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Objective Assessment of Postoperative Gastrointestinal Motility in Elective Colonic Resection Using a Radiopaque Marker Provides an Evidence for the Abandonment of Preoperative Mechanical Bowel Preparation

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Abstract

Background: It has been suggested that mechanical bowel preparation (MBP) has no benefit in terms of anastomotic healing, infection rate, or improvement in the postoperative course in patients undergoing elective colorectal surgery, and that it should be abandoned. However, the effect of MBP on postoperative gastrointestinal motility has been assessed subjectively. In this randomized trial, we objectively assessed the effect of MBP on postoperative gastrointestinal motility and mobility in elective colonic resection.

Method: In total, 79 patients scheduled to undergo elective colonic resection for cancer were randomized to MBP or no-MBP groups prior to surgery. All patients ingested radiopaque markers before surgery to evaluate postoperative gastrointestinal motility, objectively evaluated by the transition of the markers at postoperative days (PODs) 1, 3, 5 and 7. The groups were then further subdivided into open and laparoscopic-assisted colectomy (LAC) groups and evaluated in terms of gastrointestinal motility and postoperative mobility.

Results: There was no significant difference between the no-MBP and MBP groups in terms of perioperative and postoperative course. In the LAC subgroup, there was no significant difference between the no-MBP and MBP groups in terms of marker transition. However, in the open subgroup, there was a significant difference between the groups in terms of the residual ratio of markers in the small intestine at POD 3 (no-MBP 35.3% vs. MBP 69.2%; p=0.041), excretion rate of markers at POD 5 (no-MBP 49.7% vs. MBP 8.8%; p=0.005), and residual ratio in the small intestine at POD 7 (no-MBP 3.1% vs. MBP 28.8%; p=0.028). Additionally, the excretion rate in the no-MBP group was significantly higher than in the MBP group at POD 7 (74.1% vs. 33.8%; p=0.007).

Conclusions: Our data provide additional evidence to support the abandonment of MBP in elective open colonic surgery.
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Key words: mechanical bowel preparation (MBP), postoperative gastrointestinal motility, radiopaque markers

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Introduction

Postoperative inhibition of small bowel motility after elective colorectal surgery is transient and the stomach recovers within 24–48 h, whereas colonic function takes 48–72 h to return to normal[1]. Although the determination of postoperative paralytic "ileus" is somewhat controversial[2], prolonged postoperative hypomotility can lead to significant medical problems and constitutes the most common reason for delayed discharge from hospital after abdominal surgery[3]. Postoperative colonic motility is influenced by many factors, including surgical manipulation, inflammatory mediators, autonomic dysfunction, electrolyte and fluid imbalances, and analgesics (opioids)[2]. Many perioperative strategies have been instituted or modified in an attempt to prevent the development or reduce the incidence and/or duration of gastrointestinal hypomotility[3]. Preoperative mechanical bowel preparation (MBP) with, for example, oral sodium phosphate, has been used before elective colonic resection[4]. In order to reduce morbidity and mortality in postoperative complications in elective colorectal surgery, MBP has been applied routinely[5,6] and has become surgical dogma since the early 1970s[7,8]. According to the most recent survey in the US, the procedure is regularly employed by more than 99% of colorectal surgeons[5]. However, recent prospective randomized controlled trials and meta-analyses[6,9–12] have questioned the use of MBP in elective colorectal surgery. Additionally, a meta-analysis concluded that significantly more anastomotic leaks were found after MBP[12], and in studies of healthy volunteers, MBP results in dehydration, which may cause hypotension when the patient undergoes general anesthesia with an epidural. If hypotension develops, there is a high risk of the patient suffering an intravenous fluid overload during surgery. Fluid overload will, in turn, impact on gastrointestinal motility after surgery[13].

In the Enhanced Recovery After Surgery (ERAS)[14,15] protocol, MBP is tabulated as one of the negative factors for postoperative elective colonic surgery, based on evidence such as that cited above[15]. However, regarding postoperative bowel motility, the only evidence came from the subjective impressions of patients; thus, it is unclear whether any given patient's complaint is valid. Moreover, studies demonstrated that stool frequency does not correlate with colorectal motility[16] and that, inversely, many patients who complain of constipation do in fact have normal colorectal transit times[17,18]. This background led us to evaluate more precisely whether MBP affected postoperative gastrointestinal motility. The radiopaque marker SITZMARKS® (KONSYL, Easton, Maryland, USA), a useful marker for the diagnosis of hypomotility, colonic inertia and functional outlet obstruction[19–21], was used to assess bowel obstructive disease. By radiographically monitoring the transition of patients' markers, we assessed the intestinal motility as well as the location of obstructions. In this paper we report the results of a clinical trial into postoperative gastrointestinal motility in elective colonic resection by means of a laparoscopic operation or open surgery, assess the influence of MBP on improving postoperative gastrointestinal motility and evaluate the role for MBP in colonic surgery.

