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ORIGINAL ARTICLE

Modified oral antibiotics and mechanical bowel preparation (OAMBP) versus conventional OAMBP for sigmoid colon and rectal surgery: A multicenter randomized non-inferiority trial

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Abstract

Aim: To evaluate whether the use of a laxative with reduced patient burden in oral antibiotics and mechanical bowel preparation (OAMBP) could prevent surgical site infection (SSI) in left-sided colon and rectal cancers.

Methods: This multicenter, non-blinded, randomized, non-inferiority trial included patients who underwent elective colorectal surgery for colorectal cancer in a university and community hospital in Japan from April 1, 2021 to March 31, 2023. We compared conventional OAMBP (polyethylene glycol, metronidazole, and kanamycin) (cOAMBP group) with modified OAMBP (sodium picosulfate hydrate, metronidazole, and kanamycin) (mOAMBP group). The primary outcome was overall incidence of SSI. Secondary outcomes were postoperative complications, degree of patient burden, and intraoperative bowel dilatation.

Results: Among 119 patients, 112 were randomly assigned to the two groups, with 56 patients in each group. SSI occurred in three (5.4%) and five patients (8.3%) in the mOAMBP and cOAMBP groups, respectively (90% confidence interval [CI]: −12.8–5.3), with a 15% margin of non-inferiority. Anastomotic leakage occurred in no patient in the mOAMBP group and three patients (5.4%) in the cOAMBP group ($p = 0.24$). The cOAMBP group reported significantly more pain than the mOAMBP group (50 [90.9%] vs. 7 [12.5%] participants). The mOAMBP group showed significantly lesser bowel dilatation than the cOAMBP group (1 [1.8%] vs. 21 [37.5%] participants).

Conclusion: mOAMBP is safe and less burdensome, can reduce intraoperative bowel dilatation, and is non-inferior compared with cOAMBP in preventing SSI. Therefore, mOAMBP may be more suitable for sigmoid colon and rectal cancer.

Trial Registration: UMIN000043162 (http://www.umin.ac.jp/ctr/). Registered on January 28, 2021.

Yusuke Kinugasa is an editorial member of *Annals of Gastroenterological Surgery*.

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KEYWORDS
non-inferiority trial, oral antibiotics and mechanical bowel preparation, rectal cancer, robotic surgery, sodium picosulfate hydrate

1 | INTRODUCTION

Surgical site infection (SSI) remains a significant concern in colorectal cancer surgery despite advancements such as robotic procedures.[1,2] To mitigate this risk, a combination of mechanical bowel preparation (MBP) and oral antibiotics bowel preparation (OABP), known as oral antibiotics and mechanical bowel preparation (OAMBP), has gained popularity. OAMBP is strongly recommended for left-sided colon and rectal surgeries due to their high complication rates. Many reports have shown that OAMBP reduces postoperative complication rates in left-sided colon or rectal surgery.[3–10] OAMBP is strongly recommended by the American College of Surgeons and the American Society of Colon and Rectal Surgeons.[11,12] In right colon surgery, the postoperative complication rates are low, especially in minimally invasive surgeries in Japan.[13] Moreover, some reports have shown no significant reduction in the postoperative complication rate with OAMBP.[5,14] The postoperative complication rate, including that of SSI, is higher in left-sided colon and rectal surgery than in other colorectal surgeries[5,6,8]; however, several studies have reported that OAMBP significantly reduces the postoperative complication rate.[3–6,15] The more distal the tumor location, the more frequently OAMBP is used in colorectal surgery.[16] Therefore, preparation trials are more effective for left-sided colon and rectal surgeries, which have higher complication rates.

The drugs commonly used in MBP are polyethylene glycol (PEG) or PEG-based solutions,[4,5,14,15] which are administered with large volumes of water; this places a heavy burden on the patient and may interfere with the surgical operation due to edema or bowel dilatation. Sodium picosulfate hydrate (SPH) is a liquid (total volume: 10 mL) that is less painful for patients compared with PEG; if substituted for PEG, SPH may improve the patient's quality of life before surgery and make surgical procedures easier by reducing bowel dilatation. In previous studies, SPH was only used in combination with magnesium citrate.[7,17] In addition, there are no previous reports examining intraoperative bowel dilatation. Therefore, we conducted a multicenter, non-blinded, randomized controlled trial (RCT) to investigate the non-inferiority of modified OAMBP (mOAMBP) using SPH compared with conventional OAMBP (cOAMBP) using PEG in left-sided colon and rectal cancer surgeries.

