American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Gastrointestinal Dysfunction Within an Enhanced Recovery Pathway for Elective Colorectal Surgery

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Abstract

The primary driver of length of stay (LOS) following bowel surgery, particularly colorectal surgery, is the time to return of gastrointestinal (GI) function. Traditionally, delayed GI recovery was thought to be a routine and unavoidable consequence of surgery, but this has been shown to be false in the modern era owing to the proliferation of Enhanced Recovery protocols (ERP). However, impaired GI function is still common following colorectal surgery and the current literature is ambiguous with regard to the definition of postoperative GI dysfunction (POGD), or what is typically referred to as *ileus*. This persistent ambiguity has impeded the ability to ascertain the true incidence of the condition and study it properly within a research setting. Furthermore, a rational and standardized approach to prevention and treatment of POGD is needed. The 2nd Perioperative Quality Initiative (POQI) brought together a group of international experts with the objective of providing consensus recommendations on this important topic with the goal to: 1) develop a rational definition for POGD that can serve as a framework for clinical and research efforts, 2) critically review the evidence behind current prevention strategies and provide consensus recommendations, and 3) develop rational treatment strategies that take into account the wide spectrum of impaired GI function in the postoperative period.

Recommendations

Definition and Incidence

1. *We recommend foregoing the traditional definition of ileus for a more functional definition of postoperative gastrointestinal dysfunction (POGD) that takes into account the wide spectrum of signs, symptoms, and associated clinical implications.*
2. *We recommend the implementation of enhanced recovery protocols (ERP) in order to reduce the time to recovery of gastrointestinal function after colorectal surgery to an average of 1-2 days.*

Prevention of Postoperative Gastrointestinal Dysfunction

3. *We recommend active strategies to minimize the use of opioids while maintaining adequate pain control through the use of multimodal analgesia*
4. *We recommend the maintenance of euvolemia along with a normal salt and electrolyte balance in the perioperative period*
5. *We strongly recommend against the routine use of prophylactic nasogastric tubes*
6. *We recommend the use of minimally invasive surgery when appropriate*
7. *We recommend using Alvimopan if opioid-based analgesia is used; (its use could also be considered within an opioid restricted ERP in colorectal surgery.)*
8. *We recommend the use of a standardized risk-based strategy for postoperative nausea and vomiting (PONV) prophylaxis*

9. *We strongly recommend immediate resumption of eating and drinking following colorectal surgery*
10. *We recommend the use of a combined isosmotic mechanical bowel prep with oral antibiotics in elective colorectal surgery*
11. *We recommend consideration of coffee and gum chewing as adjuncts to ERPs in promoting recovery of GI function*

Treatment of Postoperative Gastrointestinal Dysfunction

12. *We recommend placement of an NGT to relieve intractable nausea and vomiting with abdominal distension.*
13. *We recommend opioid minimization, ambulation, rational fluid replacement maintaining euvolemia, electrolyte repletion, and gum chewing.*
14. *We recommend consideration of radiographic imaging with computed tomography (CT) if POGD persists beyond the 7th postoperative day or at any time based on concern for secondary causes*

Introduction

The primary driver of length of stay following bowel surgery, particularly colorectal surgery, is the time to return of gastrointestinal (GI) function. Traditionally, delayed gastrointestinal recovery was so commonplace in patients undergoing bowel surgery, that it was considered an unavoidable consequence of surgery and routine postoperative nasogastric tubes and nothing per os were ubiquitous after intestinal surgery. These practices have been challenged in the modern era owing to the proliferation of Enhanced Recovery protocols (ERP).[1] As a result, there has been a paradigm shift in traditional perioperative management towards early initiation of oral intake regardless of the perceived return of GI function. This has led to significant improvements in postoperative outcomes, including reduced length of stay (LOS) and overall complication rates. However, GI dysfunction remains one of the most common morbidities following colorectal surgery and the current literature is ambiguous with regard to the definition of postoperative GI dysfunction, or what is typically referred to as *ileus*. This persistent ambiguity precludes the ability to ascertain the true incidence of the condition and study it properly within a research setting.[2]

Although the effects of bowel surgery on postoperative GI function (POGF) are multifactorial and complex, a rational standardized approach focused on the known mediators can facilitate early restoration of GI function following colorectal surgery. The 2nd Perioperative Quality Initiative (POQI) brought together a group of international experts with the objective of providing consensus recommendations on this important topic. The POQI 2 Postoperative GI Dysfunction (POGD) group sought to: 1) develop a

rational definition for POGD that can serve as a framework for clinical and research efforts, 2) critically review the evidence behind current prevention strategies and provide consensus recommendations and 3) develop rational treatment strategies that take into account the wide spectrum of impaired GI function in the postoperative period while maintaining a normal physiologic state.

