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Quantification of the effects of coffee on postoperative ileus after laparoscopic ventral rectopexy: a randomized controlled trial

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Summary

Background Coffee consumption positively affects intestinal function following abdominal surgery with bowel resection. This study aimed to quantify the effect of coffee on intestinal activity after laparoscopic ventral rectopexy (LVR).

Methods We conducted a single-center, open-labeled, randomized controlled trial from 2014 to 2016 (UMIN-CTR, UMIN000024908). Patients who had undergone scheduled LVR for rectal intussusception or external rectal prolapse were randomly assigned to a coffee group or a water group (23 per group) and asked to drink 100 ml of either coffee or water after the procedure. Each participant was orally administered a radiopaque marker capsule the morning after surgery, and abdominal radiographs were obtained daily. The primary outcome was the total number of evacuated radiopaque markers 26 h after administration. Secondary outcomes included time to first flatus and defecation and results of segmental transit analysis of the markers on radiographs.

Results The mean number of evacuated radiopaque markers 26 h after administration in the coffee group was significantly higher than that in the water group (1 [range, 0–6] vs. 0 [range, 0–0]; $p = 0.04$), however, the mean time (hours) to first defecation (55.1 [range, 19.1–114.0] vs. 69.7 [range, 20.7–141.6]; $p = 0.13$) or time (hours) to first flatus (9.3 [range, 0.5–47.1] vs. 12.6 [range, 1.1–46.1]; $p = 0.35$) was not significant.

Conclusion Coffee consumption accelerates bowel movements, but its clinical effect after LVR is also small. Further studies about the indication of coffee for the type of surgery or the optimal amount of coffee consumption are warranted.

Keywords Coffee · Enhanced recovery after surgery · Ileus · Postoperative care · Postoperative complications

Main novel aspects

1. Previous prospective studies have shown the positive effect of coffee on intestinal function after abdominal surgery. However, these studies were related to bowel resection or lymphadenectomy, which may lead to denervation of the intestines; thus, our study aimed to show whether coffee affects patients after gastrointestinal surgery without bowel resection or rectal denervation, i.e., laparoscopic ventral rectopexy.
2. Although a clinical difference is shown, it is still relatively small, i.e., 9.4–15.4 h mean difference in the time to first defecation after operation between the coffee and water groups. Therefore, we tried to quantify whether coffee consumption accelerates intestinal activity after operations.
3. After quantification of the coffee effects, we still found that coffee provides significantly positive effects on intestinal function after abdominal surgery, but its effect is small when the same amount of coffee was administered; in previous studies, only 100 ml coffee three times daily was taken after operation. Therefore, we need to determine the optimal amount of coffee intake in future studies.

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Introduction

Postoperative ileus (POI) occurs commonly (incidence rate of 10–30%) after abdominal surgery [1]. Coffee may stimulate bowel function in healthy volunteers [2, 3]. Prospective studies have shown the positive effect of coffee on intestinal function after abdominal surgery [4–7]. However, these studies were related to bowel resection or lymphadenectomy, which may lead to denervation of the intestines; thus, whether coffee affects patients after gastrointestinal surgery without bowel resection or rectal denervation remains unknown. Therefore, we aimed to quantify whether coffee consumption accelerates intestinal activity after operations without bowel resection, such as laparoscopic ventral rectopexy (LVR).

Materials and methods

Trial design

This study was a single-center, open-label, randomized controlled trial performed to evaluate the efficacy of coffee on postoperative intestinal motility. Study protocols were approved by the ethics committee of Kameda Medical Center. The trial was registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) as UMIN000024908. Written informed consent was obtained from all participants before randomization.

Study participants

Patients with either rectal intussusception or external rectal prolapse who underwent LVR at Kameda Medical Center between July 2014 and August 2016 were enrolled. Those with slow transit constipation, aversion or allergy to coffee, American Society of Anesthesiologists physical status (ASA-PS) classification of IV or V, any central nervous system dysfunction or peripheral neuropathy with pre-existing severe constipation, age <20 years, or unable to provide written informed consent were excluded.

Randomization

Participants were stratified according to disease, sex, and age (younger than 70 years vs. 70 years or older). They were randomly assigned to either the coffee or water group using the permuted block method. Neither the surgeons nor the patients were blinded to the treatment assignments. Patients who could not continue our protocol because of severe intraoperative or postoperative complications and those who underwent open surgery after randomization were excluded.

