

## Effect of water-soluble contrast in colorectal surgery: A prospective randomized trial

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### Abstract

**AIM:** Postoperative gastrointestinal-tract motility is normally delayed. Early feeding after colorectal surgery has been reported recently, but late feeding is common. Gastrografin not only enhances bowel peristalsis, but also decreases bowel-wall edema. Whether contrast medium allows early oral feeding and reduces the duration of hospitalization requires clarification.

**METHODS:** Fifty patients underwent elective colorectal surgery in a regional medical center. Patients were prospectively randomized into a Gastrografin group or control group ( $n = 25$  each). Patients in the Gastrografin group began their feeding schedule with 100 mL of 5% dextrose water with 100 mL of Gastrografin on postoperative d 3 and were advanced to a full liquid diet when the contrast reached the colon in 4 h. Patients in the control group began their feeding schedule with 200 mL of 5% dextrose water on postoperative d 3 and were advanced to a full liquid diet after the passage of flatus and stool. Nasogastric tubes were inserted for persistent postoperative vomiting. Fullness, nausea, vomiting, complications, time of anesthesia, time of operation, time of mobilization, time of oral feeding, and duration of hospital stay were recorded and analyzed with Student's  $t$ -test.

**RESULTS:** In the Gastrografin group, one patient had aspiration pneumonia and one patient had anastomotic leakage resulting in sepsis and eventual death. This mortality was excluded from the subsequent statistical analysis. In the control group, two patients had wound infections. There was no significant difference between the two groups at the time of anesthesia, time of operation, or time of mobilization. There were significant differences between the two groups in the time of oral feeding ( $3.3 \pm 0.3$  d in

the Gastrografin group vs  $4.8 \pm 0.4$  d in the control group;  $P =$  odds ratio--, 95%CI [-0.5 to +0.7 d]) and in the length of hospital stay ( $7.6 \pm 1.1$  d in the Gastrografin group vs  $10.2 \pm 1.3$  d in the control group;  $P =$  odds ratio--, 95% CI [-1.2 to +1.4 d]).

**CONCLUSION:** Gastrografin not only allowed early oral feeding but also reduced the duration of hospitalization after elective colorectal surgery.

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**Key words:** Colorectal surgery; Contrast; Gastrografin

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### INTRODUCTION

Postoperative intestinal motility is normally delayed and returns in a predictable manner<sup>[1,2]</sup>. Recent investigations have shown that early oral feeding after abdominal surgery is safe and generally well tolerated<sup>[3]</sup>. This has potential cost-saving implications in this age of rising medical expenses and diminishing reimbursement. Patients who are fed early should be able to be discharged from hospital earlier, and this shorter hospital stay should decrease the overall cost.

The role of water-soluble contrast medium in acute small-bowel obstruction has recently been evaluated. Studies have documented the diagnostic value of this contrast medium in assessing the need for surgical treatment<sup>[4-7]</sup>. A possible therapeutic effect of this agent has also been suggested<sup>[8-11]</sup>. Gastrografin (Schering AG, Berlin, Germany) is the water-soluble contrast medium that has been most widely studied. This contrast medium may shorten the period of postoperative ileus<sup>[12]</sup> and have other therapeutic effects after elective colorectal surgery. Therefore, we designed this prospective randomized trial to determine whether Gastrografin facilitates early oral feeding and shorter hospitalization in patients undergoing elective colorectal surgery.

### MATERIALS AND METHODS

#### Patients

Between June 1 2003 and March 1 2004, 50 patients underwent elective colorectal surgery in a regional medical

center, where about 1 500 colorectal surgical procedures are performed yearly. Our patients were prospectively randomized into two different postoperative treatment arms via their case numbers: the even numbers were assigned to the Gastrografin group ( $n = 25$ ) and the odd numbers to the control group ( $n = 25$ ) after informed written consent was given by all patients.

Patients younger than 16 years or who had emergency operations were excluded. Patients with obstruction, perforation, or active intra-abdominal infection were also excluded. No laparoscopic procedures were performed.