Methods

Expert Group

The Perioperative Quality Initiative (POQI) is a previously-described collaborative of diverse international experts in anesthesia, nursing, nutrition, and surgery tasked to develop consensus-based recommendations in topics related to enhanced recovery.[3,4] The participants in the POQI consensus meeting were recruited based on their expertise in the principles of enhanced recovery after surgery and perioperative medicine. Twenty-three experts from North America and Europe met in Stony Brook, New York on December 2-3, 2016. Utilizing a modified Delphi method, an iterative process was undertaken whereby the group initially developed a list of questions related to the topic of gastrointestinal recovery following colorectal surgery, performed a literature review, and conducted a series of group sessions with structured presentation and feedback until consensus was achieved. This culminated in this consensus document. The specific wordings of the recommendation statements in this document are based upon prior work and detailed elsewhere.[4] Of note, we have chosen to follow the process detailed by the National Institute for Health and Care Excellence (NICE).[5]

Process

Over a 3-month period prior to the in-person meeting, the organizers generated topics of interest and assigned expert members of the panel to each topic subgroup. The subgroups were responsible for developing a list of relevant questions and conducting an extensive literature review prior to the meeting. During the opening plenary session, the subgroups presented their questions to the entire POQI 2 workgroup, soliciting

feedback and discussion. Over the course of the two days in ensuing group meetings and plenary sessions, the subgroups refined the relevant questions into a series of consensus statements, which were reviewed and modified by the entire POQI workgroup. (Table 1) Thereafter, this summary document was generated, encompassing feedback and modifications from all the experts in the POQI workshop.

Definition and Practical Implications

#1 - We recommend foregoing the traditional definition of ileus for a more functional definition of postoperative gastrointestinal dysfunction that takes into account the wide spectrum of signs, symptoms, and associated clinical implications.

The word ileus dates back to classical antiquity and is derived from the Latin word *īleos* meaning *"severe colic" and* the Greek word *eilein* "to turn, squeeze". Throughout much of recorded history, ileus described the clinical presentation of abdominal pain, obstipation, and fecal vomiting and was most classically associated with what is known today as volvulus.[6] As the ability to study the pathologic basis of disease flourished in the 18th century (owing to the propagation of the autopsy), the term was largely abandoned in exchange for pathological based terms such as intussusception and obstruction. It was not until the latter half of the 20th century that ileus became synonymous with a "non-mechanical obstruction," due to the lack of peristalsis.[6] As it pertained to the postoperative period, ileus was thought to represent an unavoidable consequence of bowel manipulation during surgery.[2]

There are various terms used in the modern literature to describe ileus, including pathologic or paralytic ileus, prolonged ileus, primarily ileus, and secondary ileus; ileus can also be defined as gastric, small intestinal, or colonic (which may be distinct from acute colonic pseudo-obstruction).[7,8] However, there is a lack of consistency between these various definitions. In truth, impairments in POGF occur along a spectrum ranging from transient postoperative nausea and vomiting to severe derangements in GI motility that may be secondary to life-threatening underlying pathologies, such as anastomotic leak. This variability makes it difficult to define abnormalities in POGF within the singular term of 'ileus,' particularly with regard to the incidence and the clinical implications.

In light of this clinically-relevant problem, we sought to develop a classification scheme that adequately identifies the spectrum of impaired POGF in the postoperative period to serve as a framework for discussion, structured measurement of clinical outcomes, and future research endeavors. In developing this scheme, we categorized the patients into three basic categories: Normal, postoperative gastrointestinal intolerance (POGI), and postoperative GI Dysfunction (POGD) In order to classify the functional state of the GI tract of patients, we created the I-FEED scoring system, which stands for: **I**ntake, **F**eeling nauseated, **E**mesis, physical **E**xam, and **D**uration of symptoms. It attributes points for each of the five components based on the clinical presentation of the patient (see Figure 1). The scoring system was devised to include: 1) the most important aspects of the clinical presentation of the range of postoperative GI physiology, 2) the

factors that most often drive management decisions in the postoperative period, and 3) the levels of dysfunction that correlate with increased complications and health care costs. Of note, the absence or presence of stool and flatus are not included within the I-FEED scoring system. This was purposely omitted because the group felt that was less important than the criteria in the scale. Many in the group recounted experiences with patients that continued to flatus or stool, yet had severe abdominal distention and bloating with severe intolerance to oral intake indicative of POGD. Similarly it is not uncommon for patients to be completely tolerant of oral intake in the absence of nausea or bloating prior to the return of flatus or bowel function, especially after the use of a mechanical bowel preparation.

