Gastrografin in Prolonged Postoperative Ileus
A Double-blinded Randomized Controlled Trial

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Objective: To investigate the therapeutic value of Gastrografin in shortening duration of prolonged postoperative ileus (PPOI) after elective colorectal surgery.

Background: Gut wall edema is central to the pathogenesis of PPOI. Hypersmotic, orally administered, water-soluble contrast media such as Gastrografin are theoretically capable of mitigating this edema.

Methods: A double-blinded, placebo-controlled, randomized trial was conducted. Participants were allocated to receive 100 mL of Gastrografin (Exposure Group) or flavored distilled water (Control Group) administered enterally. Other aspects of management were standardized. Resolution of PPOI was assessed 12-hourly.

Results: Eighty patients were randomized equally, with 5 in the Exposure Group and 4 in the Control Group excluded from analysis. Participants were evenly matched at baseline. Mean duration of PPOI did not differ between Exposure and Control Groups (83.7 vs 101.3 hours; P = 0.191). When considering individual markers of PPOI resolution, Gastrografin did not affect time to resolution of nausea and vomiting (64.5 vs 74.3 hours; P = 0.404) or consumption of oral diet (75.8 vs 90.0 hours; P = 0.297). However, it accelerated time to flatus or stool (18.9 vs 32.7 hours; P = 0.047) and time to resolution of abdominal distension (52.8 vs 77.7 hours; P = 0.013). There were no significant differences between groups in nasogastric output; analgesia, antimetic, or fluid requirement; complications; or length of stay.

Conclusions: Gastrografin is not clinically useful in shortening an episode of PPOI characterized by upper and lower gastrointestinal symptoms. It may however be of therapeutic benefit in the subset of PPOI patients who display lower gastrointestinal symptoms exclusively after surgery.

Keywords: colorectal surgery, Gastrografin, oral water-soluble contrast media, prolonged ileus, randomized controlled trial

METHODS
Ethics Approval and Trial Registration
Ethics approval was obtained from the Ministry of Health’s National Ethics Committee (NTX12/06/054) and Auckland District Health Board’s (ADHB’s) Research Review Committee (A+5600) before trial commencement. The trial was prospectively registered with clinicaltrials.gov (identifier: NCT01648972, US National Library of Medicine, 8600 Rockville Pike, Bethesda, MD).

Study Population
The source population included all New Zealand citizens and permanent residents living within the catchment area of ADHB. All patients 18 years or older scheduled to undergo elective laparoscopic or open colorectal surgery for any indication between September 2012 and June 2014 were screened for eligibility. Included procedures were segmental colonic or rectal resection, abdominoperineal resection, total colectomy, and formation or reversal of ileostomy or colostomy. Exclusion criteria were participants with an ASA (Australian Society of Anesthetists) grade of 4 or greater; previous allergic or adverse reaction to Gastrografin or iodinated contrast agents; hyperthyroidism; those on preoperative parenteral nutrition; and those who could not participate in trial assessments due to dementia, postoperative delirium, or language difficulties. Participants with anastomotic leak were not excluded unless they required percutaneous or operative intervention. Leak was defined as either (i) anastomotic dehiscence identified...
on reoperation; (ii) intra-abdominal collection next to the anastomosis on computed tomography (CT); or (iii) discharge of feculent material from abdominal wound or drainage tube. Patients requiring reoperation before commencement of formal day 4 assessments for PPOI were not randomized; those requiring reoperation during an episode of PPOI were excluded from subsequent analysis.

**Consent**

All patients were seen on an individual basis preoperatively by the principal investigator (R.V.) and provided with verbal and written information on trial rationale and protocol. Written informed consent was obtained before surgery.

**Participant Assessment**

Patients were assessed for the occurrence of PPOI between 8 AM and 9 AM on a daily basis from day 4 postoperatively until discharge. Those who met diagnostic criteria for PPOI were enrolled, allocated study medication, and then assessed 12-hourly for resolution of PPOI. More than 99% of these assessments were made by a single, blinded investigator who was not affiliated with the overseeing clinical team to ensure standardization of data collection (R.V.).