Operative technique

All surgeries were performed by the attending surgeon or under the surgeon's supervision. Surgical procedures were performed according to the technique described by D'Hoore et al. ([8], Figs. 1 and 2).

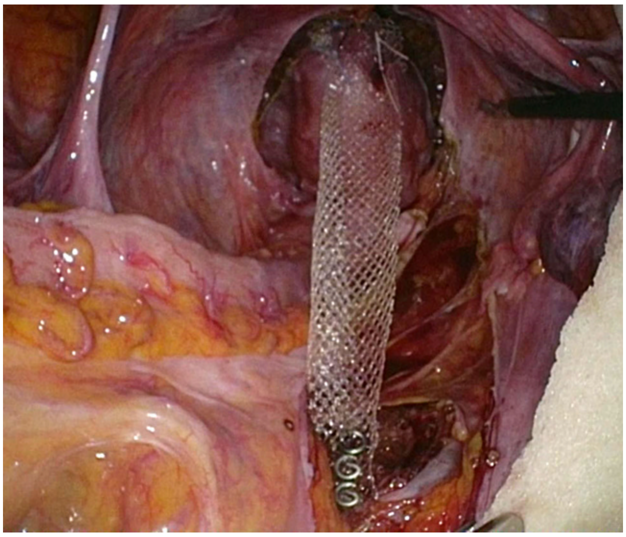

Fig. 1 Dissection exclusively anterior to the rectum, preserving the lateral ligaments. A strip of polypropylene (3 × 18 cm) mesh is introduced and positioned as distally as possible on the anterior side of the rectum and sutured on both the rectal wall and the posterior wall of the vagina. The mesh is also secured tension-free to the sacral promontory

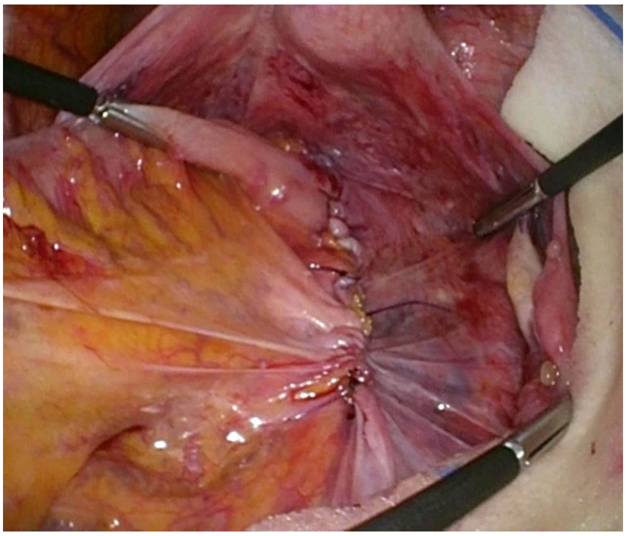

Fig. 2 The mesh is peritonealized by suturing the free edge of the previously divided peritoneum over the mesh to avoid small-bowel adhesions