Normal (I-FEED score 0 – 2)

Patients in this category are tolerating an oral diet without symptoms of bloating, but some may experience transient postoperative nausea and vomiting (PONV). PONV is common within the first 24 – 48 hours following surgery, with reported incidences of 30% in all patients and up to 80% in high-risk patients.[9] The pathophysiology of PONV is complex and not fully elucidated, but seems to be regulated by the chemoreceptor trigger zone and the nucleus tractus solitarius within the brainstem. It is stimulated by vagal afferents in the GI tract and circulating metabolites. Opioids, volatile anesthetics, anxiety, motion, and visceral manipulation can all trigger PONV. The major risk factors for PONV are well described from numerous prospective trials: female gender, non-smoking history, prior history of PONV or motion sickness, and use of opioids.[9-11] Because PONV is common following surgery, self-limited, normally able to be treated

with multi-modal pharmacologic agents, and does not typically interfere with clinical progression, it was included within the I-FEED scoring system “normal” group.

Postoperative GI Intolerance (POGI: I-FEED score 3 – 5)

In contrast to the patients without symptoms or with early PONV, these patients typically do well initially, but then start feeling nauseated after postoperative day two. They typically present with nausea, small volume non-bilious emesis (≤100mL), and may feel bloated. However, in the majority of cases, they continue to tolerate clear liquids and do not require a nasogastric tube (NGT) for decompression. They may or may not be passing stool or flatus. This feeling generally resolves within 1-2 days without significant intervention and is not associated with worse outcomes or increased healthcare costs.[2]

The pathogenesis of POGI is multifactorial.[2,12] Surgical trauma and bowel manipulation have been shown in animal models to induce a local gut inflammatory response through activation of multiple pathways, which can lead to gut injury, bowel wall edema, and dysmotility.[13-16] Surgery can also influence gut motility through neural reflexes via vagal and splanchnic routes. Additionally, hypoperfusion, disturbances of acid-base status, glucose or electrolyte imbalance, as well as both hypothermia and hyperthermia can have negative effects of gut motility.[17-19] Beyond surgical etiologies, opioids are the main contributors to anesthesia-induced gut dysmotility, although other commonly used drugs such as inhalational anesthetics, clonidine, and adrenergic agonists can contribute as well.[2,20]

Postoperative GI Dysfunction (I-FEED score ≥ 6)

POGD is the most severe form of impaired GI recovery and consistent with what is considered an ileus by most clinicians. As opposed to the two previously described groups, these patients develop abdominal distention with tympany on physical exam, nausea that is resistant to anti-emetics, and large volume (> 100 mL) bilious emesis. This is associated with an inability to tolerate any oral intake, requiring intravenous fluid (IVF) administration to maintain hydration and NG tube decompression to prevent aspiration. As opposed to POGI, which is general self-limited and not necessarily associated with prolonged LOS, POGD is associated with prolonged LOS, increased surgical complications, and increased health care costs.[21-24] The previously mentioned mediators of gut dysmotility contribute to POGD. However, POGD is also frequently associated with other underlying pathology, most notably anastomotic leak or intra-abdominal abscess, among others.[25]

Impact of ERP on POGD

#2 - *We recommend the implementation of enhanced recovery protocols (ERP) in order to reduce the time to recovery of gastrointestinal function after colorectal surgery to an average of 1-2 days.*

Traditionally, postoperative surgical management and initiation of enteral nutrition was dictated solely by the return of bowel function (i.e. the passage of flatus or bowel movement), which took three to five days on average following colorectal surgery.[26,27] It is unclear where or when this practice first originated but it became one of the fundamental bastions of surgery. The use of an ERP, based on immediate initiation of a

diet, clearly results in reduction of the time to GI recovery in colorectal surgery compared to traditional care pathways.[28-30] On average, one can expect return of flatus and or bowel movement within one to two days following elective colorectal surgery within an ERP.[31-33] Given that most surgeons continue to require the return of bowel function (as evidenced by the passage of flatus) before discharging patients following colorectal surgery, the return of bowel function remains the primary driver of LOS.[34] It is unclear whether the return of bowel function is essential beyond the tolerance of oral intake, as this practice is being challenged by the emergence of outpatient colectomy protocols.[35,36] Based on the existing evidence, we recommend that all patients undergoing colorectal surgery be cared for according to published principles of ERPs.

Prevention

#3 - We recommend active strategies to minimize the use of opioids while maintaining adequate pain control through the use of multimodal analgesia

While the mechanisms involved in POGD are varied, opioids play a significant role in reducing GI function through modulation of the Mμ-receptor.[37] Opioid-induced GI dysfunction can be caused by the release of endogenous opioids due to surgical stress or from the administration of exogenous opioids to treat perioperative pain.[1,38,39] This risk appears to be highest in colorectal surgery, although it is also elevated in surgery involving the upper GI tract, head of pancreas, and cystectomy.[40-46] Numerous studies in major intra-abdominal surgery have shown that opioid minimization is associated with earlier return of bowel function.[47-51] One study reported that the risk of delayed return of

bowel function was increased with daily doses of opioids exceeding as little as 2mg of IV hydromorphone equivalents.[44]