Patient characteristics were as follows (Table 1). The mean age was  $63.7 \pm 11.5$  years (range, 20-83 years) in the Gastrografin group and  $64.2 \pm 10.3$  years (range, 25-81 years) in the control group. The procedures were evenly matched in both groups, with the following results: segmental resection with ileocolostomy, five in the Gastrografin group and six in the control group; resection with colocolostomy, 10 in the Gastrografin group and 11 in the control group; abdominoperineal resection, three in the Gastrografin group and two in the control group; total proctocolectomy with ileoanal pouch, one in the Gastrografin group and two in the control group; and ostomy closure, six in the Gastrografin group and four in the control group. Diagnoses were also distributed evenly across groups: carcinoma was most common, with 18 in the Gastrografin group and 16 in the control group; followed by diverticular disease, with six in the Gastrografin group and seven in the control group; then inflammatory bowel disease, with one in the Gastrografin and two in the control group. Both groups had similar numbers of patients who had undergone prior abdominal surgery (Gastrografin, five; control, seven).

**Table 1** Patient characteristics

	Gastrografin group (25)	Control group (25)
Mean age (yr)	63.7 $\pm$ 11.5	64.2 $\pm$ 10.3
Operation		
Ileocolostomy	5	6
Colocolostomy	10	11
Abdominoperineal resection	3	2
Proctocolectomy and ileoanal pouch	1	2
Ostomy closure	6	4
Diagnosis		
Carcinoma	18	16
Diverticular disease	6	7
Inflammatory bowel disease	1	2
Prior abdominal surgery	5	7

## Methods

**Patient management:** Patients were maintained on a clear liquid diet from noon on the day prior to surgery. Bowel preparation, consisting of phosphosoda catharsis and oral neomycin and metronidazole, was administered the day before surgery. All patients had orogastric tubes placed intraoperatively for gastric decompression, which were removed immediately upon arrival in the postanesthetic care unit.

Patients in the Gastrografin group began their feeding schedule with 100 mL of 5% dextrose water with 100 mL of Gastrografin on postoperative d 3 and were advanced to a full liquid diet when the contrast medium reached the colon after 4 h, confirmed by plain abdominal radiography. If the patients consumed 1 000 mL or more of a full liquid diet in a 24-h period, they were advanced to a regular diet the next day. Patients were discharged when they could tolerate more than two-thirds of a regular diet.

Patients in the control group began their feeding schedule with 200 mL of 5% dextrose water on postoperative d 3 and were advanced to a full liquid diet after evidence of return to normal bowel function with the passage of flatus or stool, and no nausea or vomiting. These patients were advanced to a regular diet when they consumed 1 000 mL or more of a full liquid diet in a 24-h period. They were discharged when they could consume more than two-thirds of a regular diet.

All patients received general anesthesia and meperidine was administered during the initial postoperative phase. In both groups, nasogastric tubes were inserted for vomiting unresponsive to antiemetics. All patients were monitored for fullness, nausea, vomiting, and complications such as wound infection, aspiration pneumonia, and anastomotic leakage; and time of operation, time of anesthesia, time of early mobilization, time of oral feeding, and length of hospital stay were recorded.

## Statistical analysis

The  $\chi^2$  test was used for qualitative variables and Student's *t*-test for continuous variables. Results of the two groups were compared using Student's *t*-test. A two-day difference in the duration of hospitalization was deemed to be a clinically significant difference, and the sample size was based on the detection of this difference with 90% power. A 95% CI for the difference in duration of hospitalization was computed.  $P < 0.05$  indicated statistical significance. Analyses were performed using S-Plus®2000 for Windows statistical software (CANdiensten, Amsterdam, The Netherlands).

## RESULTS

The feeding schedule in the Gastrografin group was well tolerated, starting with 100 mL of 5% dextrose water and 100 mL of Gastrografin on postoperative d 3 in all patients. Two patients (8%) in the control group experienced fullness postoperatively, but no patient in the Gastrografin group did. Three patients (12.5%) in the Gastrografin group and six patients (24%) in the control group experienced nausea (Table 2). Three patients (12%) in the control group experienced vomiting postoperatively, but none in the Gastrografin group. All patients in both groups were treated initially with antiemetics. However, three patients (12%) in the control group required nasogastric decompression and intravenous fluids for persistent vomiting, whereas no patient in the Gastrografin group required this treatment. None of these differences was statistically significant.