2 | METHODS

2.1 | Study design and participants

This multicenter, non-blinded, randomized, non-inferiority trial compared mOAMBP with cOAMBP in patients undergoing elective colorectal surgery for colorectal cancer in Japan from April 1, 2021 to March 31, 2023. The trial was conducted at a university hospital (Tokyo Medical and Dental University Hospital) and a community hospital (Edogawa Hospital). The inclusion criteria were as follows: (1) undergoing resection for rectal cancer or left-sided colon cancer, with or without diverting ileostomy; (2) undergoing transanal anastomosis (mechanical or hand-sewn); (3) age 20–85 years; (4) Eastern Cooperative Oncology Group performance status of 0 or 1; and (5) meeting the following criteria for laboratory tests within 30 days of enrollment: (i) white blood cell (WBC) count: $3000 \leq \text{WBC} < 10000/\mu\text{L}$, (ii) neutrophil count ≥1500/μL, (iii) hemoglobin level ≥9.0 g/dL, (iv) platelet count ≥70 000/μL, (v) total bilirubin level ≤1.5 mg/dL, (vi) aspartate aminotransferase level ≤ 100 IU/L, (vii) alanine aminotransferase level ≤ 100 IU/L, and (viii) albumin level ≥2.5 g/dL.

The exclusion criteria were as follows: (1) need for emergency surgery, (2) bowel obstruction, (3) preoperative infections, (4) pregnant or may become pregnant, (5) uncontrolled diabetes mellitus (HbA1c ≥8.0%), (6) allergy to drugs used in the study (PEG, SPH, kanamycin, metronidazole), (7) undergoing neoadjuvant radiotherapy or chemotherapy, and (8) undergoing colostomy or ileostomy.

2.2 | Ethical and humane considerations

The trial protocol was approved by the Institutional Review Board of Tokyo Medical and Dental University (approval number R2020-026), and contact was made regularly for updates. Written informed consent was obtained from all patients before randomization. The trial was registered with the UMIN Clinical Trial Registry (UMIN000043162), and the study followed the CONSORT statement.

2.3 | Randomization and masking

The patients were randomly allocated in a 1:1 ratio to the mOAMBP or cOAMBP group. Randomization was performed using the minimization method to balance the distributions of the following factors between the two groups: planned approach (open surgery or minimally invasive surgery), planned diverting ileostomy (yes or no), tumor location (sigmoid or rectum), and hospital.

2.4 | Procedures

All patients underwent OABP with 1 g kanamycin and 500 mg metronidazole administered orally three times (after lunch, dinner, and before bedtime) on the day before surgery. Similar regimens were used in previous trials.[4–7,17] The patients allocated to the mOAMBP group were administered 75.0 mg SPH orally after hospitalization (1-day method; if hospitalized the day before surgery) or 37.5 mg SPH

orally after hospitalization and 37.5 mg of SPH on the morning before surgery (2-day method; if hospitalized 2 days before surgery). The patients allocated to the cOAMBP group were administered one pack of PEG/PEG-based solution dissolved in approximately 2 L of water orally after hospitalization (either the 1-day or 2-day method). Patients followed a low-residue diet until lunch the day before surgery and resumed the diet on the third postoperative day. We administered 1 g cefmetazole intravenously to both groups at the start of anesthesia before the skin incision and an additional dose every 3 h during surgery. Surgery was performed by specialists in the colorectal area.