In light of this evidence, active minimization of opioid use should be accomplished through a multimodal regimen of non-opioid analgesic strategies.[52] The goal of producing 'optimal analgesia' should be pursued, which has been defined as a pain management strategy that optimizes patient comfort and facilitates recovery of physical function including the bowel, mobilization, cough and normal sleep, while minimizing adverse effects of analgesics.[53] However, the exact combination of analgesic strategies has not yet been elucidated. Neuraxial analgesia,[54,55], lidocaine infusions,[56,57] non-steroidal anti-inflammatory drugs [58], acetaminophen,[59-61] gabapentinoids,[62-64] and ketamine [65-68] have all been shown to reduce opioid consumption and provide adequate analgesia in the perioperative period for patients undergoing intra-abdominal surgery. More details about each of these interventions and specific recommendations concerning implementation of ERP care components can be found elsewhere, including the POQI-1 multimodal analgesia consensus recommendations.[52,53]

#4 - We recommend the maintenance of euvolemia along with a normal salt and electrolyte state in the perioperative period

Hypervolemia leads to bowel wall edema, prolonging recovery of bowel function, and impairing tissue oxygenation.[22] Avoidance of hypervolemia is one of the primary tenets of ERP and may mediate earlier return of GI recovery. Lobo et al.[69] randomized 10

patients with colon cancer undergoing colorectal surgery to standard postop fluids (⩾3 L water and 154 mmol sodium per day) versus restricted (< 2L and 77 mmol sodium per day). Median solid and liquid phase gastric emptying times (T50) on the fourth postoperative day were significantly longer in the standard group than in the restricted group (175 vs 72·5 min, difference 56 [95% CI 12–132], p=0·028; and vs 73·5 min, 52 [9–95], p=0·017, respectively); median passage of flatus was 1 day later (4 vs 3 days, 2 [1–2], p=0·001); median passage of stool 2.5 days later (6.5 vs 4 days, 3 [2–4], p=0·001); and median postoperative hospital stay 3 days longer (9 vs 6 days, 3 [1–8], p=0·001) in the standard group than in the restricted group. Nisanevich et al. [70] in their analysis of 152 patients undergoing intra-abdominal surgery found that the restrictive intraoperative fluid protocol group (4 ml x kg(-1) x h(-1)) reduced time to flatus from 4 to 3 days and time to bowel movement from 6 to 4 days than the liberal group (bolus of 10 ml/kg followed by 12 ml x kg(-1) x h(-1)) . Thacker et al.[71] recently examined the correlation between fluid administration and LOS, total costs, and postoperative ileus using the Premier Research Database in patients undergoing elective colorectal surgery and hip/knee replacement. Patients were divided into quartiles for fluid administration on the day of surgery. Both high and low fluid utilization were associated with increased postoperative ileus while quartiles 2,3 were associated with lowest LOS, costs, and rates of ileus. This emphasizes that fluid restriction to the point of hypovolemia is not the goal, but rather euvolemia, also called zero-fluid balance, is the ideal physiologic state.

Conversely, MacKay et al.[72] randomized 80 patients undergoing elective colorectal surgery to restricted versus standard fluid regimens postoperatively and found no

difference in time to first flatus or bowel movement (restricted group received 4.5 L of fluids compared to over 8 in the standard group). Rollins et al.[73] performed a meta-analysis of RCTs evaluating the difference in goal directed fluid therapy (GDFT) vs conventional fluid therapy and found that GDFT was associated with a significant reduction in hospital LOS (mean difference −2.14, 95% CI −4.15 to −0.13, *P*=0.04) within a traditional care setting but not within an ERP. No difference was seen in return of flatus, or risk of paralytic ileus in patients managed within either traditional care or an ERP. However, when time to passage of stool was considered, GDFT resulted in a reduction in time to passage of stool (mean difference −1.09 days, 95% CI −2.03 to −0.15, *P*=0.02) within an ERP but not within a traditional care setting.

Taken together, the institution of zero-balance therapy seems beneficial in preventing POGD and reducing bowel edema.

#5 - We strongly recommend against the routine use of prophylactic nasogastric tubes

The preponderance of modern surgical evidence, specifically multiple meta-analyses each with several thousand patients, suggested that the routine use of a prophylactic post-operative NGT should be abandoned due to the association with an increased complication rate.[74,75] Cheatham et al.[74] examined 26 trials with 3,964 patients following laparotomy, and found that pulmonary complications, pneumonia, atelectasis, fever, and time to tolerance of oral intake all were reduced in the group without prophylactic NGTs.

There was more observed abdominal distension, nausea and vomiting but no increase in any other complication. Subsequently, a large Cochrane meta-analysis in 2007 examined a total of 33 studies with 5,240 patients.[75] They too demonstrated routine use of prophylactic NGT prolongs the time to return of bowel function and increases pulmonary complications ($p<0.01$) without an increase in anastomotic leak nor wound infections.

