

**Dietary Interventions for the Reduction of Postoperative Ileus Following Abdominal
Surgery: A Literature Review**

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A capstone project submitted to the Faculty of Graduate Studies of the University of Manitoba in
partial fulfillment of the requirements for the degree of

MASTER OF PHYSICIAN ASSISTANT STUDIES

Department of Physician Assistant Studies

Max Rady College of Medicine and Faculty of Graduate Studies

University of Manitoba

Winnipeg, Canada

May 15, 2020

ABSTRACT:

Introduction: A postoperative ileus (POI) is a common complication in patients following abdominal surgery which slows patient recovery and increases postoperative morbidity, length of hospital stay, resource use and healthcare costs. Although many interventions have been hypothesized to play a role in the prevention and management of POI, including chewing gum, coffee, and early enteral feeding, current guidelines regarding best clinical practice are lacking.

Objective: The aim of this study is to review the efficacy and safety of various dietary interventions used in the reduction of POI, to aid in providing evidence-based recommendations for future Canadian guidelines on this topic. Chewing gum, coffee, and early enteral feeding were examined.

Methods: This literature review used the PubMed database. Fifteen articles were found to meet the inclusion criteria. The primary outcomes measured were the effectiveness of each intervention in lowering the incidence of an ileus as well as their overall safety.

Results: Four of eight studies evaluated identified positive benefits from the addition of chewing gum on bowel recovery. Three primary studies identified that coffee is beneficial in reducing time to first bowel movement. Three of four studies showed that early enteral feeding significantly improves gastrointestinal motility. All studies reviewed agreed that their respective interventional measures are safe and are not associated with an increase in postoperative complications.

Conclusion: Although none of the interventions reviewed show complete consensus regarding their ability to reduce POI, there is agreement that these measures are safe, well tolerated, and not related to any major adverse effects. Therefore, chewing gum, coffee, and early enteral feeding are all postoperative measures which patients can be encouraged to adopt. The exact combination of these methods which should be included in the guidelines is unknown and requires further studies to examine the additional benefits provided by using more than one intervention.

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INTRODUCTION

A postoperative ileus (POI) is a common complication experienced by many patients following abdominal surgery. POI affects the entire gastrointestinal (GI) tract, however the sections of intestine which were directly manipulated in surgery will be most affected and will likely take longest to recover (1,2). A POI results in slowed patient recovery, delayed oral intake, and increased postoperative morbidity due to “decreased mobilization, poorer wound healing, increased risk of infection and suboptimal nutrition,” (3). This dysfunction also contributes to increased length of hospital stay, resource use and hospital costs, placing a great burden on healthcare systems. In the United States, a 2007 study estimated an average hospital stay prolongation from 5.5 to 11.5 days and an average cost increase from \$9,460 to \$18,877. They projected the management of this complication to have an annual national healthcare expenditure of \$1.46 billion (4). Due to these facts, it is very important to have a safe, inexpensive, and well-tolerated implemented solution to this problem.

While searching various sites such as Choosing Wisely, Top Alberta Doctors, UpToDate, Joule, and the Eastern Association for the Surgery of Trauma, the lack of guidelines detailing the best clinical practice for the reduction and management of POIs became apparent. Consequently, approaches used to reduce and manage POIs may vary between sites and surgeons.

Many interventions have been hypothesized to improve GI function and possibly play a role in POI reduction. However, indisputable evidence regarding the benefits of many of these interventions have yet to be seen, and not all are free of adverse events. Hypothesized techniques consist of chewing gum, coffee, carbohydrate-rich diet, early enteral feeding, early mobilization, fluid restriction, multimodal perioperative analgesia including epidurals and NSAID administration, avoidance of routine nasogastric tube use, reversal of electrolyte or metabolic

abnormalities, enhanced recovery after surgery (ERAS) perioperative care implementation, minimally invasive surgery, and new medications. Medications which have been trialed include laxatives, opioid antagonists (ie alvimopan and methylnaltrexone), prokinetic agents (i.e. gastrografin, magnesium, erythromycin, metoclopramide, and prucalopride), and ghrelin receptor agonists (2,4,5). This literature review will focus on assessing the safety and effectiveness of the following dietary methods in reducing the duration of POI: chewing gum, coffee, and early enteral feeding.

Definition

It can be expected that all patients following abdominal surgery will experience some degree of bowel function impairment, however the severity of this greatly varies. POI is generally defined as a temporary abnormal pattern of GI motility occurring most commonly following a surgical procedure. POI is a physiologically normal occurrence with many abdominal surgeries which is considered to be benign and self-limiting (1); however, the duration of GI inhibition considered to be normal has not yet been agreed upon. It is believed that after surgery, the motility of each section of the GI tract recovers at different intervals: small intestine in 12-24 hours, gastric in 24-48 hours, and colonic in 3-5 days (5). POI is characterized by nausea, vomiting, failure to tolerate an oral diet, abdominal pain, abdominal distention, as well as delayed return of GI function reflected by an absence of flatus and stool (4,6). It can be difficult to differentiate the cause of some of these symptoms as occurring from an ileus or another mechanism, thus a POI diagnosis is often confirmed by findings on radiological imaging. A greater concern emerges when the bowel's motility does not resume for an extended period of time resulting in a pathological condition known as a prolonged postoperative ileus (PPOI), which is of greater severity and related to greater morbidity.