**Diagnosis and Resolution of PPOI**

A definition of PPOI was recently proposed on the basis of systematic review and global survey and was adopted for this study. PPOI was defined as occurring if patients met 2 or more of the following 5 criteria on or after day 4 postoperatively—nausea OR vomiting over the preceding 12 hours; inability to tolerate a solid or semi-solid oral diet over the preceding 24 mealtime; abdominal distension; absence of flatus AND stool over the preceding 24 hours; and radiologic evidence of ileus on abdominal plain film or CT over the preceding 24 hours. PPOI was defined as having resolved when all 4 of the following criteria were met—absence of nausea AND vomiting for 12 hours with nasogastric tube (NGT) spigotted or removed; ability to tolerate a solid or semi-solid oral diet at the preceding mealtime; absence of abdominal distension; and passage of flatus OR stool over the preceding 24 hours. A detailed description of each diagnostic and resolution criterion can be found in Supplementary Material 1, available at http://links.lww.com/SLA/A807.

**Interventions**

**Perioperative Care**

All patients underwent routine elective in-patient abdominal surgery either by, or under the supervision of, a specialist colorectal surgeon at Auckland City Hospital. All aspects of postoperative care, which occurred before a diagnosis of PPOI were left to the discretion of the overseeing clinical team.

**Study Medication**

Patients were assessed daily from day 4 postoperatively for the occurrence of PPOI and upon diagnosis were enrolled and prescribed a single 100 mL dose of study medication. This was given orally or via NGT within 4 hours of diagnosis by a nurse not associated with the study. If administered via NGT this was spigotted for at least 2 hours but switched back to free drainage earlier if the patient experienced nausea or vomiting.

Participants in the Exposure Group received 100 mL of undiluted Gastrografin (Bayer Schering Pharma, Germany). Each 1 mL of solution contained 100 mg sodium diatrizoate and 660 mg meglumine diatrizoate in aqueous solution with flavoring agents and saccharin.

Participants in the control group received 100 mL of placebo consisting of 1 mL concentrated anise solution (2% anise oil, 72% ethanol, 26% water), 40 mL glycerol, and 59 mL distilled water. This solution mimicked the smell, taste, and consistency of Gastrografin but lacked its hypertonicity, and has been previously validated as an appropriate placebo counterpart.

**Standardized Management Guidelines for PPOI**

The clinical management of trial participants conformed to standardized evidence-based recommendations. These are outlined in detail in Supplementary Material 2, available at http://links.lww.com/SLA/A807. Nursing and medical staff were made aware of the presence of these guidelines via formal interactive ward-based teaching sessions and one-on-one reminders to involved personnel. In addition, a single page summary of guidelines was placed in the clinical notes folder of participants upon recruitment.

**Outcomes**

**Baseline Data**

Data were prospectively collected for an assortment of parameters including age at the time of surgery, sex, ASA grade, body mass index (BMI), procedure type, open versus laparoscopic versus converted technique, operative indication, and procedure duration.

**Primary Outcome**

The primary outcome for this study was the duration of PPOI, defined as the time in hours from diagnosis to resolution of PPOI as described earlier.

**Secondary Outcomes**

Data were collected on time until discharge criteria were met (from surgery and from diagnosis of PPOI), actual length of hospital stay (from surgery and from diagnosis of PPOI), and 30-day readmission rate. Discharge criteria were defined as being able to tolerate an oral diet sufficient to meet daily nutritional needs; safe and independent mobilization (or at level of baseline function); independent performance of Activities of Daily Living (or at level of baseline function); and the ability to manage pain with oral analgesia only. Occurrence of other complications were recorded and graded using the Clavien-Dindo classification system.

Volume and type of intravenous fluid required over the course of the PPOI episode was recorded. Analgesia consumption was noted with total opioid use being expressed as the mean equivalent dose (MED). MED has previously been shown to be a validated and sensitive measure of narcotic use. Antiemetic consumption was recorded with comparison being facilitated by conversion to standardized units (1 unit = 4 mg ondansetron; 25 mg cyclizine; 10 mg metoclopramide; 0.625 mg droperidol; 10 mg stemetil; 4 mg dexamethasone; 1.5 mg scopolamine). The requirement for NGT placement was noted with data prospectively collected on total output volume and time to removal. Requirement for parenteral nutrition (PN) and duration of administration were also recorded.

Data were collected on the tolerability of study medication and the occurrence of any adverse effects. Aspiration was considered a sentinel event requiring unbending of treatment allocation to the overseeing clinical team.