It is important to note that the previously mentioned studies were conducted in patients undergoing routine uncomplicated elective surgery. The efficacy of prophylactic NGT decompression in high-risk patients (for example difficult 8 hour operation with visible bowel wall edema; extensive adhesiolysis in the setting of an obstruction, emergent cases, etc.) has not been fully investigated. Since pulmonary aspiration from massive emesis can be lethal, it is imperative that perioperative teams have increased vigilance in these high-risk patients and the decision be left to the discretion of the surgeon. Additionally, the avoidance of *prophylactic* NGT decompression should also not be confused with the utility of NG decompression for *treatment* of severe POGD as addressed elsewhere in the manuscript.

#6 - We recommend the use of minimally invasive surgery when appropriate

Minimally invasive surgery has clearly been shown to improve outcomes following colorectal surgery including return of bowel function, reduction in ileus, and LOS.[76-78] As

such, the use of minimally invasive surgery should be utilized when at all possible. It is unclear whether hand-assisted laparoscopy offers the same advantages as straight laparoscopy with regard to postoperative bowel function.[79] The beneficial effects of minimally invasive surgery are likely mediated through minimization of bowel manipulation, a principle that can also be applied to open surgery.

#7 - We recommend using Alvimopan if opioid-based analgesia is used; (its use could also be considered within an opioid restricted ERP in colorectal surgery.)

The Food and Drug Administration approved Alvimopan (Entereg®) in May 2008 as an oral, peripherally acting opioid μ receptor antagonist to accelerate gastrointestinal recovery in patients undergoing bowel resection.[80,81] Alvimopan offered a significant adjunct to the fast-track protocols of the time with the potential to substantially minimize ileus rates in patients undergoing open colorectal surgery.[82] A pooled analysis of three prospective randomized and blinded Alvimopan trials demonstrated that a 12 mg dosing regimen provided optimal reduction in GI morbidity and return of GI function following abdominal surgery with a significant decrease in the incidence of ileus.[83]

Additionally, Vaughan-Shaw et al.[84] performed a meta-analysis involving three studies of 1388 patients undergoing open abdominal surgery (bowel resection and hysterectomy) within a *defined accelerated recovery program*. This study demonstrated a 16 – 20 hour reduction in the time to GI recovery and discharge order associated with Alvimopan use. It is important to note that the components of the *defined accelerated*

recovery program in each of the three studies was limited to early removal of prophylactic NG tubes, clear liquids on postoperative day number one, and encouragement of ambulation. Each of these studies utilized patient controlled analgesia with heavy doses of opioid analgesia.[85] Therefore, these trials were conducted in open surgery within the setting of an opioid-centric treatment pathway, which is not consistent with most modern day ERPs. There are no high quality prospective randomized trials examining the efficacy of Alvimopan within the setting of an opioid restricted modern day ERP or following minimally invasive surgery.

However, there are large database studies evaluating the use of Alvimopan in current practice. The Michigan Surgical Quality Collaborative (MSQC) group reported usage of Alvimopan in the community resulted in a considerable decrease in LOS (4.8 vs. 6.4 days) due principally to a reduction in prolonged ileus (7.9% vs 2.3%) associated with an average dosing of 7.6 doses.[86] Similarly, the Surgical Care and Outcomes Assessment Program (SCOAP) evaluated 14,781 patients undergoing elective colorectal surgery comparing those that did (11%) and did not receive (89%) Alvimopan and found a LOS reduction of 1.8 days and a cost reduction of $2,017 related to ileus reduction. [87] Adam et al.[88] reported on a single institution experience of 660 patients following implementation of Alvimopan as part of an established ERP (197 alvimopan; 463 no Alvimopan) and demonstrated a faster return of bowel function, a lower incidence of postoperative ileus, a shorter length of stay and a hospital cost savings of $1492 per patient. These results are also consistent with similar retrospective cohort study by Itawi et al.[89]. It should be noted that the potential benefits of Alvimopan are

likely closely related to the amount and duration of opioid analgesics as demonstrated by two separate single center studies demonstrating minimal benefit of Alvimopan in a laparoscopic colectomy population managed with a narcotic sparing analgesic regimen.[90,91]

The data suggest a reproducible benefit associated with the use of Alvimopan in open colorectal surgery, however the cost/benefit ratio must be considered within the context of the opioid administration of each institution's ERP. Bartletta et al. confirmed that the intravenous opioid dosage that results in ileus might be quite modest (2 mg hydromorphone in 24 hours).[44] Additional data would be helpful to clearly define the minimum dose exposure and route of administration of narcotics that would best guide the use of Alvimopan within a comprehensive ERP. However, if modest narcotic exposure is anticipated the agent appears to be cost effective.