Unfortunately, there are currently no set global definitions for POI and PPOI; therefore, there is great inconsistency between all studies making them difficult to compare. As seen on UpToDate, many definitions have been used in research to characterize a PPOI: “no return of bowel function postoperatively (ranging from postoperative days 4 to 6); absence of flatus or stool on postoperative day 6; postoperative nausea or vomiting requiring cessation of oral intake, intravenous support, or nasogastric tube placement by postoperative day 5; return of bowel function after postoperative day 5; absence of flatus and/or bowel movement prolonging hospitalization beyond discharge goal (ranging from postoperative days 6 to 8); [and the] lack of bowel activity more than five days after surgery,” (1).

Epidemiology

Due to the lack of standardized definitions for both POI and PPOI, there is a wide range of incidence rates found in research. A 2016 literature review identified the risk of ileus to be variable depending on the type of abdominal surgery (5). It reported the incidence of POI following colorectal surgery to be 10-30%, whereas that of pancreatic and gastric surgery was 8-13% (5).

In a 2019 primary study which included 786 patients from 40 sites in five countries following colorectal surgery within enhanced recovery after surgery (ERAS), 15% of patients developed a POI (7). Of these cases, 60% were categorized as severe which included patients requiring a nasogastric tube or hospital readmission after discharge, who developed consequences due to the POI, or those who died as a result (7).

A 2016 meta-analysis examined 54 articles published in the last two years. All articles combined included a total of 18 983 patients whom had received colorectal surgery (8). The

incidence rate for PPOI was found to be 10.2% in randomized controlled trials (RCT), and 10.3% in non-RCTs (8).

A 2018 primary study which included 323 patients from one site after colorectal surgery within ERAS identified the development of a PPOI in 19% of patients based on their primary definition (9). This study also identified the rates of PPOI using other definitions from literature and found the incidence to be between 11 and 59%; this demonstrates the importance of having standardized international definitions in order to ensure accurate statistics (9).

Pathophysiology

As research progresses and enhances the understanding of the pathophysiology of POIs and PPOIs, it will add to our ability to reduce and manage these postoperative complications. GI motility is normally controlled by its intrinsic neural network called the enteric nervous system. An extrinsic network, which is comprised of vagus, splanchnic, and pelvic nerves, connects the enteric system to the central nervous system (1). The development of POIs is complex and currently believed to occur in three phases: neural network activation, inflammatory response, and recovery of homeostasis (2,5). Features contributing to POI include anesthesia, surgical incision, tissue damage, direct bowel manipulation, abnormal electrolyte levels, and peritoneal irritation from blood and pus (1,2,5,10). Due to the lack of a standardized definition, identified risk factors for POI seem to vary between studies; however, it appears that male gender, advanced age, and significant blood loss are consistently found (5,7,9).

Objective

The objective for this literature review is to evaluate the efficacy and safety of chewing gum, coffee, and early enteral feeding as dietary interventions applied to postoperative care

following abdominal surgery to reduce the incidence of POI. This was done to aid the future development of Canadian guidelines regarding this very common postoperative complication.

METHODS

Inclusion criteria

The inclusion criteria used to determine study eligibility for this project were as follows: clinical primary research, studies originally published in English, published in the last ten years (2010-2020), and adult patients (18 years old or older) undergoing abdominal surgery. The studies could focus on abdominal surgeries broadly, or on a specific type of surgery, with the exception of gynecological and urological surgeries. An endpoint assessed must have included at least one of the following: POI, return of bowel function, time to first flatus, or time to first defecation. The study had to discuss either chewing gum, coffee or early enteral feeding. Articles which were not primary research, for example literature reviews, were included solely in the introduction portion of this study. In the end, fifteen primary research articles were eligible for inclusion and were evaluated for the results and discussion sections.

Search Strategy

An article search was completed using the PubMed database using the following words: ileus pathophysiology, postoperative ileus, prevention of postoperative ileus, post operative ileus management, ileus management, post operative ileus treatment, post operative gut motility, and postoperative gastrointestinal function. Together, these searches resulted in 13709 articles. The remaining articles included in this literature review were compiled by searching through the bibliography of relevant articles.

Primary Outcome Measures

The primary outcome examined when assessing methods studied for the reduction of POI, was their effectiveness in decreasing the occurrence or duration of an ileus; this was reflected by a direct measurement of the incidence of POI or by analyzing one of its characteristics, either the time to first passage of flatus or the time to first defecation. These were used as surrogates for POI as they represent colonic motility which is believed to recover last postoperatively (10). A $P \leq 0.050$ is considered to be statistically significant. The diagnosis of a POI followed each primary study's individual definition and criteria, which was not consistent between studies. The overall safety of each intervention's implementation into patient care was also investigated by evaluating the rate of postoperative complications and side effects related to the intervention.

RESULTS

Chewing gum

Chewing gum has commonly been applied to postoperative care to aid in reducing POI. It is believed that chewing gum mimics food intake and activates the cephalic phase of digestion and vagal reflex, thereby eliciting the release of GI hormones, secretion of saliva and secretion of pancreatic juices, which subsequently enhances GI motility. Another potential mechanism suggests that artificial sweeteners used in sugarless gum, such as xylitol and sorbitol, have promotility benefits which facilitate GI recovery. Possible side effects which have been noted are bloating, eructation, and aspiration risk (11–14). Eight primary studies were identified to analyze chewing gum and met the remaining criteria (Table 1).