**Sample Size**

An a priori power calculation was undertaken on the basis of previously published data on the incidence and duration of PPOI after elective colorectal surgery at ADHB. PPOI was identified in 50 of 255 consecutive cases with a mean duration of 4.54 days [standard deviation (SD) = 2.21] per episode. It was estimated that if therapeutically active, Gastrografin may be reasonably expected to reduce the mean duration of PPOI to 3 days. A reduction from 4.5 to 3 days would also represent a shift, which was clinically useful.

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Using a 2-tailed independent-samples t test for the difference between 2 unpaired means with an alpha error of 0.05 and power of 0.8, it was determined that to detect a 33% difference in duration of PPOI between groups, 35 patients would be required in each arm. It was anticipated some participants would be excluded from analysis because of diagnosis of an alternate pathology or return to theater. We therefore aimed to recruit 40 patients in each arm.

**Randomization**

Allocation to Exposure and Control Groups occurred in a 1:1 ratio and randomization was blocked into groups of 8 to ensure comparable allocation in the event of early termination of the trial. Randomization sequence generation was undertaken by a third party not associated with this study using an online purpose-built random number generator (www.random.org). A spreadsheet was created with consecutive numbers from 1 to 80 with treatment allocation listed adjacent to this. This spreadsheet was then sealed in an opaque envelope, signed across the seal by the third party, and delivered to the hospital pharmacy.

**Blinding**

Participants, study investigators, and clinical staff were all blinded to treatment allocation. Trial investigators arranged for study medication to be provided by the hospital pharmacy on a weekly basis. Specified participant numbers were forwarded to the pharmacy staff who, after consulting the randomization spreadsheet, either formulated placebo or repackaged Gastrografin into identical tinted glass bottles. The only discriminating feature between bottles supplied to study investigators was the allocation number printed on its label. These bottles were then collected and stored in a locked cabinet at room temperature. Upon enrolment, participants were allocated to receive the next consecutively numbered bottle of study medication.

The hospital pharmacy was not involved in any aspect of patient management, study design, data collection, or analysis. Before study commencement, external commercial testing was undertaken to ensure opened and repackaged Gastrografin maintained its stability and sterility. Data from this analysis showed the compound remained stable and sterile for at least 30 days after repackaging.

**Statistical Analysis**

Analysis was performed on an intention-to-treat basis. No interim or subgroup analyses were planned or undertaken. Statistical analysis was performed using SPSS for Windows (Version 19; SPSS, Chicago, IL). Parametricity was determined using histograms, Q-Q plots, and the Shapiro-Wilk test. Normally distributed data were expressed as mean ± SD and nonparametric data as median ± interquartile range (IQR). Univariate analysis was carried out using the χ² test for categorical variables, the Mann-Whitney U test for nonparametric continuous variables, and an independent samples t test for parametric continuous variables. Kaplan-Meier curves were constructed for primary outcome measures with resolution of symptoms as the survival event. Differences in survival distribution were compared using the log-rank test. Results were considered statistically significant if P < 0.05.

**RESULTS**

Patient flow is detailed in the CONSORT diagram (Fig. 1). Between September 2012 and June 2014, 351 patients were assessed for eligibility. Six patients declared consent and a further 5 were unable to provide consent. Four patients met exclusion criteria of receiving preoperative parenteral nutrition (n = 3) or having previous anaphylaxis to an iodinated contrast agent (n = 1). Nine patients were excluded before commencement of formal assessments of PPOI because of reoperation before day 4 (n = 7); intubation and ventilation in intensive care unit for sepsis (n = 1); and postoperative ischemic stroke on day 2 (n = 1). In total, 88 of the remaining 327 screened patients developed PPOI (incidence 26.9%). Eight patients were excluded before treatment allocation for the following reasons—withdrawal of patient consent (n = 1); withdrawal of clinical team consent because of concerns relating to patient age (92 years old) and frailty (n = 1); hemodynamic instability of cardiac origin (n = 1); transfer to geriatric ward where staff were unaware of trial protocol and standardized management guidelines (n = 1); Gastrografin charted in error by on-call intern (n = 1); reoperation for anastomotic leak on morning of diagnosis (n = 1); vomiting with aspiration of gastric contents leading to intubation and ventilation in intensive care unit (n = 1); and inability to participate in trial assessments because of postoperative delirium (n = 1).