Similar complication rates were seen in both groups; one case of aspiration pneumonia and one of anastomotic leakage in the Gastrografin group; two cases of wound

infection in the control group.

There were no significant differences between the two groups at the time of anesthesia, time of operation, or time of mobilization.

There were significant differences between these two groups in the time of oral feeding (Gastrografin,  $3.3 \pm 0.3$  d *vs* control,  $4.8 \pm 0.4$  d;  $P < 0.05$ , 95%CI, -0.5 to +0.7 d) and duration of hospital stay (Gastrografin,  $7.6 \pm 1.1$  d *vs* control,  $10.2 \pm 1.3$  d;  $P < 0.001$ , 95%CI, -1.2 to +1.4 d).

**Table 2** Clinical features and complications of Gastrografin and control groups

	Gastrografin group (24)	Control group (25)
Fullness	0	2
Nausea	3	6
Vomiting	0	3
Nasogastric decompression	0	3
Complications		
Wound infection	0	2
Aspiration pneumonia	1	0
Anastomotic leak	1	0
Time of operation (h)	$4.3 \pm 1.2$	$4.2 \pm 1.1$
Time of anesthesia (min)	$34.3 \pm 5.4$	$32.7 \pm 6.3$
Time of mobilization (d)	$5.1 \pm 1.0$	$5.3 \pm 1.2$
Time of oral feeding (d)	$3.3 \pm 0.3^1$	$4.8 \pm 0.4$
Hospital stay (d)	$7.6 \pm 1.1^1$	$10.2 \pm 1.3$

<sup>1</sup>Significantly different.

## DISCUSSION

A dynamic ileus after abdominal surgery is characterized by a lack of mobility caused by neuromuscular inhibition with sympathetic overactivity. It occurs after all abdominal procedures and motility typically returns to the small bowel within 24 h, to the stomach within 48 h, and to the colon within 3-5 d<sup>[1,2]</sup>. Because of this phenomenon, we designed our study so that our patients began their feeding schedule with 5% dextrose water on postoperative d 3, after which a liquid diet was initiated and advanced to a regular diet over 1-2 d.

Reissman *et al*<sup>[3]</sup>, reported a prospective, randomized trial of 161 patients who underwent elective colon resection, and compared early postoperative feeding with traditional postoperative feeding. This study showed that early oral feeding was safe and also demonstrated no difference in the duration of ileus, the incidence of nausea and vomiting, or major postoperative morbidity. Hartsell *et al*<sup>[13]</sup>, also showed that early oral feeding after elective colorectal surgery was safe. Most patients tolerated early feeding. However, there was no significant difference in the duration of hospitalization in these patients.

Given this information, it is reasonable to suppose that patients who tolerate early oral feeding after treatment with Gastrografin can be discharged from hospital sooner, thereby reducing the duration of hospitalization and medical costs.

The role of water-soluble contrast medium in predicting the need for surgery for adhesive small-bowel obstruction has recently been evaluated. Other studies have evaluated its possible therapeutic effects<sup>[8,9]</sup>. Gastrografin is the contrast

medium most commonly cited. It is an ionic bitter-flavored mixture of sodium diatrizoate, meglumine diatrizoate, and a wetting agent (polysorbate 80), with an osmolality of 1 900 mOsm/L, approximately six times that of extracellular fluid<sup>[8]</sup>. It promotes the shifting of fluid into the bowel lumen and increases the pressure gradient across the anastomotic site<sup>[8]</sup>. The bowel contents are diluted, and in the presence of the wetting agent, the passage of the bowel contents through the anastomotic site is facilitated. Gastrografin also decreases edema of the bowel wall and enhances bowel motility<sup>[6,9,14]</sup>. Gastrografin is water-soluble and relatively safe, even if anastomotic leakage occurs. Complications from the use of Gastrografin are rare, although anaphylactoid reactions and lethal aspiration have been reported<sup>[15-17]</sup>. Gastrografin may also shorten postoperative ileus<sup>[12]</sup>, thus providing another therapeutic effect in elective colorectal surgery. We designed this prospective randomized trial to determine whether treatment with Gastrografin facilitates early oral feeding and shorter hospitalization in patients undergoing elective colorectal surgery.