Topcu and Oztekin conducted a randomized control trial (RCT) in 2016 examining 60 patients following open colorectal surgery (11). The study design involved gum chewing three times a day for 15 minutes compared to routine care alone. They reported chewing gum shortened time to first flatus (51.07 vs 87.83 hours, $P < 0.001$) and time to defecation (73.33 vs 137.2 hours, $P < 0.001$) compared to the control (11).

Forrester et al. conducted a RCT in 2014 with 47 patients who underwent open or laparoscopic sigmoid colectomy (15). They were randomized into three groups: standard care (control), standard care with silicone-adhesive patch (attention control), and standard care with sugarless chewing gum (intervention). Gum chewing was scheduled three times a day for greater than one hour each time. Neither time to first flatus (2.99 vs 2.81 vs 3.42 days, $P = 0.744$) nor bowel movement (5.21 vs 3.36 vs 3.33 days, $P = 0.198$) were identified as significantly shorter in the chewing gum group compared to the attention control and control groups. Gum chewing was noted to be safe postoperatively (15).

A 2014 RCT by van den Heijkant et al. evaluated 112 patients undergoing open colorectal surgery (12). The intervention used in this study was sugarless gum chewing before and after surgery and the control was a dermal patch. Chewing gum was found to positively affect presence of flatus within 48 hours (65% vs 50%, $P = 0.044$), presence of stool within four days (85% vs 57%, $P = 0.006$) and incidence of POI (27% vs 48%, $P = 0.020$) compared to the control group. No significant difference in total rate of postoperative complications ($P = 0.860$) was seen (12).

A 2016 multicentre study by Shum et al. included 82 patients after laparoscopic colorectal surgery who were randomized into two groups: sugarless chewing gum three times a day for 30 minutes added to a standardized ERAS programme or ERAS alone (13). Both time to

first flatus (18 vs 34 hours, $P = 0.007$) and bowel movement (19 vs 44 hours, $P = 0.001$) were significantly shorter in the chewing gum group. Incidence of postoperative complications were similar between the two groups. No patients experienced any adverse events from the chewing gum (13).

Studies by de Leede et al. (14) and Atkinson et al. (16), consisting of 1941 and 402 patients respectively, also studied the benefits of adding sugarless chewing gum to ERAS, however in contrast, no benefits to GI recovery were observed. Control and intervention groups resulted in similar times to first flatus ($P = 0.873$ and $P = 0.586$, respectively) and times to first bowel movement ($P = 0.562$ and $P = 0.153$, respectively) (14,16). Atkinson et al. did not identify any significant change in incidence of POI between study groups ($P = 0.197$) (16). Both de Leede et al. and Atkinson et al. did not identify any change in rate of postoperative complications ($P = 0.113$ and $P = 0.840$, respectively) or any adverse events due to gum chewing (14,16).

A 2013 study by Zaghiyan et al. chose to evaluate the effects of chewing sugared gum for 45 minutes three times a day compared to no gum (17). 114 patients after major colorectal surgery were randomized into these groups and all started on early enteral feeding in an ERAS setting. No significant differences were found between the intervention and control groups regarding time to flatus (48.6 vs 47.4 hours, $P = 0.83$), time to defecation (56.9 vs 63.2 hours, $P = 0.40$), and incidence of POI (7.5% vs 6.7%, $P = 0.5$). Increased incidence of bloating, indigestion, and eructation was present in the gum group (13% vs 2%, $P = 0.03$), however its influence on postoperative complications was deemed insignificant (15% vs 18%, $P = 0.46$) (17).

Liu et al. conducted a meta-analysis in 2017 consisting of 18 RCTs and 1736 patients following colorectal surgery (18). Studies contrasted chewing, either sugared or sugarless gum for 5 to 60 minutes three or four times a day, to groups with no gum. Overall, time to first flatus

($P = 0.0002$), time to first bowel movement ($P < 0.00001$) and incidence of POI ($P = 0.003$) all decreased with chewing gum. No significant change in risk of other postoperative complications, nausea, vomiting, bloating, readmission, or reoperation was revealed (18).

Coffee

Drinking coffee is well known to stimulate bowel motility, yet the exact mechanism of action for this event is not yet understood; it is believed that a chemical component is more likely responsible for this advantage rather than one of its physical properties (19–21). Three RCTs analyzing coffee drinking for the benefit of reducing POI were examined in this paper (Table 2).

A 2012 multicentre RCT by Müller et al. examined 71 patients having elective open or laparoscopic colectomy (19). They compared drinking 100mL three times a day of warm water versus caffeinated coffee without additives. They determined that time to first bowel movement was significantly shorter in the coffee than the control arm (62.1 vs 73.7 hours, $P = 0.028$). Time to first flatus (40.6 vs 47.1 hours, $P = 0.191$) and total complications ($P = 0.344$) were not affected by coffee. No complications associated with drinking coffee were identified (19).

A 2015 single centre RCT by Dulskas et al. included 90 patients undergoing elective laparoscopic left colectomy due to malignancy (20). They contrasted the effects of drinking 100mL three times a day of caffeinated coffee, decaffeinated coffee and water on POI. Time to first bowel movement was identified to be significantly shorter in the decaffeinated coffee arm than the caffeinated coffee and water groups (3 vs 3.75 vs 4.14 days, $P < 0.05$). Time to flatus was not found to be of significant difference in the decaffeinated coffee arm than in the caffeinated coffee and water groups (1.47 vs 1.57 vs 1.77 days, $P > 0.05$). No significant change in postoperative complications ($P = 0.347$) was found (20).

