications (doses in OR only)
- Ambulate 5 times in hallways every day
- Remove Foley on POD #1 for laparoscopic and POD #2 for open cases

DIETARY MANAGEMENT

- Chewing gum, 1 stick x 60 minutes tid
- Clear liquids given as tolerated after surgery
- Boost[®] nutritional drink, 1 can twice daily po
- No dietetic consult unless specifically clinically indicated
- Soft diet on POD #1 for laparoscopic and POD #2 for open cases

MEDICATIONS:

- Open surgery: morphine or hydromorphone PCA



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- Laparoscopic surgery: Morphine 1–2 mg iv prn or PCA
 - Gabapentin 300 mg po tid for 2 days (off-label use)
 - Ketorolac 30 mg iv q6h around the clock for open and laparoscopic patients, except in those with renal dysfunction, hypertension, elderly, etc as per manufacturers' guidelines
 - Diclofenac 50 mg tid as supplement on discharge, same restrictions
 - Use hydroxyzine 25 mg IM q6 hours prn (generally for first 24–48 hours), or metoclopramide 10 mg iv q6h (generally after first 24–48 hours) as first line treatments for nausea
 - Zolpidem 5 mg or temazepam 15 mg po qhs from POD #1
 - Hydrocortisone 50 mg iv tid for patients with hx of steroids within 6 months
 - Avoid dolasetron in postoperative patients, and discontinue if ordered by another service, unless there is a specific indication
-
- POD #1: Hold morphine except for break through pain. Start acetaminophen/codeine, 1–2 q4–6 hours prn (write for oral analgesia to be given 30–60 minutes prior to stopping PCA or epidural)

STOMA CLOSURE PATIENTS:

- POD #1: GI soft as tolerated
- POD #1: Hold morphine except for break through pain. Start acetaminophen/codeine, 1–2 q4–6 hours prn (write for oral analgesia to be given 30–60 minutes prior to stopping PCA or epidural)

OPEN CASES:

- POD #1: Full liquids as desired by patient
 - POD #1: chewing gum, 1 stick x 60 minutes tid
 - POD #2: D/C Foley in am
 - POD #2: D/C GI soft as tolerated
-
- POD #2: Hold morphine except for break through pain. Start oxycodone 5/325, 1–2 q4–6 hours (write for oral analgesia to be given 30–60 minutes prior to stopping PCA or epidural)
 - POD #2: D/C suction drains unless specific reason for use

POSTOPERATIVE CARE ON FLOOR:

- NG tube generally inserted for 2 or more episodes of vomiting
- Postoperative fever is generally not evaluated for the first 48–72 hours, unless clinically indicated. Encourage incentive spirometry, and check that it is being done properly
- Unless Hb < 7 g, or HCT < 21, PRBC transfusions should be discussed with the staff surgeon



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DISCHARGE CRITERIA & INSTRUCTIONS:

- Discharge criteria:
 - Tolerating 3 meals without nausea or vomiting
 - Pain adequately controlled
 - Ambulating independently
 - Adequate support at home
 - DCR 2007 criteria
- If not removed prior to discharge, staples are to be removed by local nurse (home care), or have the patient return to the office. Local doctors should not be asked to remove staples
- Patients are seen in the office 6 weeks postoperatively
- Patients with defunctioning ileostomy and IPAA/CAA need gastrograffin enema (GGE) order for morning of office visit
- Ileostomy patients get Metamucil[®] instructions, and loperamide 2 qac/qhs prn, #240
- Steroid taper: prednisone 20 mg per day, and wean 5 mg per week, unless symptomatic

Abbreviations: CBC: complete blood count; POD: postoperative day; BMP: basic metabolic panel; PAS: pneumatic antiembolism stockings; PCA: patient controlled analgesia; HCT: hematocrit; PRBC: packed red blood cells; IPAA: ileal pouch-anal anastomosis; CAA: coloanal anastomosis

Disclaimer: The protocols in this care plan are provided as an example from Case Western Reserve University. No responsibility is assumed by the authors or those who have provided this guideline.