In our study, there were significant differences between the two groups in the duration of hospitalization and time of oral feeding. The primary hypothesis that treatment with Gastrografin leads to early oral feeding and shorter hospitalization in patients undergoing elective colorectal surgery was confirmed in this series.

No difference in the incidence of complications was noted between the two groups. In the Gastrografin group, an anastomotic complication occurred that was related to surgical technique. However, Gastrografin allowed early detection of the site of anastomotic leakage. Another patient suffered aspiration pneumonia that may have been due to Gastrografin, but there was no subsequent lethal effect. In the control group, two patients suffered wound infections that were unrelated to feeding. Furthermore, the fact that the anastomotic leak and aspiration pneumonia noted in two patients receiving Gastrografin might have been caused by the fact that they got Gastrografin in the first place. Certainly, the fluid loaded in the gut could have led to the anastomotic leak and the aspiration pneumonia might have been made worse if the patient aspirated Gastrografin. Thus, Gastrografin was not only safe, but also provided a further diagnostic advantage in patients undergoing gastrointestinal-tract surgery. However, we could not forget the lethal complications of Gastrografin when using it.

No patient suffered from fullness in the Gastrografin group, whereas 8% suffered from fullness in the control group, leading to a delay in oral feeding. Although no significant difference between the two groups was observed, Gastrografin may have reduced the incidence of fullness, contributing to the shorter hospitalization in the Gastrografin group.

There were some defects in our study because the study was single blinded. When taking care of the patients and making decisions regarding whether or not to give them food and whether or not to send them home might have been influenced by knowing which group they were in. Therefore, another double blinded study should be designed to overcome the disadvantage in the future.

In recent years, several studies have demonstrated that routine nasogastric decompression is unnecessary in colorectal

surgery<sup>[13,18]</sup>. In the Gastrografin group, only 12% of patients suffered from nausea and none required a nasogastric tube. In the control group, 24% patients suffered from nausea and 12% of patients required nasogastric tubes because of vomiting. Although none of these differences was statistically significant, perhaps the lower incidence of nausea and vomiting in the Gastrografin group was related to the effects of the contrast medium.

The time of anesthesia and the time of operation did not differ significantly between the two groups, so there was no effect on postoperative care and consequently no significant difference in the time of mobilization between the two groups. Therefore, in our study, early oral feeding and shorter hospitalization might be attributable to the effects of Gastrografin rather than to other causes.

The type of anesthesia and appropriate analgesia also have important effects on postoperative care in colorectal surgery. Bradshaw *et al.*<sup>[9]</sup>, reported that the return of bowel function and the duration of hospitalization of patients undergoing colon surgery were improved if perioperative epidural anesthesia and analgesia were provided. Carli *et al.*<sup>[20]</sup>, showed that thoracic epidural analgesia had distinct advantages in providing superior quality analgesia and shortening the duration of postoperative ileus.

Our patients received general anesthesia and analgesia agents during the initial postoperative phase. Gastrografin not only allowed early oral feeding but also reduced the hospital stays of our patients. Further randomized studies, including larger doses of Gastrografin and perioperative epidural anesthesia, may enhance this effect and allow even shorter hospitalization.

We conclude that Gastrografin not only facilitates early oral feeding but also reduces hospitalization after elective colorectal surgery.