A 2019 RCT by Hasler-Gehrer et al. included 115 patients having elective colorectal surgery and compared drinking 150mL three times a day of coffee to non-caffeinated tea (21). All patients also followed an early enteral feeding schedule to determine the possibility of additive benefits. In the coffee arm, time to first bowel movement (66.8 vs 77.3 hours, $P = 0.006$) was significantly shorter, but time to first flatus (40 vs 30 hours, $P = 0.05$) was significantly longer compared to the tea arm. No difference in morbidity ($P = 0.47$) between groups was identified (21).

Early enteral feeding

Traditionally, postoperative nutrition entailed nasogastric decompression and delayed oral feeding until the POI resolved, indicated by first flatus or stool without presence of abdominal distention or vomiting, in order to prevent its symptoms and protect the anastomosis from dehiscence. Conversely, the current belief is that consuming a normal oral diet postoperatively should begin as soon as possible in order to ensure adequate nutrition. Using early enteral nutrition can encourage GI recovery, reducing the risk of a clinically apparent POI and other morbidities, bridging the patient to a normal diet (22–25). Four studies analyzing early enteral feeding were examined (Table 3).

Pragatheeswarane et al. (22) and Dag et al. (23) both conducted similar RCTs contrasting early to traditional oral feeding. Early feeding started at 24- and 12-hours post operation, respectively. Pragatheeswarane et al.'s 2014 study consisted of 120 patients following open bowel surgery while Dag et al.'s 2011 study had 199 patients post open colorectal surgery. Both studies demonstrated the positive benefits of early feeding on time to first flatus (2.6 vs 4.5 days, $P < 0.0001$; 1.76 vs 3.27 days, $P = 0.0001$, respectively) and time to first bowel movement (3.8 vs 6.1 days, $P < 0.0001$; 3.41 vs 4.38 days, $P = 0.0001$, respectively). The studies agree that early

oral feeding is safe, well-tolerated and resulted in similar incidence of postoperative complications, including anastomotic leakage ($P = 0.309$ and $P = 0.279$, respectively), compared to traditional feeding (22,23).

Boelens et al. conducted a 2014 RCT consisting of 123 patients following extensive rectal surgery (24). The intervention, early enteral nutrition via naso-jejunal tube starting eight hours after surgery, was compared to the control, parenteral nutrition via central line, and all patients were also able to eat and drink as much as they desired. Time to first defecation ($P = 0.04$) and rate of anastomotic leak ($P = 0.009$) were found to be significantly shorter in the intervention group. Early enteral feeding is believed to be safe as no significant changes in POI incidence ($P = 0.12$) and surgical or infectious complications were noted (24).

A 2011 meta-analysis by Osland et al. examined 15 studies and 1240 patients following GI resection and compared early enteral feeding (by mouth or tube proximal to anastomosis) with nutritionally significant food and fluids starting within 24 hours post-surgery, to traditional feeding (25). No significant effect by early enteral feeding was found regarding time to first flatus ($P = 0.23$), time to first defecation ($P = 0.55$), or anastomotic leak ($P = 0.39$). A significant decrease in total complications ($P = 0.01$) with early enteral feeding was seen (25).

DISCUSSION

The current literature review demonstrates confidence in the safety of these three interventions following abdominal surgery, however their effectiveness in reducing the duration of POI requires further investigation.

The studies reviewed display confounding evidence regarding the ability of chewing gum to ameliorate POI; only four of eight studies displayed concrete evidence in favour of the

intervention. These four articles demonstrated faster GI recovery by shorter time to first flatus and defecation, and two of the four also directly showed lowering in POI incidence (11–13,18). Many of the articles examining chewing gum agreed this was a safe, inexpensive, and widely accessible method which is easily enacted and does not have a contributory relation with postoperative complications (11–13,15,18). All six papers which commented on rate of postoperative complications all showed these were comparable between the chewing gum and control groups (12–14,16–18). Not all authors agreed on the tolerability of chewing gum by patients; Zaghiyan et al. noted an increased risk of bloating, eructation, and indigestion, whereas de Leede et al. identified no difference between groups regarding complaint of nausea, vomiting, or bloating (14,17). The inconsistent results regarding POI reduction and patient tolerability may be explained by the wide variety of sample sizes, surgery types, and compliance rates as well as use of multiple interventions. Four articles had mention of patients not complying with the gum chewing protocol, ranging from an unspecified amount to 78% (12,14–16). Some studies compensated for non-compliance by removing those patients from their analysis. Another factor which may have affected the outcomes is the diversity in the amount of chewing that was requested from patients, thus the true amount required to produce sufficient cephalic stimulation to enhance GI motility is unclear. Overall, chewing gum has been shown to be a safe option with minimal adverse effects and not associated with increased complications. Therefore, as gum is inexpensive and readily available, it would be a feasible option to add to post abdominal surgery protocols.