2.5 | Outcomes

The primary outcome was the overall incidence of SSI within 30 days of surgery. SSI was defined using the Center for Disease Control and Prevention criteria.[18] The SSI diagnosis was made by the surgeon, attending physician, or other physicians or nurses when there was purulent drainage from the incision, isolation of organisms from an aseptically obtained fluid or tissue culture, or symptoms of infection.[18] The secondary outcomes were degree of patient burden, operative procedure, operative approach, operation time, blood loss, diverting ileostomy creation rate, degree of intraoperative bowel dilatation, conversion to open surgery, incidence of superficial SSI, deep SSI or organ-space SSI, incidence of 30-day postoperative complications excluding SSI, intraoperative adverse events, length of intra-abdominal drain placement, and length of postoperative hospital stay. The grades of postoperative complications were evaluated based on the Clavien–Dindo (CD) classification.[19] All events related to preoperative bowel preparation were graded according to the National Cancer Institute Common Toxicity Criteria (CTCAE v5.0), and CTCAE grade ≥2 events were considered the secondary outcomes. The degree of patient burden was assessed using a questionnaire comprising three items: drug compliance (3-point scale: full dose, half dose, and almost none), degree of burden (4-point scale: very painful, painful, somewhat painful, and not painful), and frequency of evacuation (number of evacuations between laxative intake and 8:00 the following morning). These questionnaires were distributed after hospital admission and collected on the morning of the surgery. The degree of intraoperative bowel dilatation was assessed using a questionnaire answered by surgeons. The questionnaire was an intraoperative evaluation of the operative field in the abdominal cavity rated on a 3-point scale (dilated to interfere with the procedure, dilated but not interfering with the procedure, and no dilatation).

2.6 | Sample size

Previous studies of rectal surgery have shown that the incidence of SSI varied from 9.8% to 15.3% in patients undergoing OAMBP and from 22.5% to 26.2% in patients undergoing MBP.[4–6] Accordingly, we assumed that SSI would occur in 9.8% of patients undergoing cOAMBP and mOAMBP. We set the non-inferiority margin at 15%, ensuring it does not exceed the previously reported high values and the feasibility of completing case enrollment.[6] With a non-inferiority margin of 15%, one-sided significance level of 5%, and power of 80%, the required number of patients was 98. We planned to enroll 108 patients to account for dropouts.

2.7 | Statistical analysis

All the randomized populations who met the criteria of the study population received the study treatment at least once and had at least one data point after randomization, which was used for all analyses.

Baseline characteristics are presented as medians and interquartile ranges for continuous variables and as frequencies and percentages for categorical variables. Distributions were compared using the Wilcoxon rank-sum test for continuous variables and the Fisher's exact test for categorical variables. In analyzing the primary outcome, the statistical inference for non-inferiority was based on the upper boundary of the exact Clopper–Pearson 90% confidence interval (CI) of the difference in the overall incidence rate of SSI between the two groups. To ensure consistency between the significance level set in the sample size calculation and that employed in the primary outcome analysis, we applied a 90% CI in the analysis. We also compared the overall incidence rate of SSI between the groups using Fisher's exact test.

The same analyses for the primary outcome were performed for the incidence rates of superficial, deep, and organ-space SSI. We estimated the incidence rates of complications and their exact Clopper–Pearson 95% CIs and compared the difference between the two groups using the Fisher's exact test. Since the analyses for secondary outcomes were exploratory, the 95% CI was applied. For other secondary outcomes, the Wilcoxon rank-sum test was performed to compare the distributions of the frequency of evacuation, operation time, blood loss, length of intra-abdominal drain placement, and postoperative hospital stay. Further, the Fisher's exact test was performed to compare the distributions of drug compliance, degree of burden, operative procedure, operative approach, diverting ileostomy, and bowel dilatation. Adverse events were summarized as frequencies and percentages. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3 | RESULTS

3.1 | Patient characteristics

In total, 119 patients were included in this study (Figure 1). Overall, 61 patients were randomly assigned to the cOAMBP group and 58 to the mOAMBP group. Five patients in the cOAMBP group (three received incorrect bowel preparation, one was considered ineligible

after allocation, and one did not undergo transanal anastomosis) and two patients in the mOAMBP group (no transanal anastomosis) were excluded, resulting in 56 patients each in the cOAMBP and mOAMBP groups. Ultimately, 112 patients were included in the analysis. Table 1 summarizes patients' background characteristics, which were well-balanced in both groups owing to the randomized allocation.