#8 - We recommend the use of a standardized risk-based strategy for PONV prophylaxis to prevent postoperative GI dysfunction within an ERP for colorectal surgery

PONV is a significant component in the spectrum of impaired GI recovery and a frequent source of patient discomfort if aggressive prophylaxis and treatment is not employed.[49,50] Consensus guidelines propose that a risk-based strategy of prophylaxis should be employed, along with a structured treatment for when PONV occurs.[9] In summary, a preoperative assessment of risk factors should be undertaken in all patients

and PONV prophylaxis administered based upon that assessment (see Table 2). Of note, a core tenet of effective treatment for PONV once it develops involves switching classes of medications from those used for prophylaxis. Thus, if an ERP prescribed the steps for PONV prophylaxis, including classes of medications to be used, a structured postoperative plan for treating PONV should include use of alternative classes of medications than those used intraoperatively. Finally, it is known that PONV in the PACU is associated with a higher risk of both nausea and vomiting in the subsequent 24-48 hours.[92,93] Thus, one could consider scheduling anti-emetics for the first 24 hours postoperatively for patients requiring treatment for PONV in the PACU.

#9 - We strongly recommend immediate resumption of eating and drinking following colorectal surgery

Postoperative feeding

As mentioned previously, traditional perioperative care dictated the return of bowel function prior to initiation of feeding following intestinal surgery. In 2006, Andersen et al. published a Cochrane meta-analysis comparing oral feeding within 24 hours to later feeding after elective colorectal resection.[94] They analyzed 13 randomized trials, with 1173 patients, and found a non-statistical trend toward reduction in complications in the early feeding group. This supported that early feeding was safe and at least equivalent to later feeding.

Subsequently in 2011, Osland et al. performed a meta-analysis of 15 studies including 1240 patients demonstrating a 45% reduction in total complications (OR 0.55, C.I. 0.35 – 0.87, p=0.01).[95] There was no difference between the groups with respect to NGT insertion, mortality, anastomotic leak, return of bowel function, nor LOS. In 2013, Zhuang et al. performed a meta-analysis of randomized trials with stricter inclusion criteria based on the presence of at least one of the following outcomes: anastomotic leak, pneumonia, wound infection, NGT reinsertion, vomiting, mortality, LOS, hospital costs, and quality of life. [96] They included 7 studies with a total of 587 patients, and found that early oral feeding was associated with reduced complications RR 0.70 (p=0.04), but also found an association with reduced LOS by 1.58 days (p=0.009). There were no differences in rates of NGT re-insertion, vomiting, anastomotic leaks, SSI, or mortality. The authors concluded that early oral feeding is safe & effective in patients undergoing elective colorectal surgery. Based on these data, we recommend immediate introduction of eating and drinking in patients following elective colorectal surgery.

#10 - We recommend the routine use of a combined isosmotic mechanical bowel prep with oral antibiotics before elective colorectal surgery.

The use of a combined isosmotic mechanical bowel prep *with oral antibiotics* (MBP-OAB) was initially recommended as part of the POQI-1 Infection Prevention Consensus statement (currently in press). We briefly revisit this topic as the MBP-OAB not only results in a lower SSI rate, but is also associated with decreased rates of POGD as well.

For a full discussion of the benefits of combined bowel prep, please refer to the POQI-1 Infection paper.[97]

In terms of modern literature showing a beneficial relationship between the MBP-OAB and rate of POGD, Englesbe et al. evaluated 2,011 elective colectomies in the MSCQ and found that patients receiving MBP-OAB had lower rates of prolonged ileus (3.9% vs. 8.6%, p=0.01).[98] Subsequently, both Kiran *et al.* and Morris et al. looked at over 8,000 patients in NSQIP stratified by MBP undergoing elective colorectal resection, and found the MBP-OAB group had significant reductions in SSI, anastomotic leak, and ileus ($p < 0.0001$ for all).[99,100] The pathophysiology behind the effect of MBP-OAB of gut motility remains to be seen. It may be that MBP-OAB simply attenuates POGD through the reduction of intra-abdominal infection and anastomotic leak, which are known causes of secondary POGD.[25]

#11 – We recommend consideration of coffee and gum chewing as adjuncts to ERPs in promoting recovery of GI function

Coffee - There have been several RCTs evaluating the effect of coffee on the return of bowel function following abdominal surgery. Gungorduk et al.[101] randomized 114 patients undergoing gynecologic oncology surgery to coffee three times daily vs placebo. Time to recovery of bowel function and tolerance of a diet were reduced significantly in patients who consumed coffee compared with control subjects. Ileus was reduced from 30.4% in the control group to 10.3% in the coffee group (P=.01). Muller et

al.[102] randomized 80 patients undergoing elective colorectal surgery to coffee or water three times daily. Time to first bowel movement was shorter in the coffee arm with no difference in time to first flatus or tolerance of solid food. Taken together, these data suggest that coffee taken three times daily may shorten GI recovery in patients undergoing major abdominal surgery.