All three of the analyzed studies have revealed the promising effects of coffee in the reduction of POI when compared to water or tea. All protocols consisted of similar amounts of coffee per day starting on the first day after surgery. Although caffeinated coffee had been shown

to enhance GI motility in the study by Müller et al., Dulskas et al.'s study examined this relationship further and concluded that decaffeinated coffee provided greater assistance in relieving bowel dysmotility than caffeinated coffee (19,20). Hasler-Gehrer et al.'s study does not differentiate between caffeinated and decaffeinated coffee thus no statement on this matter can be extracted (21). This comparison showcases the likelihood that the mechanism of action contributing to coffee's benefits on GI function are due to its chemical properties compared to physical properties. While caffeine is known to have stimulatory effects, the fact that decaffeinated coffee outperformed caffeinated coffee proves there must be another component or components with similar or greater stimulatory effects. It has also been questioned if the decaffeination process may result in unique chemicals providing further advantages (20).

All three studies have concluded that coffee is a simple, safe, readily accessible, cheap, and easily implemented intervention with few adverse effects (19–21). The only adverse event listed was the fact that caffeine may overstimulate the nervous and cardiovascular systems, also making decaffeinated coffee a safer option (20,21). In addition, all three studies presented similar incidence of postoperative complications between intervention and control groups (19–21). Although coffee is a popular beverage, strong distaste as well as cultural preferences for other beverages, such as tea, may negatively affect patient compliance in daily practice. Hasler-Gehrer et al. and Müller et al. performed per protocol analysis, removing 19 and 8 patients, respectively, from the equation, in order to limit the effect of non-compliance on their results (19,21). Based on this review, it can be concluded that coffee, both caffeinated and decaffeinated, have been shown to be safe and beneficial in the activation of bowel motility. This reflects a likely advantage in the reduction of POI, however incidence of POI was not directly measured in any of the three articles reviewed.

Early feeding usually consists of starting an enteral diet within 24 hours after surgery. Most protocols called for beginning with small amounts of clear fluids and slowly progressing until a normal solid diet is tolerated (22–24). The meta-analysis by Osland et al. focused solely on trials which skipped the clear fluid stage and jumped directly to nutritionally significant food or fluids (25). Three of the four studies have shown significantly shorter time to first defecation, and two of those three have shown shorter time to first flatus (22–25). Only one study examined POI incidence directly and did not discover an advantageous effect from early feeding (24). All studies agreed that early enteral feeding was a safe intervention to add to postoperative care. Boelens et al. was the sole study to report a positive benefit of early feeding on rate of anastomotic leak. Osland et al. stated that early feeding significantly reduced incidence of total postoperative complications. The other studies showed similar incidence of these endpoints between groups (22–25). The various discrepancies between each of the four studies' results may be explained by various factors. The four studies reviewed varied regarding their study design, such as the timing of feeding, type of surgery, type of enteral feeding, and type of control. Other factors which may have influenced results include the reliance of correct self-reporting and possible protocol deviation. All in all, early enteral feeding is safe, not causing increased harm to patients, however its effect on POI may be variable dependent on numerous factors.

The reasoning and benefits behind traditionally delaying enteral feeding is not well documented. Now that new research has shown patients' health being compromised by withholding nutrition and is supporting the use of early enteral feeding by demonstrating its advantages, early feeding is becoming a popular option in postoperative care (22–25). The main reason for the use of traditional fasting is to protect the anastomosis; however, Osland et al. and Dag et al. explain that the digestive system secretes two to seven liters of fluid per day which

passes through the intestines. This fact invalidates the fear of harming the anastomosis as the bowel is not fully resting even with traditional fasting (23,25). Pragatheeswarane et al. and Dag et al. report that the nutrition from early enteral nutrition can actually strengthen the anastomosis, reducing complications and promoting wound healing (22,23). The benefits of adequate nutrition in postoperative care is the reason Osland et al. decided to focus on studies providing nutritionally significant foods from the start of early feeding, which has been shown to be tolerated, and they were the only study to report a significant decrease in complication rates (25). A great detriment associated with traditional fasting is that the prolonged period of malnutrition undesirably affects metabolism which will in turn influence insulin resistance, muscle function, and weight loss, negatively affecting postoperative outcomes (23,25). In some cases this can be an additive effect to poor nutritional status already existing prior to surgery related to the nature of their condition (25). Studies have stated that early feeding can decrease septic complications, modulate surgical stress response, and reduce morbidity, thus improving surgical recovery. These studies have proven, that in the majority of cases, there is no merit in continuing to use traditional postoperative fasting and risking the damaging effects of malnutrition as there are no repercussions associated with early enteral feeding (22–25).

The benefits of using a combination of methods, which have been individually hypothesized to decrease the incidence of POI, is widely unknown. A few of the studies reviewed have trialed multimodal approaches. Shum et al have attempted to determine if sugarless chewing gum can further reduce POI when it is combined with laparoscopic surgery and ERAS protocol (which includes early enteral feeding), two interventions which are also believed to alleviate POI themselves. Possible side effects consist of bloating and eructation as well as a risk of aspiration; however, no patients experienced any of these events in this study.