3.2 | Preoperative impact of MBP

The results of MBP compliance and patient burden questionnaires are presented in Table 2. All patients in the mOAMBP group were selected for the 2-day method; thus, the comparison of patient burden was between full dose of PEG and half SPH. No significant difference was noted between the two groups in MBP compliance, but one patient (1.8%) in the mOAMBP group and five (8.9%) in the cOAMBP group discontinued MBP at half dose owing to patient burden. For the patient burden questionnaire, 49 patients (87.5%) in the mOAMBP group and 5 (9.1%) in the cOAMBP group reported "not painful," 19 (34.5%) in the cOAMBP group reported "very painful," and significantly more patients in the cOAMBP group reported "painful" than those in the mOAMBP group (51 patients [90.9%] vs. seven patients [12.6%], respectively [$p < 0.01$]). The median number of evacuations from the start of MBP to the following morning was four and nine in the mOAMBP and cOAMBP groups, respectively, with a significant difference ($p < 0.01$). No adverse events attributable to the MBP were observed.

3.3 | Operative outcomes

Table 3 presents a summary of operative outcomes. The rate of anterior resection was 73.2% and 69.6% in the mOAMBP and cOAMBP groups, respectively; the rate of robotic surgery was 91.1% and 85.7% in the mOAMBP and cOAMBP groups, with no significant difference ($p = 0.56$). The results of the surgeon's questionnaire for intraoperative bowel dilatation after surgery revealed that intraoperative bowel dilatation was significantly more frequent in the cOAMBP group than in the mOAMBP group ($p < 0.01$).

3.4 | Postoperative outcomes

Table 4 presents the postoperative results, and Figure 2 depicts the differences in the incidence of postoperative complications between the mOAMBP and cOAMBP groups. In this study, organ-space SSIs other than AL were not observed, resulting in organ-space SSI and AL being synonymous. As shown in Figure 2, 90% CIs are shown for all SSI, superficial SSI, and organ-space SSI (AL). Meanwhile, 95% CIs are shown for all complications, complications by CD grade, and complications other than SSIs. All SSIs were found