Successful implementation of a multimodal approach requires organization, time, communication, and commitment. Objective program evaluation and monitoring improvement should be part of a multimodal program and a shared learning experience for the multidisciplinary team. Improvement may be reflected in measures of adherence/compliance with new protocols, collective analysis of the frequency of POI, the time to tolerance of food, time to first bowel movement, general measures of patient satisfaction, and cost. It should be pointed out that while the focus of the current discussion relates to POI, implementation of a multimodal pathway is associated with benefits in other endpoints, such as pulmonary function, fatigue, cardiovascular response to exercise, preservation of body composition, risk of infection, morbidity, patient satisfaction, and length of hospital stay.^{46,48,49}



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Several studies have documented the success of a multimodal/fast-track approach for colorectal surgeries with reduced duration of POI and length of hospital stay.^{46,49-55} Wind et al presented results of a systematic review of enhanced recovery programs for colonic surgeries that included 6 studies (N = 512 patients; 3 randomized, controlled trials, and 3 controlled clinical trials).⁵⁶ Compared with traditional care, fast-track/multimodal protocols were associated with a reduction in hospital stay (-1.56 days; 95% CI, -2.61-0.50; $P = 0.004$), less morbidity (relative risk = 0.54; 95% CI, 0.42-0.69; $P < 0.001$), and earlier time to first bowel movement and tolerance of normal diet ($P < 0.05$). Readmission rates were not different between the fast-track (range: 0%-21%) and traditional care (range: 0%-20%) approaches ($P = 0.52$). Despite such success, according to the results of a multinational survey, evidence-based strategies that are part of a multimodal approach following colonic surgeries are not consistently applied clinically in the United States and Europe.⁵⁷ Among the barriers to the implementation of multimodal protocols are lack of awareness, skepticism, institutional limitations, time involved, insufficient expertise or staff support, reimbursement or liability issues, and the engagement of a multidisciplinary team.⁴⁹

As mentioned previously, POI is associated with a significant economic burden. Prolonged hospitalization is accompanied by costs related to occupancy of beds, nursing care, equipment, supplies, laboratory, and pharmaceutical resources. Implementation of multimodal/fast-track programs that reduce the length of stay for patients undergoing bowel resection procedures by even 1 to 2 days may result in tremendous cost savings. Although the cost of initial postoperative days exceeds that of the days prior to discharge, cumulative savings associated with accelerated recovery pathways could be significant. In a small study by Bosio et al, open colectomy with standard care was compared with laparoscopic colectomy and fast-track/multimodal care.⁵⁸ Components of the multimodal pathway included preoperative patient instruction, early ambulation and diet, avoidance of NG tubes, limited use of drains, and transition from IV PCA to oral NSAIDs supplemented with narcotics. Laparoscopic colectomy/fast-track care was associated with a significantly shorter length of stay (3.6 vs 8.3 days; $P < 0.001$) and significantly lower direct costs (\$4,993 vs \$11,383; $P < 0.001$).



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Interdisciplinary collaboration is at the heart of the multimodal approach. Future improvements of this strategy will include better identification of patients at risk for the development of POI, patient-centered care, pharmacologic modification of the stress response to minimize the negative effects on GI motility, multidisciplinary post-anesthesia care units, updated clinical pathways, and incorporation of services to facilitate postsurgical patient rehabilitation.⁵⁹ Such improvements should help to minimize the burden of POI for the patient, but also reduce the burden of POI on the health care system.



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**The Evolving Multimodal Management Plan for Postoperative Ileus
 CME Credit Attestation/Evaluation Form**

Instructions:

In order to obtain *AMA PRA Category 1 Credits™* participants are required to:

- (1) Read the learning objectives and review the activity in its entirety.
- (2) Complete the CME Credit Attestation/Evaluation Form and mail or fax it to:
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Activity Release Date: September 10, 2009

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Indicate the number of credits you are claiming _____ (May not exceed 1 credit)

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I certify that I have completed this CME activity as designated.

Degree(s): MD/DO PharmD/RPh NP PA RN Other _____

Specialty: Pharmacist Surgeon Nurse Anesthesiologist Other _____

BIAS, FAIR BALANCE

Was this activity fair, balanced, objective, and free from commercial bias? Yes No

If no, please state reason(s) _____



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PRACTICAL APPLICATION

4 = strongly agree; 3 = agree; 2 = disagree; 1 = strongly disagree

- (a) ___ What I learned in this activity has increased my understanding of postoperative ileus
- (b) ___ What I learned in this activity will improve my ability to manage patients at risk for developing postoperative ileus
- (c) ___ What I learned in this activity will result in an improvement in my patients' health

Do you intend to make changes or apply new information to your practice as a result of this activity?