There were also no significant differences between groups regarding rate of postoperative complications. This trial concluded that the addition of chewing gum did in fact provide additional benefits to the ERAS protocol and laparoscopic surgeries, by resulting in further reduction of POI duration (13). De Leede et al. and Atkinson et al. both conducted similar trials assessing the effects of sugarless chewing gum combined with an ERAS programme (including early enteral feeding) on the reduction of length of stay and time to bowel recovery. However, in contrast to Shum et al., they found no significant changes in time to flatus or time to defecation and determined gum chewing had no further benefit on GI motility (14,16). Due to lack of protocol supervision, de Leede et al.'s results may have been greatly impacted by low compliance of gum chewing as 78% of patients reported they did not chew gum on postoperative day one to three due to nausea, malaise, or fear the gum would stick to their dentures. Nevertheless, they still believe their results are relevant as they showcase how the use of chewing gum, if added to POI guidelines, will be encouraged and not forced in daily practice (14). Regarding Atkinson et al.'s study, they had a lower non-compliance rate of only 11%, however those who did chew gum only did so on average in 58% of the instances when the gum was dispensed (16). Shum et al.'s study does not provide any data on their patients' compliance to their protocols, thus the possibility of this issue contributing to the discrepancy between these three studies cannot be fully analyzed. Another reason for this inconsistency could be that while Shum et al only focused on colorectal surgeries, de Leede et al.'s research included both intestinal and non-intestinal abdominal surgeries (13,14). POI following non-intestinal abdominal surgeries are likely related to a different pathophysiology than that of intestinal surgeries as the degree of intestinal manipulation and damage experienced would greatly differ. It is also possible that ERAS alone provides maximal reduction in POI, making gum chewing

clinically irrelevant in this setting. De Leede et al. and Atkinson et al.'s studies were both conducted with sample sizes much larger than Shum et al., however due to each study's heterogeneity in perioperative protocols within and between studies, it makes comparison and drawing a conclusion on the benefits of adding chewing gum to an ERAS protocol challenging (13,14,16).

Although neither chewing gum nor early enteral feeding have consensus between their studies regarding their individual benefits on bowel function, all studies have shown these methods are individually safe and well-tolerated. The importance and usefulness of adding chewing gum to early enteral feeding to further reduce POI has been raised. The study by Zaghiyan et al. examined this issue. They studied the effects of sugared gum instead of sugarless gum to try and isolate the effects of gum chewing on cephalic-vagal stimulation from the promotility effects of artificial sweeteners. This trial did not result in any significant changes in time to flatus, time to defecation, or POI incidence, and therefore concluded that there were no additional benefits of combining early enteral feeding with gum chewing. This could potentially be explained by the benefits of sugared gum being masked by early enteral feeding as it had already maximally optimized activation of the cephalic-vagal pathway (17). However, due to certain circumstances such as patient preference or their ability to tolerate oral intake soon after surgery, chewing gum may still be a useful intervention in certain individuals to aid in reducing the duration of POI and therefore, it deserves further research. In contrast to the addition of chewing gum to early enteral feeding, Hasler-Gehrer et al. have shown positive benefits on GI recovery from adding coffee instead of tea to early enteral feeding plans (21).

The majority of studies reviewed aimed to determine the effect of their intervention on the recovery of bowel function and the reduction of POI. All three of these methods have been

shown to be safe, well-tolerated, feasible, and in some studies, able to reduce the duration of POI. These measures have ultimately been shown to be safe options which could aid in the management of a physiologically normal POI, and thereby prevent a clinically diagnosed pathological POI and PPOI from occurring.

STUDY LIMITATIONS AND FURTHER DIRECTIONS

A required step before guidelines can be developed for the reduction and management of POIs and PPOIs is the national or international agreement of their standardized definitions. The lack of consistent definitions makes it difficult to appropriately compare the results between primary studies, making this a major limitation in this study. This may require further studies to determine the acceptable length of time to allow for return of GI motility, which may also be variable between types of surgical procedures. A 2013 systematic review proposed standardized clinical definitions for both POI and PPOI to be used by future studies (6); however, as later studies still have inconsistencies in their definitions of these terms, it appears their definitions were never authoritatively accepted.

Possible surrogates for duration of POI used by many studies include time to first flatus, time to first bowel movement, time to tolerability of solid food, and length of hospital stay. The surrogates for POI used in this literature review, time to passage of first flatus and time to passage of first stool, are considered to be subjective in nature and thus the results presented by the reviewed studies rely on the patients properly self-reporting these events to the healthcare team as well as the accurate documentation by the team. It has also been questioned if these endpoints truly reflect the return of motility to the entire GI tract (12). Boelens et al.'s study revealed that a significant decrease in time to defecation does not always necessarily correlate

with significant reduction in POI (24). Although, as there is no standardized definition for POI, the use of surrogates eases comparison between studies.

Several of these studies focused on patients undergoing elective surgeries as well as a specific type of abdominal surgery such as rectal resection or colectomy. It is unknown if these results can be extrapolated to create standardized guidelines for emergency surgeries or other categories of abdominal surgery. It is known that the GI function of different segments of bowel recover at different rates postoperatively, colonic taking the longest, and therefore colorectal surgeries are associated with longer durations of POI (11). Therefore, each type of abdominal surgery may also be affected by preventative measures for POI differently. For those studies which focused broadly on abdominal surgeries and thus included an assortment of operative procedures, their results may have been compromised due to this heterogeneity and the differing response of each technique to the intervention. Some studies attempted to investigate this concern by analyzing subgroups, where some differences in the effectiveness of interventions to reduce POI were seen (13,14,18). It should also be noted that this literature review only focused on abdominal surgeries while it is well known that non-abdominal surgeries can also result in a POI due to spread of inflammation, however this is much less well understood.

The heterogeneity present within and between trials, including aspects such as section of GI pathology, severity of pathology, surgical approach, perioperative analgesia and anesthesia, study design, combination of interventions, stoma versus anastomosis, as well as recent treatment (i.e. chemoradiotherapy), raises questions regarding their validity and affects comparability between studies. In addition, multiple studies had small sample sizes of less than 100-150 individuals, and a few did not fulfill the required sample size to meet the desired power after exclusions. Therefore, larger multicenter studies with limited heterogeneity or adequate

subgroup analysis, directly investigating the incidence of POI regarding various interventions for reduction, would be useful to solidify the research related to the efficacy, safety as well as cost-effectiveness of these reduction techniques.