The remaining 80 patients were randomized equally to receive either Gastrografin or placebo. Diagnostic criteria most frequently met were presence of nausea or vomiting (n = 74 [92.5%]), inability to tolerate an oral diet (n = 77; 96.3%), and abdominal distension (n = 68; 85%); absence of flatus and stool (n = 37; 46.3%) and radiologic evidence of ileus (n = 13; 16.3%) were observed less commonly. Three or more diagnostic criteria were met in 72 (90%) patients.

All 80 participants were administered study medication within 4 hours of diagnosis with the exception of 2 (both in the Gastrografin group), who received it at 8 hours and 14 hours postdiagnosis because of nursing delay. A single patient in the placebo group consumed 50 mL of study medication per orally before declining the rest because of taste; all other participants consumed the study medication in its entirety. Five patients were excluded from analysis in the Exposure Group because of reoperation for anastomotic leak (n = 3), early postoperative SBO (n = 1), and fascial dehiscence (n = 1). Four patients were excluded in the Control Group because of reoperation for early postoperative SBO (n = 2), reoperation for anastomotic leak (n = 1), and occurrence of outlier data (n = 1). This latter participant’s duration of PPOI was 660 hours, whereas all remaining durations of PPOI were normally distributed between 12 and 264 hours (Fig. 2). Data from this participant were excluded to avoid skewing results toward the Exposure Group thereby providing a more conservative estimate of any observed treatment effect.

Seventy-one patients were analyzed with 35 in the Exposure Group and 36 in the Control Group. There was complete follow-up for all primary and secondary endpoints. Groups were evenly matched at baseline with no significant differences in age, sex, race/ethnicity, ASA grade, BMI, indication for surgery, procedure type, or operative technique (Table 1).

The mean duration of PPOI did not differ significantly between the Gastrografin and placebo groups (83.7 vs 101.3 hours; P = 0.191) (Table 2). When considering individual markers of PPOI resolution, Gastrografin did not significantly affect time to resolution of nausea and vomiting (64.5 vs 74.3 hours; P = 0.404) or consumption of an oral diet (75.8 vs 90.0 hours; P = 0.297) compared to placebo. However, it accelerated time to flatus or stool (18.9 vs 32.7 hours; P = 0.047) and time to resolution of abdominal distension (52.8 vs 77.7 hours; P = 0.013). Kaplan-Meier analyses concordantly showed no significant difference in resolution distributions between groups for overall duration of PPOI (Fig. 3), time to resolution of nausea and vomiting, and time to consumption of an oral diet. Time-to-event was however accelerated in the Gastrografin group for passage of flatus or stool (log-rank test, P = 0.029) and resolution of abdominal distension (P = 0.016).

There were no significant differences between groups in time until objective discharge criteria—actual length of stay, occurrence of other complications, and 30-day readmission rate—were met (Table 3). The volume of intravenous crystalloid, paracetamol and antiemetic administered over the episode of PPOI was similar.
between groups. There was however a trend toward increased use of opioid analgesia in the Gastrografin cohort (19.8 vs 8.8 MED; \( P = 0.050 \)). An equivalent number of participants in each group required NGT insertion with a similar median duration of insertion and median total output volume. No significant differences were noted in the number of patients requiring postoperative PN or the median duration of administration if commenced. Study medication was generally well-tolerated with watery diarrhea/high stoma losses being the principal adverse events in each study arm.

**DISCUSSION**

Understanding of the changes in gastrointestinal contractility which accompany PPOI is lacking, and current thought is that generalized hypomotility predominates rather than dysmotility or...
FIGURE 2. Histogram of duration of PPOI.