Materials and Methods

Participants

This study included patients who underwent an elective open or laparoscope-assisted colonic resection (LAC) for cancer at our institution between January and December 2009. The protocol was approved by our IRB committee. All patients were invited to participate in this trial, which compared the outcomes after surgery with or without preoperative MBP. The general inclusion criteria were patients with (1) a primary tumor located somewhere between the cecum and the sigmoid colon and (2) an American Society of Anesthesiologists grade of I or II.

The patients were staged according to the TNM classification[22], with reference to preoperative examinations such as a colonoscopy, abdominopelvic computed tomography, PET and a barium enema.

Patients were randomized to the MBP or no-MBP groups by a central allocation system. Written consent was obtained from each patient following the provision of verbal and written information. Exclusion criteria comprised a stoma, a complete intestinal obstruction that needed decompression or a past history of another colonic resection.

Preoperative MBP

All patients began a low-residue diet upon arrival at the hospital. Patients in the MBP group were prohibited from eating, starting on the morning of the day before surgery, and received a bowel preparation of 10 mL of sodium picosulfate hydrate (Laxoberon®) in the evening 2 days before surgery, followed by 2,000 mL of an oral agent consisting of polyethylene glycol (PEG; Niflec®) in the morning of the day before surgery. Patients in the no-MBP group ate in the evening of the day before surgery and did not receive any special pretreatment. Patients in both groups received an intravenous infusion of the prophylactic antibiotic flomoxef (1 g) at the induction of anesthesia and every 3 h during surgery.

Endpoints and Assessment of Postoperative Gastrointestinal Motility

To assess the influence of MBP on the improvement of postoperative gastrointestinal motility, we used the radiopaque marker SITZMARKS®; this product contains 20 radiopaque 4.5-mm-diameter rings per capsule (**Fig. 1**). All patients took SITZMARKS® 2 h before surgery. Postoperative gastrointestinal motility was clinically assessed by counting the number of markers and radiographically monitoring their transition on postoperative days (PODs) 1, 3, 5 and 7.

Using abdominal radiography on PODs 1, 3, 5 and 7, the markers were counted in each intestinal region: (1) as far as the small intestine, (2) as far as the rectum and (3) excretion (**Fig. 2**).

The primary endpoints were the small intestinal and colonic residual rates (=the number of residual markers per 20) and the excretion rate (=the number of excreted markers per 20) at individual PODs.

Surgical Technique and Postsurgical Management

In the open abdominal surgery, the surgical procedure was performed through a midline laparotomy. In the LAC, the abdomen was entered via an incision of approximately 4 cm in the appropriate area. When a right or left colectomy was performed, a small transrectus or midline incision was made on the epigastrium close to the umbilicus. In a left colectomy, a transverse incision was made on the lower mid-hypogastrium. Exclusion criteria for the LAC operation are 1) the patients with the cancer infiltrating to the other organs and 2) the patients with the huge cancer. Both techniques involved complete mobilization of the hepatic or splenic flexure. Vessel ligation was performed according to the location and depth of the tumor in each case. Bowel reconstructions were performed by hand-sewing or functional end-to-end anastomosis in a right colectomy, and by hand-sewing or double-stapling end-to-end anastomosis in a left colectomy. Suction drains were inserted when a left side colectomy was performed. Nasogastric tubes were removed soon after extubation. All patients received 48 h of mid-thoracic epidural anesthesia/analgesia after surgery and began taking oral fluids on POD 1, with a fluid diet and antiflatulents commencing on POD 4. Patients were allowed a regular diet on POD 5. As prophylaxis for deep vein thrombosis, they received an intravenous infusion of an antithrombocytic agent for 24 h postoperatively.

Statistics

Statistical analyses to compare the two groups were conducted using the Mann-Whitney U-test and Student's *t*-test. The Kruskal-Wallis test, followed by Bonferroni's post hoc test were used to compare the four groups. Multivariate analysis was performed using logistic regression analysis. A p value of <0.05 was considered to indicate statistical significance. All analyses were performed using SPSS ver.12J Base System.

Results

Characteristics of the Participants

In total, 79 patients matched the criteria for this study: 38 (17 males, 21 females) were randomly assigned to the no-MBP group and 41 (24 males, 17

Fig. 1 Photograph of the SITZMARKS®, which includes 20 radiopaque rings per capsule.