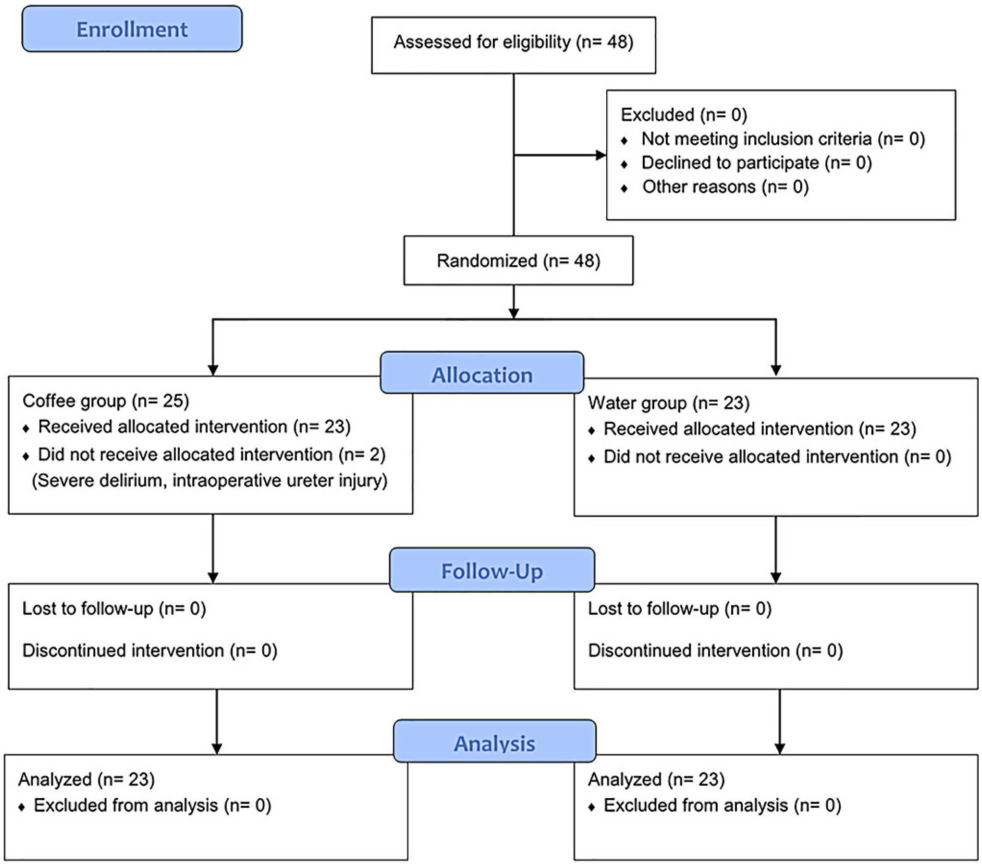

Fig. 3 CONSORT diagram of the trial

Perioperative care

The enhanced recovery after surgery (ERAS) protocol was used for all patients undergoing LVR at our institute [9, 10]. Bowel preparation was not performed. All patients received a glycerin enema in the evening before the surgery. Surgery was performed with the patient under general anesthesia. A nasogastric tube was inserted at the start of surgery and removed after completion. A thoracic epidural catheter was also used and removed the next morning. Additionally, flurbiprofen axetil and acetaminophen were subsequently administered as needed.

The postoperative feeding regimen and mobilization were standardized. Patients were discharged after the first defecation on day 2 or later if they had stable vital signs, tolerated a regular diet, and had no postoperative complications. Other details about perioperative care are described in the Supplementary file.

Intervention

Patients in the coffee group drank 100 ml of coffee 5 h after surgery on the day of surgery. They drank coffee three times daily (100 ml at 9:00 AM, 1:00 PM, and 5:00 PM) beginning on the day after surgery (postoperative day 1) until the first defecation. In the water group, coffee was replaced by 100 ml of water and was consumed according to the same schedule.

Each cup of coffee or water was heated to 50–60 °C. Patients were requested to consume them within 10 min without any additives such as milk or sugar. Other than the coffee or warm water, they were only allowed to drink water. The same brand and type of commercially available regular black coffee was prepared and served for the coffee group (UCC BLACK; UCC Ueshima Coffee Co., Ltd., Kobe, Japan).

Data collection and endpoints

Each participant was administered a radiopaque marker capsule (SITZMARKS®; Konsyl Pharmaceuticals, Fort Worth, TX, USA) containing 20 pellets of barium sulfate-impregnated polyethylene at 7:00 AM on the day of surgery. Radiopaque marker capsules enable quantification of intestinal motility [11, 12]. Therefore, the primary outcome was defined as the total number of evacuated radiopaque markers 26 h (9:00 AM on postoperative day 2) after their administration. Secondary outcome measurements were time to first flatus, time to first defecation, and results of the segmental transit analysis used to evaluate the radiopaque marker distribution to enable estimation of the whole intestinal movement. Abdominal radiographs were obtained at 6 h (1:00 PM on postoperative day 1) and 26 h after administration of the radiopaque marker and 9:00 AM daily thereafter until the first defecation. Radiopaque marker distribution was confirmed using a previously reported method [11, 12]. The first flatus was self-reported, and the first defecation was verified by a nurse. During segmental transit analysis, the markers identified on radiographs in five locations, namely, stomach, small intestine, right colon, left colon, and rectum, were counted by two physicians. The right and left colon were distinguished according to the appearance of the spine. Because 20 markers were included in the capsule, we calculated the number of markers evacuated.