CONCLUSION

Although none of the interventions reviewed demonstrate complete consensus in their respective trials regarding their ability to reduce POI, there is agreement that these measures are safe, well tolerated, and not related to any major adverse effects. Therefore, chewing gum, coffee, and early enteral feeding are all postoperative measures which patients can be encouraged to adopt. These three interventions may ultimately result in a faster recovery for patients and thus an earlier discharge and decreased healthcare costs for abdominal surgeries. The exact combination of these methods which should be included in the guidelines is unknown and requires further studies to examine the additional benefits provided by using more than one intervention. Future studies should include large sample sizes, multicentre examination, greater control of perioperative regimens, subgroup analysis, and have an endpoint analyzing the incidence of clinical POI directly, and not solely interpreted through the examination of surrogates.

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APPENDIX

Table 1. Summary of Primary Studies on Chewing Gum

Study	Objective	Type of surgery	Study specific POI definition	Study design & sample size (= #)	Outcomes and P-value	Conclusion
Topcu and Oztekin, 2016 (11)	"Determine the effect of gum chewing on the reduction of postoperative ileus and recovery after surgery"	Planned open colorectal surgery		Chewing gum for 15 minutes 3 times a day (30) vs no chewing gum (30)	First flatus time, P < 0.001; First defecation time, P < 0.001	"It is recommended to use gum chewing in nursing care for patients who have undergone colorectal surgery and to inform patients about gum chewing in helping to reduce POI"
Forrester et al, 2014 (15)	"Whether postoperative gum chewing reduces the duration of postoperative ileus symptoms"	Elective open or laparoscopic sigmoid colectomy		Standard care (18) vs silicone patch (16) vs standard care with sugarless chewing gum for greater than 1 hour 3 times a day (13)	Time to first flatus, P = 0.744; Time to first bowel movement, P = 0.198	"Gum chewing was not found to be more effective ... in reducing the duration of postoperative ileus symptoms, length of stay, or complications among patients following open/ laparoscopic sigmoid colectomy"
van den Heijkant et al, 2014 (12)	"Evaluate the effect of gum chewing on POI, length of hospital stay and inflammatory parameters"	Elective open colorectal surgery	"Lack of passage of flatus or stool and intolerance to oral intake for at least 24 h," if met on day 5 after operation	Sugarless chewing gum before and after surgery (52) vs dermal patch (60)	Flatus within 48 hours, P = 0.044; Defecation within 4 days, P = 0.006; POI, P = 0.020; Complications, P = 0.860	"Gum chewing is a safe and simple treatment to reduce POI, and is associated with a reduction in systemic inflammatory markers and complications"
Shum et al, 2016 (13)	"Whether chewing gum could lead to a further reduction in ileus"	Laparoscopic colorectal resection		Sugarless chewing gum for 30 minutes 3 times a day (41) vs no chewing gum (41) in context of ERAS	Time to first flatus, P = 0.007; Time to first bowel motion, P = 0.001	"Chewing gum is a simple intervention that speeds intestinal transit in patients managed with a recovery programme after laparoscopic colorectal resection"
de Leede et al, 2018 (14)	"Evaluated whether chewing gum after elective abdominal surgery reduces LOS and time to bowel recovery in the setting of ERAS-based perioperative care"	Elective laparotomy or laparoscopic abdominal surgery	"Mention of ileus or gastroparesis in the patient's record by the treating physician"	Sugarless chewing gum for 30 minutes 3 times a day (976) vs no chewing gum (966) in context of ERAS	Time to first flatus, P = 0.873; Time to first defecation, P = 0.562; Complications, P = 0.113	"The addition of chewing gum to an ERAS postoperative care pathway after elective abdominal surgery does not reduce the LOS, time to bowel recovery or the rate of postoperative complications"
Atkinson et al, 2016 (16)	"Look at the effects of chewing gum on postoperative recovery"	Elective colorectal resection		Sugarless chewing gum for 10 minutes 4 times a day (199) vs no chewing gum (203) in context of ERAS	Day to first flatus, P = 0.586 Day to first bowel movement, P = 0.153; Vomiting/nausea/ileus, P = 0.197; Complications, P = 0.840	"Chewing gum did not alter the return of bowel function or LOS after colorectal resection"
Zaghiyan et al, 2013 (17)	"Evaluate the effect of sugared chewing gum in combination with early enteral feeding on recovery of GI function"	Elective or urgent major colorectal surgery	Postoperative nausea/vomiting, accompanied by abdominal distention, absence of bowel function, and x-ray findings consistent with ileus	Sugared chewing gum for 45 minutes 3 times a day (54) vs no chewing gum (60) in context of early enteral feeding	Time to flatus, P = 0.83; Time to bowel movement, P = 0.40; POI, P = 0.5; Complications, P = 0.46	"There does not appear to be any benefit to sugared chewing gum in comparison with no gum in patients undergoing major colorectal surgery managed with early feeding in the postoperative period. There may be increased incidence of bloating, indigestion, and eructation, possibly related to swallowed air during gum chewing"
Liu et al, 2017 (18)	"Evaluate the effect of chewing gum on ameliorating ileus following colorectal surgery"	Open and laparoscopic colorectal surgery		1736 patients; sugared or sugarless chewing gum for 5-60 minutes 3-4 times a day vs no chewing gum	Time to flatus, P = 0.0002; Time to first bowel movement, P < 0.00001; POI, P = 0.003	"Chewing gum offers an inexpensive, well-tolerated, safe and effective method to ameliorate ileus following colorectal surgery"