TABLE 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Gastrografin (n = 35)</th>
<th>Placebo (n = 36)</th>
<th>All (n = 71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs*</td>
<td>62.7 (16.1)</td>
<td>66.2 (14.4)</td>
<td>64.5 (15.3)</td>
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<td>1</td>
<td></td>
</tr>
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<td>19</td>
<td>21</td>
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</tr>
<tr>
<td>3</td>
<td>16</td>
<td>14</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²†</td>
<td>28.1 (7.0)</td>
<td>29.6 (8.6)</td>
<td>28.6 (7.7)</td>
<td>0.593</td>
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<td>Indication</td>
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<td>Procedure</td>
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<td>R hemicolectomy</td>
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<tr>
<td>Reversal Hartmann’s or end ileostomy</td>
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<td>3</td>
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<tr>
<td>Open</td>
<td>22</td>
<td>26</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Lap-assisted</td>
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<td>4</td>
<td>11</td>
<td></td>
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<tr>
<td>Laparoscopic</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td></td>
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<tr>
<td>Converted</td>
<td>4</td>
<td>3</td>
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*Parametric data were expressed as mean (SD).
†Nonparametric data were expressed as median (IQR).
complete atony.5,20 This is supported by the fluctuating clinical features of ileus—such as obstipation, abdominal distension, tympany, the absence of bowel sounds, and presence of air-fluid levels on imaging—as well as the predicted gastrointestinal response to the processes of inflammation, autonomic dysfunction, and exogenous activation of opioid receptors thought to be central to its pathogenesis.5,21 OWSC media such as Gastrografin act as osmotic laxatives, and their therapeutic properties in adhesive SBO are believed to relate to their ability to shift fluid from edematous bowel wall to lumen, which in turn serves to improve coordinated myocyte activity, cause bolus-induced peristalsis, and create a longitudinal pressure difference across the site of obstruction.9 It was therefore hypothesized that Gastrografin may exert an effect similar to SBO in PPOI albeit with an absence of any discrete differences in pressure.

The potential benefit of OWSC media in resolving ileus has received limited attention in the literature. Watkins and Robertson20 first published in 1985 a retrospective review of 40 patients with apparent PPOI who had received OWSC media with good effect; there was however no control arm with which this was compared. This was followed a decade later with a case-control study, which showed in a gynecologic surgical cohort that OWSC media conferred no apparent benefit with respect to return of bowel function or oral intake. The incidence of PPOI was particularly high in this study with 57 of 115 screened patients meeting inclusion criteria.11 Chen et al performed an unblinded randomized trial investigating the routine administration of Gastrografin after colorectal surgery. With 25 patients in each arm, it was shown that Gastrografin allowed oral feeding to commence 1.5 days earlier and shortened length of stay from 10.2 to 7.6 days when compared to placebo; no inference was however made on its value in ileus.12 The role of Gastrografin in PPOI was therefore unclear, and adequately powered, randomized, and blinded prospective appraisal was thought necessary to assess its clinical utility.

An important feature of this study was the attempt to use standardized and reproducible definitions for the diagnosis and resolution of PPOI. Previous prospective work has used varying definitions for PPOI, which has precluded comparison of competing interventions and translation to clinical practice.1 Moreover, although symptoms such as the presence or absence of flatus or stool are relatively easy to qualify, “softer” symptoms such as nausea and the ability to tolerate an oral diet are not as transparent and may be subject to differing interpretations.22,23 Diagnostic criteria have been explicitly defined in this study in what is hoped to be a clinically useful and readily appraisable manner. It is anticipated that this will serve to improve external validity and encourage homogeneity in subsequent endpoint reporting.

We have demonstrated that while Gastrografin accelerated time to flatus or stool and resolution of distension in patients with PPOI, it did not influence time to tolerance of an oral diet or resolution of nausea and vomiting. These findings were foreshadowed by a recent clinical consensus update, which subclassified ileus on the basis of the relative prominence of presenting symptom clusters. In descending prevalence—type I ileus was represented by “panintestinal” symptoms, type II by upper gastrointestinal symptoms exclusively, and type III by lower gastrointestinal symptoms exclusively.24 Although this classification system was designed primarily to lend expediency to the clinical description of an ileus syndrome, it also strongly alludes to the pathophysiologic mechanisms, which may explain our results. Dysfunction associated with ileus may affect segments of the gastrointestinal tract autonomously and to varying degrees.9 Indeed, it has been shown that after surgery motility returns first to the small bowel, then stomach, and finally large bowel.20 This suggests that although Gastrografin may successfully counteract edema and promote peristalsis within the small and/or large bowel, it lacks an equivalent effect in the stomach. We postulate that this may be related to the anatomical shape of the stomach whereby its large internal volume and noncylindrical shape hinders Gastrografin’s ability to effectively shift fluid from wall to lumen and induce sufficient distension for peristalsis. Alternatively, absence of effect may be explained by pathophysiologic mechanisms such as autonomic dysfunction or gastrointestinal hormone derangement, which are unrelated to edema and known to manifest more prominently in the stomach than small or large bowel.5,24,25 More than 90% of the patients in our cohort demonstrated symptoms of upper gastrointestinal dysfunction on diagnosis of PPOI and may have therefore been less susceptible to the mechanical effects of Gastrografin. A regimen, which combines an