Clinical data such as age, sex, body mass index, ASA-PS, primary disease indicated for LVR, comorbidities, and operative data (such as operative time, infusion amount, bleeding amount, and postoperative complications) were collected from clinical records. Postoperative ambulation time was calculated daily using self-reported questionnaires. Pain and fatigue were evaluated using a standardized scale ranging from 1 to 10 points. Nausea and vomiting were recorded by a nurse.

Statistical analysis

We designed the primary analysis to detect between-group difference in the number of evacuated markers 26 h after administration. To calculate the sample size, we assumed that the mean and variance of the number of evacuated markers in the control group normally would be distributed as 3 and 1, respectively, and coffee was expected to increase the mean number by 60%. Based on the assumption, 23 patients per group (total of 46 patients) were required to provide 80% power to detect a difference at a 5% level of significance during a two-sample *t* test. All outcomes were assessed using a per-protocol analysis. Univariate analyses were performed using a non-parametric analysis (Mann–Whitney *U* test) for continuous variables and chi-square test or Fisher's exact test for categorical variables. Parametric analyses (Student's *t* test) were performed based on the assumption for equality of variance, which was not actually met in the collected data. Therefore, a post hoc analysis with a non-parametric comparison was applied. A value of $p < 0.05$ was considered statistically significant.

As part of the transit analysis, we estimated the association between coffee administration and marker distribution in the gastrointestinal tract at 26 h (ordinal variable) using a generalized estimating equation (GEE) logistic regression model with patient-level clustering. Statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria; [13]).

Results

A total of 48 patients were randomly assigned to the two groups. Two patients in the coffee group were excluded because one had an intraoperative ureter injury and the other developed severe delirium postoperatively (Fig. 3). Patient characteristics (Table 1) and perioperative outcomes (Table 2) were not significantly different between the groups. One patient in the coffee group had pneumonia, which resolved rapidly after antibiotic administration.

The mean number of evacuated radiopaque markers 26 h after administration in the coffee group was significantly higher than that in the water group (1 [range, 0–6] vs. 0 [range, 0–0]; $p = 0.04$) (Table 3). Markers found on the anal side of the stomach, small bowel, right colon, and left colon in the groups per segmental transit analysis are presented in Table 3. The mean number of radiopaque markers that passed the small bowel 6 h after administration in the coffee group was significantly higher than that in the water group (12 [range, 0–20] vs. 7 [range, 0–20]; $p = 0.04$). The mean number of radiopaque markers that passed the left colon 26 h after administration in the coffee

Table 1 Patient characteristics

	Coffee *N* = 23	Water *N* = 23	*p*
Age, mean [range]	74.0 [48.0, 90.0]	80.2 [66.0, 90.0]	0.09
Sex (%)			
Female	18 (78.3)	16 (69.6)	0.74
Male	5 (21.7)	7 (30.4)	–
BMI, mean [range]	22.1 [16.0, 30.5]	22.4 [18.6, 26.6]	0.49
ASA-PS (%)			
1	2 (8.7)	0 (0.0)	0.50
2	18 (78.3)	21 (91.3)	–
3	3 (13.0)	2 (8.7)	–
Disease (%)			
External rectal prolapse	12 (52.2)	11 (47.8)	1
Rectal intussusception	11 (47.8)	12 (52.2)	–
Medical history			
Cardiovascular (%)	3 (13.0)	3 (13.0)	–
Digestive (%)	4 (17.4)	5 (21.7)	–
Orthopedics (%)	2 (8.7)	7 (30.4)	–
Psychiatry (%)	2 (8.7)	1 (4.3)	–
Pulmonary (%)	3 (13.0)	1 (4.3)	–
Cerebrovascular (%)	1 (4.3)	0 (0.0)	–
Diabetes (%)	4 (17.4)	3 (13.0)	–
Hyperlipidemia (%)	3 (13.0)	5 (21.7)	–
Hypertension (%)	10 (43.5)	14 (63.6)	–
History of abdominal surgery (%)	12 (52.2)	12 (52.2)	–

ASA-PS American Society of Anesthesiologists Physical Status Classification System, *BMI* body mass index