Table 2. Summary of Primary Studies on Coffee

Study	Objective	Type of surgery	Study specific POI definition	Study design & sample size (= #)	Outcomes and P-value	Conclusion
Müller et al, 2012 (19)	"Assess whether coffee consumption accelerates the recovery of bowel function after elective colectomy"	Elective open or laparoscopic colectomy		Coffee (35) vs warm water (36)	Time to first flatus, P = 0.191; Time to first bowel movement, P = 0.028; Complications, P = 0.344	"Coffee consumption after colectomy was safe and was associated with a reduced time to first bowel action"
Dulskas et al, 2015 (20)	"Determine whether consuming a 100-ml cup of coffee is effective in preventing or reducing postoperative ileus"	Elective laparoscopic left colectomy		Decaffeinated coffee (30) caffeinated coffee vs (30) vs water (30)	Time until first flatus, P > 0.05; Time until first bowl movement, P < 0.05; Complications, P = 0.347	"Coffee consumption after colectomy was safe and in the decaffeinated group associated with a reduced time to first bowel action. Caffeine is not a main ingredient affecting the length of postoperative ileus"
Hasler-Gehrer et al, 2019 (21)	"Evaluate the effect of standardized coffee intake on postoperative bowel movement after elective laparoscopic colorectal resection"	Elective colorectal surgery		Coffee (49) vs non-caffeinated tea (47)	Time to first flatus, P = 0.05; Time to first bowel movement, P = 0.006; Complications, P = 0.47	"Coffee intake after elective laparoscopic colorectal resection leads to faster recovery of bowel function. Therefore, coffee intake represents a simple and effective strategy to prevent postoperative ileus"

Table 3. Summary of Primary Studies on Early Enteral Feeding

Study	Objective	Type of surgery	Study specific POI definition	Study design & sample size (= #)	Outcomes and P-value	Conclusion
Pragatheeswarane et al, 2014 (22)	"Compare the safety, tolerability and outcome of early oral feeding vs. traditional feeding in patients undergoing elective open bowel surgery"	Elective open bowel surgery		Early feeding (60) vs traditional feeding (60)	First flatus, P < 0.0001; First stool, P < 0.0001; Anastomotic leak, P = 0.309	"In patients undergoing elective open bowel surgeries, early post-operative feeding is safe, is well tolerated and reduces the length of hospitalization"
Dag et al, 2011 (23)	"Evaluate the safety and tolerability of early oral feeding after colorectal operations"	Elective open colorectal surgery		Early feeding (99) vs regular diet (100)	Time of intestinal movements, P = 0.0001; Time to defecation, P = 0.0001; Anastomotic leak, P = 0.279; Complications, P = 0.541	"The present study indicated that early oral feeding after elective colorectal surgery was not only well tolerated by patients but also affected the postoperative outcomes positively. Early postoperative feeding is safe and leads to the early recovery of gastrointestinal functions"
Boelens et al, 2014 (24)	"Investigate whether early enteral nutrition (EEN), as a bridge to a normal diet, can reduce postoperative ileus"	Major rectal surgery	"Early ileus if 1 or more of the following symptoms occurred: nausea or vomiting for more than 1 episode in the first 5 days, reinsertion of the nasogastric tube in the first 5 days, presence of the nasogastric tube for more than 4 days, no return to normal diet after 5 days, or first-time normal defecation after 7 days. Prolonged ileus was defined as an early ileus lasting more than 5 days. Late ileus was defined as nausea or vomiting after the first 5 days, influencing normal intake and defecation, or reinsertion of the nasogastric tube"	Early enteral nutrition via naso-jejunal tube (61) vs early parenteral nutrition via central line (62)	Time to first defecation, P = 0.04; POI, P = 0.12; Early ileus, P = 0.02; Anastomotic leak, P = 0.009	"Early enteral nutrition is safe and associated with significantly less ileus. Early enteral nutrition is associated with less anastomotic leakage in patients undergoing extensive rectal surgery." "We would suggest a preoperative plan for postpyloric enteral feeding in patients at high risk of POI"
Osland et al, 2011 (25)	"Evaluating surgical outcomes following nutritional provision provided proximal to the anastomosis within 24 hours of gastrointestinal surgery compared with traditional postoperative management"	GI resection		1240 patients; Nutritionally significant early oral or enteral feeding vs traditional feeding	Passage of flatus, P = 0.23; First bowel motion, P = 0.55; Anastomotic dehiscence, P = 0.39; Complications, P = 0.01	"Early postoperative nutrition is associated with significant reductions in total complications compared with traditional postoperative feeding practices and does not negatively affect outcomes such as mortality, anastomotic dehiscence, resumption of bowel function, or hospital length of stay"

ACKNOWLEDGEMENTS

I would like to thank Dr. Pamela Hebbard for sharing her expertise and guidance throughout this capstone project. I would like to thank Rebecca Muller for her comments on this review. I would also like to thank the MPAS program faculty and staff for their continued support over the past two years.