### TABLE 2. Primary Outcome Measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Gastrografin (n = 35)</th>
<th>Placebo (n = 36)</th>
<th>All (n = 71)</th>
<th>P</th>
<th>Log-rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of PPOI, h</td>
<td>83.7 (58.8)</td>
<td>101.3 (53.9)</td>
<td>92.6 (56.6)</td>
<td>0.191</td>
<td>0.311</td>
</tr>
<tr>
<td>Time to flatus or stool</td>
<td>18.9 (20.0)</td>
<td>32.7 (35.2)</td>
<td>25.9 (29.4)</td>
<td>0.047</td>
<td>0.029</td>
</tr>
<tr>
<td>Time to resolution of nausea and vomiting</td>
<td>64.5 (54.5)</td>
<td>74.3 (44.2)</td>
<td>69.5 (49.5)</td>
<td>0.404</td>
<td>0.370</td>
</tr>
<tr>
<td>Time to resolution of distension</td>
<td>52.8 (35.6)</td>
<td>77.7 (45.6)</td>
<td>65.4 (42.5)</td>
<td>0.013</td>
<td>0.016</td>
</tr>
<tr>
<td>Time to consumption oral diet</td>
<td>75.8 (61.9)</td>
<td>90.6 (52.0)</td>
<td>83.0 (57.1)</td>
<td>0.297</td>
<td>0.348</td>
</tr>
</tbody>
</table>

All data are parametric and expressed as mean (SD).

*FIGURE 3.* Kaplan-Meier survival curves for time to resolution of PPOI (log-rank test, P = 0.311).
inhalational hyperosmotic agent with an agent that promotes gastric emptying, may be expected to promote resolution of PPOI and warrants investigation in future research.

There was a trend toward an increased consumption of opioid analgesia in the Gastrografin cohort compared to placebo. It is speculated that this may relate to the increased peristaltic activity Gastrografin is believed to precipitate, which could feasibly be associated with increased pain in a patient who has undergone abdominal surgery.

The presentation of early postoperative SBO (EPSBO) closely resembles that of PPOI, and it may be difficult to differentiate these syndromes clinically after surgery. This represents an important potential confounding factor in this trial whereby participants with self-limiting EPSBO could have been mislabeled as having PPOI and administered study medication. This in turn may partly explain the lack of statistical significance. CT has been shown to distinguish PPOI and EPSBO with high sensitivity and specificity. The lack of statistical significance. CT has been shown to distinguish PPOI and EPSBO with high sensitivity and specificity.

A trial which employs routine CT scanning in all patients with suspected ileus will resemble that of PPOI, and it may be difficult to differentiate these syndromes clinically after surgery. This represents an important potential confounding factor in this trial whereby participants with self-limiting EPSBO could have been mislabeled as having PPOI and administered study medication. This in turn may partly explain the lack of statistical significance. CT has been shown to distinguish PPOI and EPSBO with high sensitivity and specificity.

A second limitation relates to the relatively broad distribution of duration of PPOI. This is likely a reflection of inherent variation in the severity of the clinical syndrome and the fact that diagnosis and resolution of PPOI required the presence and absence of separate symptom clusters. Nonetheless, the standard deviations for duration of PPOI noted here are consistent with those observed previously. Finally, larger patient numbers would have reduced the chance of a type II error in this study. However, it was shown on subanalyses that there was earlier occurrence of the 2 markers of PPOI related to resolution of small and large bowel symptoms, without any significant improvement in the remaining 2 markers associated with the upper gastrointestinal symptom cluster. Increased numbers may therefore not necessarily show a difference in PPOI, which uses all these symptoms in its definition.

**CONCLUSIONS**

Gastrografin reduces the time taken to passage of flatus or stool and resolution of distension, but not the time taken to tolerance of an oral diet or resolution of nausea and vomiting. It is therefore not clinically useful in shortening an episode of PPOI characterized by all of these features. Gastrografin may however be of therapeutic benefit in the subset of patients with PPOI who display lower gastrointestinal symptoms exclusively after surgery and further prospective appraisal in this scenario is warranted.

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