Table 2 Perioperative outcomes

	Coffee *N* = 23	Water *N* = 23	*p*
Operative time, min, mean [range]	181.6 [120.0, 266.0]	177.0 [107.0, 333.0]	0.44
Intraoperative infusion, ml, mean [range]	1443.5 [850.0, 2050.0]	1534.8 [900.0, 2500.0]	0.81
Amount of bleeding, ml, mean [range]	18.4 [0.0, 260.0]	21.7 [0.0, 320.0]	0.56
Food intake, %, mean [range]			
POD 1	67.6 [10.0, 100.0]	58.3 [5.0, 100.0]	0.34
POD 2	73.9 [10.0, 100.0]	77.7 [30.0, 100.0]	0.93
Ambulation time, min, mean [range]			
POD 1	227.0 [0.0, 680.0]	214.4 [30.0, 660.0]	0.91
POD 2	348.5 [0.0, 850.0]	302.7 [0.0, 860.0]	0.40
Fatigue, mean [range]			
POD 1	3.3 [0.0, 7.0]	3.6 [0.0, 10.0]	0.93
POD 2	2.6 [0.0, 6.0]	2.2 [0.0, 7.0]	0.34
Pain, mean [range]			
POD 1	4.5 [0.0, 8.0]	4.7 [0.0, 10.0]	0.91
POD 2	2.2 [0.0, 6.0]	3.2 [0.0, 10.0]	0.48
Nausea (%)			
POD 1	2 (8.7)	6 (26.1)	0.24
POD 2	0 (0.0)	0 (0.0)	NA
Vomiting (%)			
POD 1	1 (4.3)	3 (13.0)	0.61
POD 2	0 (0.0)	0 (0.0)	NA
Postoperative complications			
Pneumonia (%)	1 (4.3)	0 (0.0)	–
Orthostatic hypotension (%)	4 (17.4)	3 (13.0)	–
Urinary retention (%)	1 (4.3)	0 (0.0)	–

POD postoperative day

Table 3 Outcomes

		Coffee *N* = 23	Water *N* = 23	*p*
Number of markers on the anal side, mean [range][a]				
6 h	Stomach	20 [20, 20]	19 [0, 20]	0.14
	Small bowel	12 [0, 20]	7 [0, 20]	0.04
	Right colon	0 [0, 0]	0 [0, 0]	NA
	Left colon	0 [0, 0]	0 [0, 0]	NA
	Rectum	0 [0, 0]	0 [0, 0]	NA
26 h	Stomach	20 [20, 20]	20 [16, 20]	0.32
	Small bowel	20 [14, 20]	18 [0, 20]	0.82
	Right colon	4 [0, 17]	4 [0, 20]	0.44
	Left colon	2 [0, 14]	1 [0, 11]	0.10
	Rectum	1 [0, 6]	0 [0, 0]	0.04
Time to first defecation, h, mean [range]		55.1 [19.1, 114.0]	69.7 [20.7, 141.6]	0.13
Time to first flatus, h, mean [range]		9.3 [0.5, 47.1]	12.6 [1.1, 46.1]	0.35
Distribution of markers at 26 h[b]		–	–	0.80

[a]The number of markers that passed through each segment in each participant. For example, the number of markers on the anal side of the small bowel is the total number of markers in the right colon, left colon, rectum, and evacuated markers
[b]Analyzed by the generalized estimating equations logistic regression model

group tended to be higher than that in the water group (2 [range, 0–14] vs. 1 [range, 0–11]; $p = 0.10$). However, the marker distribution in the entire gastrointestinal tract at 26 h analyzed by GEE was not significantly different between the groups ($p = 0.80$; Fig. 4). The time to the first flatus and time to the first defecation were not significantly different between the groups either.

Discussion

Summary of results

After quantification of coffee effects, coffee showed positive effects on the intestinal activity of patients who underwent LVR; the total number of evacuated radiopaque markers 26 h after administration was significantly higher in the coffee group than in the water group. However, we could not find significant positive effects on clinical outcomes, such as time to the first flatus and time to the first defecation. In addition, the distribution of the radiopaque markers was not significantly different either. Although we found that coffee provides significantly positive effects on intestinal function after abdominal surgery, its effect is relatively small when the same amount of coffee was administered; in previous studies, only 100 ml of coffee three times daily was taken after operation.