Gum chewing – Gum chewing has been associated with reduced GI recovery in prospective RCTs of patients undergoing major abdominal surgery.[103] However, the majority of these studies were conducted in the era of prolonged fasting after surgery when gum chewing was used as a method of sham feeding. It is doubtful that sham feeding offers an advantage when the patients are actually being fed, as is the case with ERPs. Shum et al.[104] randomized 41 patients in each group *within an ERP* to gum chewing three times daily from day 1 until discharge. There was a 16-hour reduction in time to passage of flatus within no difference in hospital stay. Ho et al.[105] performed a meta-analysis of 10 RCTs and found that gum chewing had no advantage within the setting of early feeding. Therefore, it seems that the effect of gum may be negated by actual early feeding. However, given the minimal risk and low cost, gum chewing may serve as an adjunct to ERPs, particularly in patients with minimal oral intake following surgery for one reason or another.

Treatment

#12 - We recommend placement of an NGT to relieve intractable nausea and vomiting with abdominal distension.

#13 - We recommend the following for treatment of postoperative POGD: opioid minimization, ambulation, rational fluid replacement maintaining euvolemia, electrolyte repletion, and gum chewing.

#14 - We recommend consideration of radiographic imaging CT imaging if POGD persists beyond the 7th postoperative day or at any time based on concern for secondary causes

Treatment for POGD should focus on bowel rest with nutrition support, continuation of ERP principles to the extent possible, and radiographic imaging to rule out secondary causes such as anastomotic leak and intra-abdominal infections. Specific treatment recommendations will depend on POGD severity and associated signs and symptoms. (Figure 2)

Patients with POGI who have mild nausea, small volume non-bilious emesis (≤100mL), and bloating are generally managed with a clear liquid diet advanced as tolerated and anti-emetics. These patients do not typically require a NGT for decompression and usually do not require nutrition support as the symptoms are generally mild and self-limited.

Early recognition of the patient that has progressed to POGD is critical in preventing aspiration pneumonitis, which is a potentially fatal complication following elective colorectal surgery. Patients with intractable nausea, bilious vomiting, abdominal distension and tympany require NGT placement, which oftentimes provides immediate

symptomatic relief and may also reduce the risk of aspiration, especially in the elderly or frail patient. There are many different approaches to NGT management, and unfortunately research is lacking to guide clinical practice. Some surgeons leave the NGT until the patients have demonstrated return of bowel function as evident by the return of flatus, while others remove the NGT when it reaches a certain color and volume. Additionally, practices vary with regard to suction versus gravity drainage. Although, there was uniform agreement in the importance of early NGT placement for treatment of POGD, there were wide variations in subsequent NGT management within the group and consensus could not be reached with regard to NGT removal. Thus, this should be left to the surgeon's discretion. This topic represents an opportunity for further research efforts.

Once a patient develops POGD, ERP principles still should be continued to the extent possible, including opioid minimization, ambulation, rational fluid replacement maintaining euvolemia, electrolyte repletion, and gum chewing. As all but the final two components have been discussed above, those will be the focus of this discussion. In the setting of POGD, administration of maintenance fluid requirements and replacement of volume losses from NGT drainage should be approached in a rational manner with goals of maintaining euvolemia and normal electrolyte balance, especially since gastric contents have high concentrations of chloride and potassium. While no specific data exists for this situation, certain principles of fluid management have been shown to correlate with patient benefit and harm. Additionally, recent research has noted a wide variability in the practice of fluid management by many trainees[106]; thus, a structured,

principle-based approach is needed, as both hypervolemia and hypovolemia throughout the perioperative period are associated with much worse outcomes for surgical patients.[71] First, euvolemia should be targeted and individualized to the patient such that patients are only given fluid boluses when there is a demonstrated need for augmentation of perfusion status *and* when they have been shown to be volume responsive.[107-109] Weighing the patient daily to target zero weight gain and closely following hemodynamic targets and urine output may be of benefit. Second, fluids should be treated as drugs with potentially harmful side effects.[110] Thus, in a patient with one instance of organ failure, in this case POGD, frequent careful bedside assessment should be undertaken to guide appropriate therapy. A simple maneuver such as the passive leg raise test can help determine if a patient will be responsive to IVF therapy, or possibly if a higher level of care with more sophisticated monitoring is needed.[111] This level of individualized patient care should be given as compared to empiric administration of large volumes of intravenous fluids that may not be indicated, and potentially could be of harm. Third, fluid choice should be guided by the electrochemical balance of the patient, taking care to avoid hyperchloremia (>110mmol/L) as this has been associated with worse patient outcomes.[112,113] While routine labs are often avoided today, in this setting a frequent assessment of the biochemical profile of the patient is likely warranted to guide fluid therapy. The patient with prolonged POGD (> 7 days) may require parenteral nutrition according to standard guiding principals.[114]

Finally, the group agreed uniformly that it is important to rule out secondary causes of POGD such as small bowel obstruction or anastomotic leak, which are frequently associated with POGD and may alter management.[25] If bowel function has not returned by POD seven or if there are signs and symptoms suggestive of an alternative underlying etiology (fever, tachycardia, abdominal tenderness, leukocytosis, etc.), further radiologic investigation is recommended, including abdominal CT.