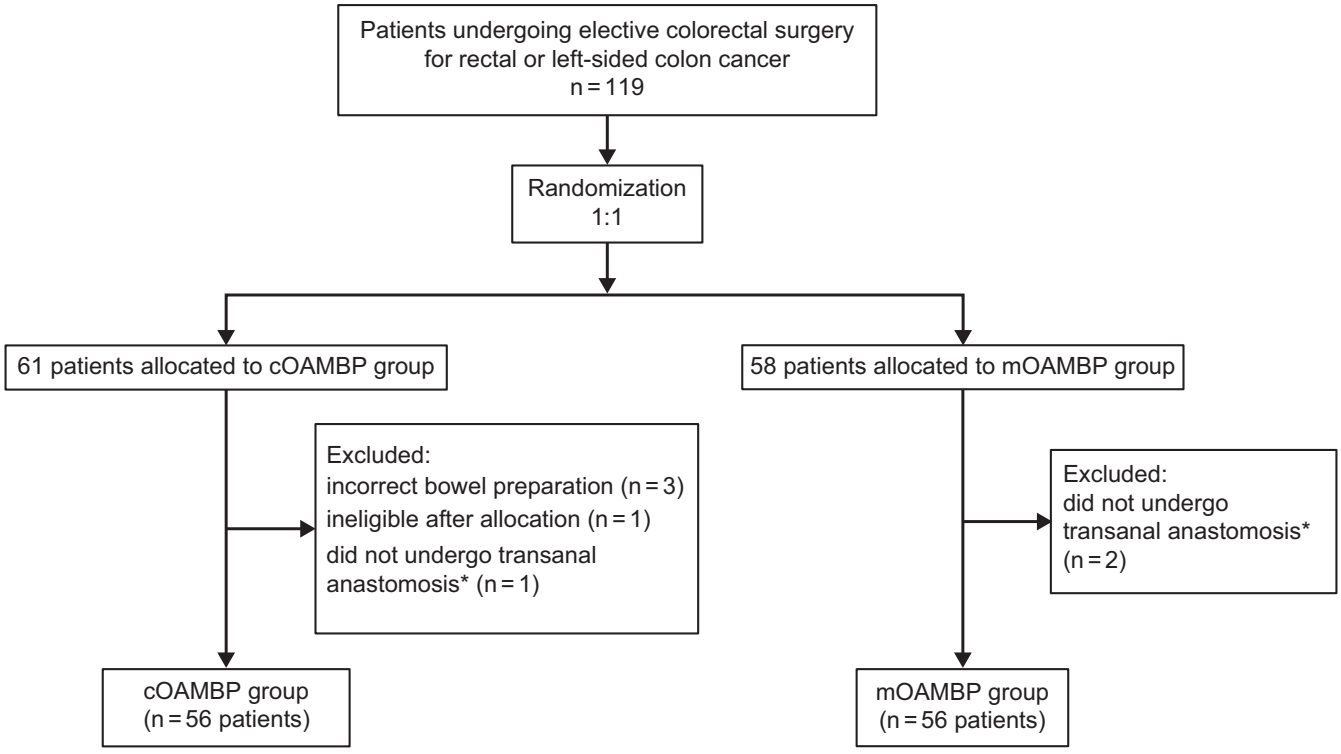

FIGURE 1 Trial flowchart. A total of 119 patients were enrolled in the study, and seven patients were excluded because they did not satisfy the inclusion criteria.
mOAMBP: modified oral antibiotics and mechanical bowel preparation; cOAMBP: conventional oral antibiotics and mechanical bowel preparation.

TABLE 1 Preoperative patient characteristics.

		Total	mOAMBP	cOAMBP	
		n = 112	*n* = 56	*n* = 56	*p*-value
Age (years)[a]		66.5 (57.0–75.5)	66.0 (57.5–74.0)	68.0 (56.0–77.0)	0.68
Sex ratio (M: F)		72:40	38:18	34:22	0.55
Nationality	Japanese	111 (99)	55 (98)	56 (100)	1
	Others	1 (1)	1 (2)	0 (0)	
BMI (kg/m^2)[a]		23.6 (21.3–26.0)	23.7 (21.5–25.6)	23.6 (20.9–26.4)	1
ASA classification	I	25 (22)	11 (20)	14 (25)	0.32
	II	82 (73)	44 (78)	38 (68)	
	III	5 (5)	1 (2)	4 (7)	
Previous abdominal surgery	Yes	26 (23)	10 (18)	16 (29)	0.26
Diabetes	Yes	28 (25)	12 (21)	16 (29)	0.51
	HbA1c (%)[a]	5.8 (5.5–6.2)	5.8 (5.5–6.1)	5.8 (5.5–6.3)	0.69
Steroid use history	Yes	3 (3)	1 (2)	2 (4)	1
Anticoagulant use	Yes	7 (6)	3 (5)	4 (7)	1
Smoking within 1 year	Yes	17 (15)	8 (14)	9 (16)	1
Albumin (g/dL)[a]		4.3 (4.0–4.5)	4.4 (4.1–4.5)	4.2 (4.0–4.4)	0.03
CEA (ng/mL)[a]		2.7 (1.7–4.2)	2.7 (1.7–4.0)	2.8 (1.8–5.4)	0.53
CA19-9 (ng/mL)[a]		9.8 (5.4–16.6)	8.4 (5.5–13.4)	10.8 (5.0–19.2)	0.39
Tumor location	Sigmoid	26 (23)	12 (21)	14 (25)	0.82
	Rectum	86 (77)	44 (79)	42 (75)	
Planned approach	Open surgery	0 (0)	0 (0)	0 (0)	–
	Minimally invasive surgery	112 (100)	56 (100)	56 (100)	
Planned diverting ileostomy	Yes	20 (18)	9 (16)	11 (20)	0.81
Hospital	University hospital	82 (73)	41 (73)	41 (73)	1
	Community hospital	30 (27)	15 (27)	15 (27)	

Note: Values in parentheses are presented as percentages unless indicated otherwise.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CA19-9; carbohydrate antigen 19–9; CEA, carcinoembryonic antigen; cOAMBP, conventional oral antibiotics and mechanical bowel preparation; IQR, interquartile range; mOAMBP, modified oral antibiotics and mechanical bowel preparation.

[a]Values are presented as median (i.q.r.).