Fig. 2 Representative X-ray films of the patient at POD 7 following an open colectomy with MBP. **Arrowheads**: the markers which are located in the small intestine (2 markers); **Arrows**: the markers which are located in the colon (16 markers). Two markers had already been excreted (excretion rate was 2/20=10%).

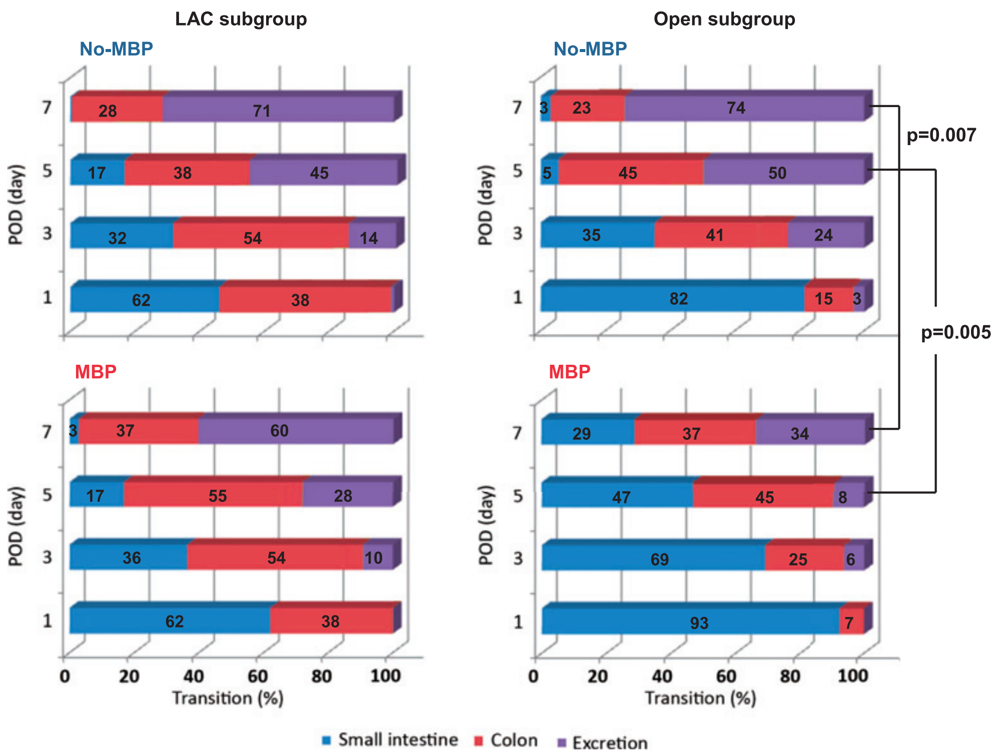

Fig. 3 The location and transition of the markers in patients following colonic surgery. The graph represents transition of markers between the small intestine, the colon and the outside of the body via excretion. The numbers indicate the residual or excretion rate (%). The p-value was calculated using Student's t-test.

Table 1 Characteristics of the participants

Variables	Total (*n*=79)	no-MBP (*n*=41)	MBP (*n*=38)	P value
Baseline characteristics				
Age, years (range)	68.8 (44–92)	66.2 (44–84)	69.3 (52–92)	0.192
Gender (male/female)	41/38	24/17	17/21	0.223
BMI	21.3 (15.0–27.8)	21.8 (16.0–26.4)	20.8 (15.0–27.8)	0.147
Tumor location (rt/lt)	42/37	17/24	25/13	0.041
Pathological stage				
I	23	14	9	0.313
II	19	7	12	0.135
III	24	13	11	0.793
IV	13	7	6	0.880
Operation and Complications				
Surgical procedure (open/LAC)	31/48 (convert 1)	12/29 (convert 1)	19/19 (convert 0)	0.061
Type of anastomosis (hand-sewn/stapled)	42/37	25/26	17/21	0.223
Blood loss, mL (range)	213.7 (0–1,715)	235.0 (0–1,715)	185.9 (0–660)	0.449
Operation time, min (range)	240.1 (126–597)	241.0 (155–597)	232.9 (126–365)	0.629
First flatus, day	1.85	1.9	1.8	0.916
First defecation, day	3.45	3.3	3.4	0.778
Postoperative hospital stay, days (range)	18.0 (8–105)	15.5 (8–81)	19.9 (8–105)	0.279
Complications (%)				
Wound infection	0	0	0	
Intra-abdominal infection	2 (2.5)	1 (2.4)	1 (2.6)	0.957
Anastomotic leakage	4 (5.1)	3 (7.3)	1 (2.6)	0.346
Ileus	3 (3.8)	2 (4.9)	1 (2.6)	0.346
Others	1 (1.3)	1 (2.4)	0	0.938