Unanswered questions

Question #1 - The I-FEED scoring system was created out of the need for a consistent objective definition of POGD based on discussion amongst experts in the field. However, prospective validity and reliability testing along with usability assessment needs to be performed in order to evaluate the utility of it as a clinical and research tool.

Question #2 - Surprisingly, the science behind detection of POGD is relatively limited. In general, the sensitivity and positive predictive value of the bedside clinical exam is poor in identifying the return of bowel function. [115] Emerging non-invasive biosensor technology such as acoustic GI surveillance and bedside ultrasound have shown promise in measuring gut motility within small case series following surgery.[116,117] These studies, although interesting, will need multi-institutional validation prior to incorporation into clinical practice.

Question #3 - There is a plethora of research on preventative strategies for delayed gastrointestinal function. However, there is a paucity of literature in the ERP era

pertaining to management of this condition, particularly with regard to fluid management, NGT management, and pharmacologic interventions as treatment of POGD in the otherwise stable patient who is nil per os.

Interest still exists in finding prokinetic agents to stimulate peristalsis as a treatment of POGD. Unfortunately, most trials have been small and of poor methodologic quality. Erythromycin is a weak motilin receptor agonist that has been shown to be effective in treating gastroparesis but not POGD. In a Cochrane analysis, erythromycin was shown to have a consistent lack of effect.[118] A variety of other medications had inconsistent or insufficient data including chylecystokinin-like drugs, cisapride, dopamine-antagonists, propranolol or vasopressin. However, they did find that intravenous lidocaine and neostigmine were promising, but there was a lack of evidence on clinically relevant outcomes. To date, the efficacy of several ghrelin analogs (TZP-101, ulimorelin, ipamorelin) have been assessed by randomized trials in post-colectomy patients but have *not* been shown to be effective for reducing POGD.[119-121] Given the societal costs of POGD, pharmaceutical companies will continue their quest to develop an effective small and large bowel prokinetic enteric neuroendocrine peptides.

Question #4 - Although the data are quite convincing for the efficacy of Alvimopan in open colorectal surgery and patients receiving significant opioid pain medication, high quality prospective studies in laparoscopic surgery and/or within an ERP are lacking, representing an opportunity for future research. This is especially true in the setting of ERPs that use very minimal doses of opioids in the perioperative period.

Table 1

Consensus Statements Concerning Prevention and Treatment of POGD	
Recommendation	**Strength***
Prevention	
Use of enhanced recovery protocol	Strongly Recommend
Minimize the use of opioids while maintaining adequate pain control through the use of multimodal analgesia	Recommend
Maintenance of euvolemia along with a normal salt and electrolyte state in the perioperative period	Recommend
No routine use of prophylactic nasogastric tubes	Strongly Recommend
Use of minimally invasive surgery when appropriate	Recommend
Use of Alvimopan if opioid-based analgesia is used	Recommend
Use of a standardized risk-based strategy for PONV prophylaxis	Recommend
Immediate eating and drinking following colorectal surgery	Strongly Recommend
Use of mechanical bowel prep with oral antibiotics in elective colorectal surgery	Recommend
Coffee and gum chewing as adjuncts to ERPs in promoting recovery of GI function	Consider
Treatment	
Placement of an NGT to relieve intractable nausea and vomiting with abdominal distension.	Recommend
Continuation of opioid minimization, ambulation, rational fluid replacement maintaining euvolemia, electrolyte repletion, and gum chewing.	Recommend
Abdominal CT if POGD persists beyond POD7 or at any time based on concern for secondary causes	Consider

*based upon NICE guidelines for strength of recommendations. [NGT = nasogastric tube; CT = computerized tomography; POD = postoperative day; POGD = Postoperative Gastrointestinal Dysfunction]

Table 2

Major Risk Factors for PONV*
Female
Non-smoker
Prior PONV or history of motion sickness
Postoperative opioids

Need for PONV treatment in PACU

[PONV = postoperative nausea and vomiting; PACU = postanesthesia care unit]
*based on Gan TJ, et al. *Anesth Analg* 2014;118: 85-113 and Apfel, CC et al. *Anesthesiology, 2012;* 117: 475-486.

Figure Legend

Figure 1: The I-FEED scoring system was created out of the need for a consistent objective definition of impaired postoperative GI function. I-Feed stands for: **I**ntake, **F**eeling nauseated, **E**mesis, physical **E**xam, and **D**uration of symptoms. The scoring system attributes 0-2 points for each of the five components based on the clinical presentation of the patient and categorizes patients into Normal (0-2), Postoperative GI Intolerance (3-5), Postoperative GI Dysfunction (≥ 6).

Figure 2. A treatment algorithm was developed based on the I-FEED scoring system for the management of patients with impaired postoperative GI function according to the clinical presentation of the patient in real time.

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