TABLE 2 Drug compliance and patient burden.

		mOAMBP	cOAMBP	
		n = 56	*n* = 56	*p*-value
Drug compliance of MBP	Full dose	55 (98.2)	51 (91.1)	0.21
	Half dose	1 (1.8)	5 (8.9)	
	Almost none	0 (0)	0 (0)	
Patient burden	Very painful	1 (1.8)	19 (34.5)	<0.01
	Painful	3 (5.4)	14 (25.5)	
	Somewhat painful	3 (5.4)	17 (30.9)	
	Not painful	49 (87.5)	5 (9.1)	
Frequency of evacuation (times)[a]		4.0 [2.0–5.0]	9.0 [6.0–10.0]	<0.01

Note: Values in parentheses are presented as percentages unless indicated otherwise.

Abbreviations: cOAMBP, conventional oral antibiotics and mechanical bowel preparation; MBP, mechanical bowel preparation; mOAMBP, modified oral antibiotics and mechanical bowel preparation.

[a]Values are medians (i.q.r.).

TABLE 3 Operative outcomes.

		mOAMBP *n* = 56	cOAMBP *n* = 56	*p*-value
Procedure	Sigmoidectomy	11 (19.6)	12 (21.4)	0.97
	HAR	13 (23.2)	11 (19.6)	
	LAR	28 (50.0)	28 (50.0)	
	ISR	4 (7.1)	5 (8.9)	
Approach	Robot	51 (91.1)	48 (85.7)	0.56
	Laparoscopy	5 (8.9)	8 (14.3)	
Operative time (min)[a]		225.0 (178.0–278.0)	229.0 (176.5–287.5)	0.79
Blood loss (mL)[a]		5.5 (0.0–20.0)	9.0 (0.0–20.0)	0.70
Diverting ileostomy	Yes	10 (17.9)	12 (21.4)	0.81
Bowel dilatation	Interfere with procedure	0 (0.0)	5 (8.9)	<0.01
	Dilated but did not interfere with procedure	1 (1.8)	16 (28.6)	
	No dilatation	55 (98.2)	35 (62.5)	
Conversion to open surgery	Yes	0 (0.0)	0 (0.0)	

Note: Values in parentheses are presented as percentages unless indicated otherwise.

Abbreviations: cOAMBP, conventional oral antibiotics and mechanical bowel preparation; HAR, high anterior resection; ISR, intersphincteric resection; LAR, low anterior resection; mOAMBP, modified oral antibiotics and mechanical bowel preparation.

[a]Values are presented as median (i.q.r.).

TABLE 4 Postoperative outcomes.

		mOAMBP *n* = 56	cOAMBP *n* = 56	*p*-value
SSI	All	3 (5.4)	5 (8.3)	0.72
	Superficial	3 (5.4)	2 (3.6)	1
	Deep	0	0	–
	Organ space	0	3 (5.4)	0.24
All complications		7 (12.5)	9 (16.1)	0.79
CD grade ≥ III		1 (1.8)	4 (7.1)	0.36
CD grade ≥ II		6 (10.7)	8 (14.3)	0.78
Anastomotic leakage		0	3 (5.4)	
Ileus		1 (1.8)	2 (3.6)	
Urinary dysfunction		1 (1.8)	0	
Anastomotic bleeding		1 (1.8)	0	
Others		2 (3.6)	3 (5.4)	
Length of intra-abdominal drain placement (day) (median [range])		5 [4–6]	5 [4–62]	0.95
Postoperative hospital stay (day)[a]		6 [6–7]	6 [6–7]	0.64

Note: Values in parentheses are presented as percentages unless indicated otherwise.

Abbreviations: CD, Clavien–Dindo classification; cOAMBP, conventional oral antibiotics and mechanical bowel preparation; mOAMBP, modified oral antibiotic and mechanical bowel preparation; SSI, surgical site infection.

[a]Values are presented as median (i.q.r.).

in three patients (5.4%) in the mOAMBP group and five (8.3%) in the cOAMBP group; the 90% CIs of the difference in incidence rate was −12.8% to 5.3%, with a 15% margin of non-inferiority, proving non-inferiority, but no significant difference was recorded between the groups ($p = 0.72$). AL was found in zero patients (0%) in the mOAMBP group and three (5.4%) in the cOAMBP group,