- ___ Yes, I plan to make changes*
- ___ I'm not sure, but I'm considering changes*
- ___ No, I already practice these recommendations

*If yes or you are considering changes, please check off/list what thing(s) you intend to do differently or incorporate into your clinical practice as a result of this educational activity

- ___ Work with multidisciplinary team members to implement a multimodal management plan for patients undergoing bowel resection procedures
- ___ Incorporate evidence-based therapeutic options for the management of postoperative ileus
- ___ Other _____

BARRIERS

What are the top 3 barriers that might inhibit your ability to incorporate any of the above changes into your clinical practice?

- 1. _____
- 2. _____
- 3. _____

DEMOGRAPHIC QUESTIONS

How did you hear about this CME activity?

- Downloaded from www.POIeducation.org
- Received copy from colleague
- Other: _____

Number of years in practice: < 5 6–10 11–15 16–20 21–25 > 25

What percent of your patients are affected by postoperative ileus?

- < 5% 5–10% 11–20% > 20%

ACTIVITY EVALUATION 4 = strongly agree; 3 = agree; 2 = disagree; 1 = strongly disagree

Upon completion of this activity, I will be able to:

- (a) ___ Describe the prevalence, pathophysiology, and defining criteria for postoperative ileus (POI)
- (b) ___ Distinguish evidence-based therapeutic options for the management of POI
- (c) ___ Describe how to implement a multimodal management plan in my institution for patients undergoing bowel resection procedures to improve time to bowel recovery

Please rate the overall content presented at this activity: Too basic Appropriate Too complex

ONGOING UNMET EDUCATIONAL NEEDS

Recommendations for future topics in this disease area: _____



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Posttest

1. Prolonged postoperative ileus is associated with:
 - A. Abdominal pain, nausea, and vomiting
 - B. Delayed passage of flatus and stool
 - C. Prolonged hospitalization
 - D. Abdominal pain, nausea, vomiting, and delayed passage of flatus and stool
 - E. All of the above
2. Which of the following contributes to the pathogenesis of POI?
 - A. Opioids—endogenous and exogenous
 - B. Inflammatory mediators
 - C. Sympathetic activation
 - D. All of the above
 - E. None of the above
3. According to data from the Health Care Financing Administration for 1999 to 2000, the incidence of POI for common abdominal surgeries ranged from 4.1% to 19.2%. Which of the following procedures is associated with the highest incidence of POI?
 - A. Small or large bowel resection
 - B. Cholecystectomy
 - C. Appendectomy
 - D. Abdominal hysterectomy
 - E. Nephroureterectomy
4. Which of the following statements is true regarding nonpharmacologic management options for POI?
 - A. Postoperative nasogastric tube decompression improves patient comfort and hastens the return of bowel function
 - B. Early mobilization has direct effects on the GI tract and reduces POI
 - C. Meta-analyses/systematic reviews of early feeding and gum chewing have demonstrated reduced length of hospital stay following GI surgeries
 - D. Restricting perioperative fluid intake reduces cardiovascular stress
 - E. All of the above
5. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) for POI is beneficial because:
 - A. NSAIDs block inhibitory sympathetic reflexes
 - B. Opioid-sparing analgesia can help to minimize the inhibitory effects of opioids on GI motility
 - C. Prokinetic properties of NSAIDs reduce the duration of POI
 - D. NSAIDs have a higher affinity for the κ -opioid receptor than morphine
 - E. Clinical trials demonstrate a reduction in nausea and vomiting following bowel resection procedures



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6. Why are peripheral-acting μ -opioid receptor antagonists beneficial for postoperative ileus?
- A. They are active in the gastrointestinal tract and also cross the blood-brain barrier
 - B. They directly stimulate segmental contractions in the large intestine
 - C. They reverse GI opioid side effects without compromising analgesia
 - D. They have a lower affinity for the μ -opioid receptor than morphine
 - E. They stimulate release of nitric oxide from the muscularis externa
7. Which of the following pharmacologic agents is FDA approved to accelerate the restoration of normal bowel function in adult patients who have undergone partial large or small bowel resection surgery?
- A. Metoclopramide
 - B. Lubiprostone
 - C. Erythromycin
 - D. Alvimopan
 - E. Tegaserod
8. Which of the following is typically a component of a multimodal accelerated care pathway?
- A. Early ambulation
 - B. Early oral feeding
 - C. Limited postoperative use of nasogastric tubes
 - D. Opioid-sparing analgesia
 - E. All of the above