## REFERENCES

- 1 Condon RE, Sarna SK. Motility after abdominal surgery. *Clin Gastroenterol* 1982; **11**: 609-620
- 2 Smith J, Kelly KA, Weinshilboum RM. Pathophysiology of postoperative ileus. *Arch Surg* 1977; **112**: 203-209
- 3 Reissman P, Teoh TA, Cohen SM, Weiss EG, Noguera JJ, Wexner SD. Is early oral feeding safe after elective colorectal surgery? A prospective randomized trial. *Ann Surg* 1995; **222**: 73-77
- 4 Blackmon S, Lucius C, Wilson JP, Duncan T, Wilson R, Mason EM, Ramshaw B. The use of water-soluble contrast in evaluating clinically equivocal small bowel obstruction. *Am Surg* 2000; **66**: 238-242; discussion 242-244
- 5 Chen SC, Chang KJ, Lee PH, Wang SM, Chen KM, Lin FY. Oral Urografin in postoperative small bowel obstruction. *World J Surg* 1999; **23**: 1051-1054
- 6 Chen SC, Lin FY, Lee PH, Yu SC, Wang SM, Chang KJ. Water-soluble contrast study predicts the need for early surgery in adhesive small bowel obstruction. *Br J Surg* 1998; **85**: 1692-1694
- 7 Wilson MS, Ellis H, Menzies D, Moran BJ, Parker MC, Thompson JN. A review of the management of small bowel obstruction. Members of the Surgical and Clinical Adhesions Research Study (SCAR). *Ann R Coll Surg Engl* 1999; **81**: 320-328
- 8 Choi HK, Chu KW, Law WL. Therapeutic value of gastrografin in adhesive small bowel obstruction after unsuccessful conservative treatment: a prospective randomized trial. *Ann Surg* 2002; **236**: 1-6
- 9 Assalia A, Schein M, Kopelman D, Hirshberg A, Hashmonai M. Therapeutic effect of oral Gastrografin in adhesive, partial small-bowel obstruction: a prospective randomized trial. *Surgery* 1994; **115**: 433-437
- 10 Feigin E, Seror D, Szold A, Carmon M, Allweis TM, Nissan A, Gross E, Vromen A, Freund HR. Water-soluble contrast material has no therapeutic effect on postoperative small-bowel obstruction: results of a prospective, randomized clinical trial. *Am J Surg* 1996; **171**: 227-229
- 11 Fevang BT, Jensen D, Fevang J, Sondenaa K, Ovrebø K, Rokke O, Gisslasson H, Svanes K, Viste A. Upper gastrointestinal contrast study in the management of small bowel obstruction--a prospective randomised study. *Eur J Surg* 2000; **166**: 39-43
- 12 Watkins DT, Robertson CL. Water-soluble radiocontrast material in the treatment of postoperative ileus. *Am J Obstet Gynecol* 1985; **152**: 450-455
- 13 Hartsell PA, Frazee RC, Harrison JB, Smith RW. Early postoperative feeding after elective colorectal surgery. *Arch Surg* 1997; **132**: 518-520; discussion 520-521
- 14 Strodahl A, Laerum F, Gjolberg T, Enge I. Water-soluble contrast media in radiography of small bowel obstruction. Comparison of ionic and non-ionic contrast media. *Acta Radiol* 1988; **29**: 53-56
- 15 Skucas J. Anaphylactoid reactions with gastrointestinal contrast media. *AJR Am J Roentgenol* 1997; **168**: 962-964
- 16 Ridley LJ. Allergic reactions to oral iodinated contrast agents: reactions to oral contrast. *Australas Radiol* 1998; **42**: 114-117
- 17 Trulzsch DV, Penmetsa A, Karim A, Evans DA. Gastrografin-induced aspiration pneumonia: a lethal complication of computed tomography. *South Med J* 1992; **85**: 1255-1256
- 18 Delaney CP, Fazio VW, Senagore AJ, Robinson B, Halverson AL, Remzi FH. 'Fast track' postoperative management protocol for patients with high co-morbidity undergoing complex abdominal and pelvic colorectal surgery. *Br J Surg* 2001; **88**: 1533-1538
- 19 Bradshaw BG, Liu SS, Thirlby RC. Standardized perioperative care protocols and reduced length of stay after colon surgery. *J Am Coll Surg* 1998; **186**: 501-506
- 20 Carli F, Trudel JL, Belliveau P. The effect of intraoperative thoracic epidural anesthesia and postoperative analgesia on bowel function after colorectal surgery: a prospective, randomized trial. *Dis Colon Rectum* 2001; **44**: 1083-1089