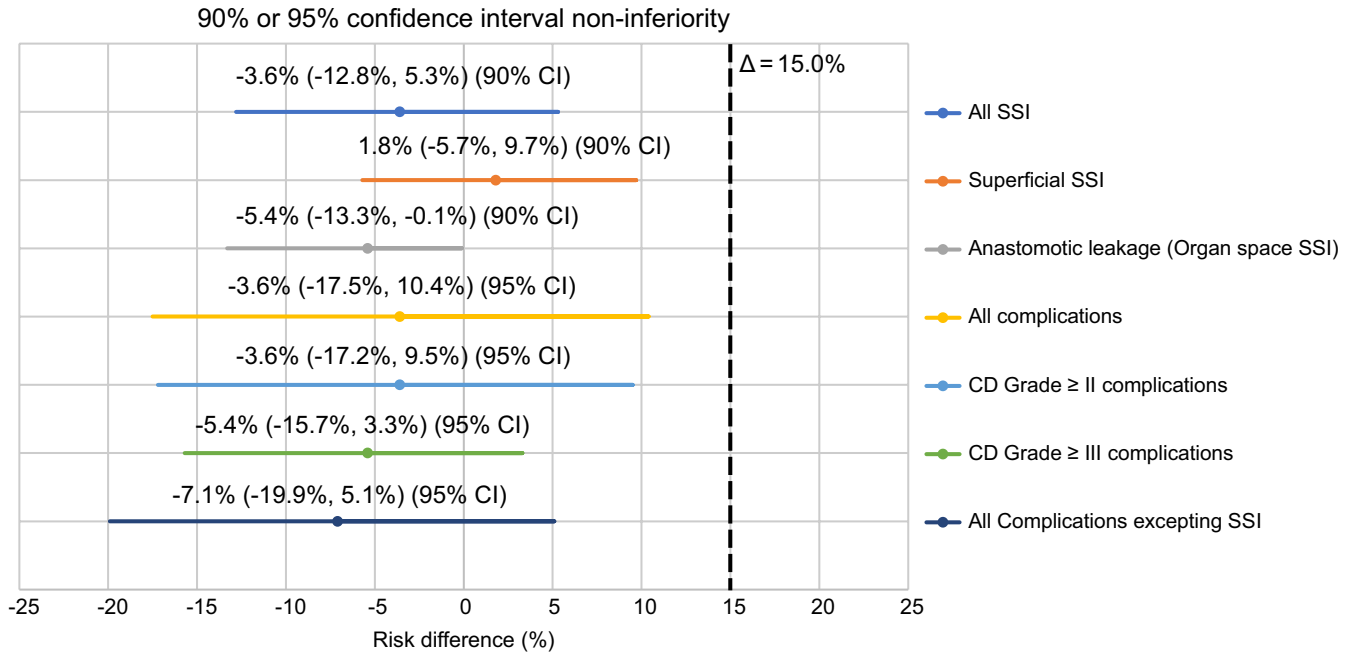

FIGURE 2 Analyses of non-inferiority of mOAMBP compared with cOAMBP.
The primary outcome, SSI, was analyzed with a 90% CI, while other complications were analyzed with a 95% CI. mOAMBP: modified oral antibiotics and mechanical bowel preparation; cOAMBP: conventional oral antibiotics and mechanical bowel preparation; SSI: surgical site infection; CI: confidence interval.

with a 90% CI of −13.3% to −0.1% for the difference in incidence rate, with no significance ($p = 0.24$). Two of three patients in the cOAMBP group with AL required additional surgical treatment. The incidence of grade II or higher complications was 10.7% in the mOAMBP group and 14.3% in the cOAMBP group, with a 95% CI of −17.2% to 9.5% for the difference in the incidence rate and no significant difference between both groups ($p = 0.78$). The median duration of abdominal drain placement and median postoperative hospital stay in both the groups were five and six days, respectively, with no significant difference.

4 | DISCUSSION

This is the first RCT to examine MBP content in preoperative bowel preparation for sigmoid colon and rectal cancer. Conventional PEG is used in MBP with a very high volume (approximately 2 L), whereas the volume of SPH, this current study drug, was only 10 mL. This study demonstrated that mOAMBP with SPH was non-inferior to cOAMBP with PEG in terms of the incidence of SSI. The incidence of other complications was not significantly different between the two groups; mOAMBP was found to be superior to cOAMBP in terms of patient burden and intraoperative bowel dilatation, indicating that mOAMBP can be a basic preparation alternative to cOAMBP.