Reason for the small clinical difference

Four randomized controlled studies have investigated the effects of coffee on the recovery of POI [4–7] and showed small clinical difference (9.4–15.4 h) in terms of the operation-to-first-defecation time between the coffee and water groups. Based on previous clinical studies, the present study was designed to offer 100 ml of coffee three times a day for each patient. In fact, a previous experimental study offered 200–280 ml of coffee at a time [3, 14, 15]. One reason for the small clinical difference is that the amount of coffee might be insufficient. Moreover, the preserved colon and rectum may serve as reservoir of stools, which may have caused the ambiguous clinical effect. Because the previous experimental study showed that coffee may stimulate more the transverse until the descending colon, its effect did not appear to be a promoter of defecation [3]. In addition, because the ERAS protocol was already successfully in use and LVR is a less invasive surgery, the postoperative period and time to the first defecation were already shortened, and the clinical effect may be less apparent in this study than

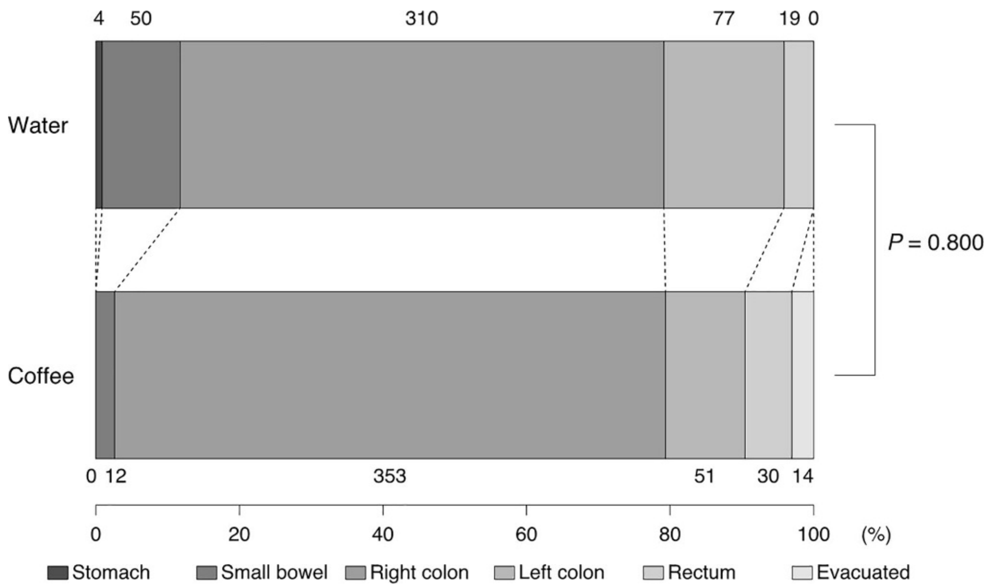

Fig. 4 Distribution of markers at 26 h after administration. All radiopaque markers in patients were counted for each segment and presented as the proportion of the total. The total number in each segment is also shown

in previous studies. Therefore, based on the assumption of the smaller clinical effect, further clinical trials with larger sample size are needed to test the benefit of coffee on patients undergoing abdominal surgery.

What we knew through the quantification of coffee effect on POI

A transit analysis using radiopaque markers enabled quantification of the intestinal motility and demonstrated possibly increased left colon motility, which was consistent with that of previous studies with healthy volunteers. Brown et al. [2] reported a positive effect of coffee on rectosigmoid motor activity. Rao et al. [3] demonstrated that coffee consumption induced significantly greater motor activity in the colon, especially in the transverse or descending colon.

We also found that coffee may promote small bowel function at 6 h. However, Boekema et al. [14] reported that coffee did not affect gastric emptying or small bowel transit in healthy patients. Thus, we should consider which operation coffee can be used for as a POI treatment; coffee intake may not be an anti-POI treatment after gastric operation, which raises a question of whether coffee improves POI after small intestinal operation.

Limitations

This study had several limitations. First, we could not perform a blinded intervention because coffee has a distinct aroma, color, and taste compared with water. Second, this study was performed according to a protocol analysis. Because we studied the effects of coffee on bowel movements rather than clinical outcomes, we weighed the coffee consumption.

Conclusion

In conclusion, the consumption of coffee accelerated bowel movements and facilitated faster passage of radiopaque markers through the bowel of patients who underwent elective LVR. However, its clinical effect was very small. Further research to identify which operation coffee can be used for as a POI treatment or to determine the optimal amount of coffee intake is warranted.

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Compliance with ethical guidelines

Conflict of interest K. Hayashi, A. Tsunoda, A. Shiraishi, and H. Kusanagi declare that they have no competing interests.

Ethical standards All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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