females) to the MBP group. The clinical characteristics at baseline as well as operation data and postoperative complications are given in **Table 1**. The two subgroups were comparable in terms of clinical background details with the exception of tumor location; the no-MBP group had a significantly higher rate of left colon tumors (p=0.041; **Table 1**). Additionally, there was no difference in the operation time, intraoperative blood loss, postoperative hospital stay, or rate of surgical infectious complications between the two groups. In the no-MBP group, the procedure for one patient was changed to open surgery because of invasion of the small intestine. There was no significant difference in the mean time of the first bowel movement between the two groups, which was assessed using the patients' subjective reports of flatus and defecation (no-MBP vs. MBP, 1.9 vs. 1.8 and 3.3 vs. 3.4, respectively).

Characteristics of the Variables in the LAC and Open Subgroups

When the patients were divided into the LAC and open subgroups, 48 patients were treated laparoscopically (19 no-MBP and 29 MBP) and 31 were treated by conventional open surgery (19 no-MBP and 12 MBP). There was no significant difference between the two groups in terms of patient baseline characteristics, operative data, or postoperative complications (**Table 2**). Again, there was no significant difference between the two groups in terms of the time to first bowel movement, which was assessed by subjective reports of flatus and defecation (**Table 2**).

Assessment of Location and Transition of the Radiopaque Markers

To objectively assess the influence of MBP on postoperative gastrointestinal motility, the transition of the markers was analyzed in both the LAC and open subgroups (**Fig. 3**). In the open subgroup, the no-MBP group had a significantly higher excretion

Table 2 Characteristics of the variables in the LAC and open subgroups

	LAC group				Open group			
	Total (n=48)	no-MBP (n=19)	MBP (n=29)	P value	Total (n=31)	no-MBP (n=19)	MBP (n=12)	P value
Baseline characteristics								
Age, years (range)	66.7 (44–87)	66.7 (52–87)	66.7 (44–84)	0.979	69.3 (47–91)	71.3 (57–91)	66.6 (47–84)	0.271
Gender (male/female)	27/21	9/10	18/11	0.321	14/17	7/12	7/5	0.486
BMI (range)	21.4 (14.7–27.7)	21.1 (15.0–27.8)	21.6 (14.7–27.7)	0.638	21.2 (16.6–26.4)	20.5 (16.6–24.2)	22.2 (17.9–26.4)	0.055
Tumor location (rt/lt)	22/26	11/8	11/18	0.215	23/8	15/4	8/4	0.447
Operation and Complications								
Type of anastomosis (hand-sewn/stapled)	25/23	9/10	16/13	0.601	14/17	8/11	6/6	0.484
Blood loss, mL (range)	123.4 (0–865)	124.2 (0–865)	123 (0–660)	0.983	338.8 (15–1,715)	253.1 (15–1,170)	474.6 (15–1,715)	0.100
Operation time, min (range)	231.8 (126–430)	235.4 (126–365)	229.4 (155–430)	0.754	251.4 (168–597)	232 (168–335)	282.2 (168–597)	0.125
First flatus	1.74	1.8	1.7	0.681	2.01	1.9	2.2	0.278
First defecation	3.2	3.2	3.2	0.994	3.56	3.6	3.5	0.966
Postoperative hospital stay, days (range)	14.4 (7–105)	11.1 (7–16)	16.5 (7–105)	0.195	23.2 (10–96)	20.3 (10–82)	27.9 (10–96)	0.313
Complications (%)								
Wound infection	0	0	0		0	0	0	
Intra-abdominal infection	1 (2.1)	1 (5.3)	0	0.216	1 (2.1)	0	1 (8.3)	0.719
Anastomotic leakage	2 (4.2)	0	2 (6.9)	0.247	2 (4.2)	1 (5.3)	1 (8.3)	0.920
Ileus	3 (6.3)	1 (5.3)	2 (6.9)	0.821	1 (2.1)	0	1 (8.3)	0.719
Others	3 (6.3)	1 (5.3)	2 (6.9)	0.821	1 (2.1)	0	1 (8.3)	0.719

rate of markers versus that of the MBP group at POD 5 (no-MBP 49.7% vs. MBP 8.8%; p=0.005) and POD 7 (74.1% vs. 33.8%; p=0.007). In accordance with the excretion rate, there was a significant difference between the two groups in the residual ratio of markers in the small intestine at POD 3 (no-MBP 35.3% vs. MBP 69.2%; p=0.041) and POD 7 (no-MBP 3.1% vs. MBP 28.8%; p=0.028). In the LAC subgroup, although the no-MBP group seemed to have an earlier recovery from postoperative hypomotility, there was no significant difference between the no-MBP and MBP groups in terms of markers localization after surgery. For example, in the LAC subgroup, the excretion rate of markers at POD 7 was 70.6% in the no-MBP group and 60.6% in the MBP group (p=0.365). Moreover, the MBP group of the open subgroup had a significantly lower excretion rate at POD 7 compared with the other three groups (LAC no-MBP vs. LAC MBP vs. open no-MBP vs. open MBP; p=0.037). In order to determine the independent and significant factors in the modulation of bowel motility after colonic surgery, we used logistic regression analysis. We set a threshold of a 50% excretion rate and assigned other possibly important variables including age, gender, tumor location, type of anastomosis, bleeding volume and operation time **(Table 3)**. The variable of no-MBP was found to be the sole independent and

Table 3 Multivariate analysis was performed according to logistic regression analysis. The 50% of excretion rate was set as a threshold.

Variables	Odds ratio	P value
Age	0.95 (0.84–1.07)	0.390
Gender	0.31 (0.026–3.63)	0.350
Location	4.13 (0.37–46.37)	0.251
Anastomosis	0.15 (0.010–2.35)	0.188
Bleeding	0.999 (0.99–1.008)	0.884
Operation time	1.004 (0.97–1.038)	0.813
no-MBP	52.52 (2.55–1,082.82)	0.010

significant factor for the prediction of a higher excretion rate of the markers (odds ratio 52.5, 95% confidence interval 2.55–1,082.82, p=0.010), indicating that no-MBP was an important factor for earlier recovery of bowel motility after open colonic surgery.

Discussion

In this RCT we studied the effect of MBP on postoperative bowel motility using an objective evaluation system in patients undergoing elective open/laparoscopic colon surgery. Administration of preoperative MBP resulted in a delay in the excretion of the markers on POD 5 and 7 in the open subgroup, indicating that MBP negatively affected the recovery of bowel movement from postoperative gastrointestinal hypomotility. Moreover, multivariate analysis demonstrated that a lack of MBP was an independent and significant factor in postoperative gastrointestinal motility. The results of a previous report by Jung et al.[23] are consistent with our data; they showed that preoperative bowel preparation was stressful for colonic surgery and prolonged postoperative ileus. Shafii et al.[24] evaluated 86 patients undergoing cystectomy and urinary diversion and reported that bowel preparation significantly increased the incidence of postoperative ileus and length of hospital stay. The underlying mechanism by which MBP negatively affects recovery from postoperative bowel hypomotility remains unclear. Huge et al.[25] demonstrated a decrease in colonic tone in patients following left colonic surgery on POD 2 and 3 and severely impaired postoperative colonic motility. Additionally, a past report demonstrated that bowel irrigation, despite the use of PEG, caused an unduly large amount of congestion, edema and inflammation of the intestinal mucosa.[26] We believe that this result indicates that various changes in the intestinal mucosa caused by bowel preparation restricts gastrointestinal motility and slows postoperative recovery. One possible explanation for the relationship between MBP and late onset of postoperative bowel movement is that preoperative MBP caused dehydration and fluid and electrolyte abnormalities[27], followed by intraoperative salt and water overload, which could result in hypotonus of the bowel.

Many other methods of stimulating postoperative colonic motility have been studied in addition to MBP. However, postoperative gastrointestinal hypomotility has many causes, and the most effective treatment may be a multimodal strategy; this was also recently recommended by the ERAS clinical care protocol[15].

We suggest that in cases of laparoscopic surgery it is necessary to collapse the bowel with MBP because feces left in the bowel influences manipulation during the operation. Nevertheless, in laparoscopic surgery we found no difference between the two groups in terms of postoperative bowel motility or postoperative complications. This may have been because the procedure was less invasive and the postoperative gut function improved earlier than for open surgery[28]. On the other hand, we noted a negative effect in some patients in the no-MBP group: during the operation on the lower sigmoid colon, we often found that solid feces hindered transanal artificial anastomosis. In these cases, we were able to safely create an anastomosis after washing the transanal route and removing the feces from the intestinal lumen. Thus, to more safely and effectively perform an anastomosis, fecal stasis at the planned anastomosis site should be avoided. In conclusion, according to our results and those of past reports, it can be omitted in other cases of colon surgery.

Taken together, we suggest that our data provide additional evidence supporting the abandonment of MBP for elective open colonic surgery, and that the results of this study are consistent with the ERAS protocol.

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