In previous studies on OAMBP, the incidence of SSI was reported to be 3.5%–15.3%.[4–8,15,17] In our study, the incidence of SSI was 6.8%, comparable to the previous results. However, previous studies on OAMBP used PEG or PEG-based solutions,[4,5,15] and no reports have focused on only SPH as the MBP. We showed that MBP with only SPH was less burdensome on patients and had better results than PEG, with an SSI incidence of 5.4% and a grade II or higher complication rate of 10.7%. Therefore, MBP with SPH may be appropriate for these patients.

AL is an important complication in colorectal surgery, with a reported incidence of approximately 10% for rectal cancer surgery.[20,21] While good outcomes with robotic surgery have been reported in Japan,[22–24] robotic surgery was performed in 88% of patients in the present study, and AL was observed in 2.7% of the patients, consistent with the findings of the above-mentioned previous reports. Notably, AL was not observed in the mOAMBP group, even though no significant difference was found.

PEG is the most common bowel cleansing agent used in colonoscopy and the most popular MBP content in Japan.[25] However, it poses a significant burden on patients and is associated with many adverse events.[26,27] SPH requires a much lower dosage than PEG and is associated with reduced patient burden, as indicated by our questionnaire. Several studies on colonoscopy have reported that SPH and magnesium citrate are as effective as PEG in bowel cleansing,[27,28] and the preference for a less burdensome preparation supports the results of our study. SPH alone may have a decreased laxative effect compared with that of PEG, but preoperative bowel preparation, unlike colonoscopic preparation, does not require complete clearance. Regarding safety, a few serious adverse events were reported in previous studies,[27,28] whereas none were observed in our study related to SPH.

We evaluated the burden of MBP based on patients' responses to questionnaires and found that PEG imposes a great patient burden, whereas SPH, with only 10 mL, imposes a small patient burden and is a useful MBP. Although SPH had a significantly lower frequency of evacuation than PEG, it was associated with lower incidences of SSI and AL; additionally, intraoperative bowel dilatation was significantly less common with SPH than with PEG. This reduced bowel dilatation may be attributed to two factors: (1) residual physical bowel dilatation, as PEG is rarely absorbed in the intestinal tract, and (2) PEG increasing the moisture content of feces through osmosis.[29] Bowel dilatation has a greater impact on surgical manipulation in minimally invasive surgeries than in open surgeries. Although several studies on bowel preparation exist, all minimally invasive surgeries were performed via laparoscopy;[4,5,7,8,15,17] our study is the first report on bowel preparation in which almost all procedures were performed by a robot. Therefore, transitioning from PEG to SPH in MBP may prove beneficial in reducing patient burden and intraoperative bowel dilatation.

No significant differences were noted in operative time or blood loss, incidence of complications other than SSI or AL, and length of postoperative hospital stay between the two groups. No other adverse events were observed in either group, and the trial was conducted safely in the mOAMBP and cOAMBP groups.

This study has some limitations. First, we set the estimated incidence of SSI at 9.8% based on previous reports and the margin of non-inferiority at 15%; however, the overall incidence of SSI was 6.8%, which was lower than expected, and the incidence in the mOAMBP group was lower than that in the cOAMBP group. This lower-than-expected event rate may be attributed to the relatively small sample size and few number of events in our study. Moreover, all cases in this study involved minimally invasive surgeries, with robotic procedures accounting for 88% of surgeries. Robotic surgery has been reported to have a lower complication rate than laparoscopic surgery.[22–24] We could not demonstrate superiority in this study because most cases involved robotic surgeries. Second, all patients in the mOAMBP group were selected for the 2-day method. All patients in this study were admitted 2 days before surgery, following the standard clinical pathways at the participating facilities. The 2-day method was chosen at the discretion of the surgeon because it was uncertain whether SPH would effectively cleanse the intestinal tract with a single oral dose compared with PEG, making it necessary to check the daily evacuation volume with the 2-day method. Third, this RCT was not blinded, indicating a possibility of surgeon bias. Fourth, although this was a multicenter study, it was conducted at only two centers. Fifth, all patients except one were Japanese. Finally, OABP is currently not covered by the Japanese public health insurance system, despite OAMBP being strongly recommended in the ASCRS guidelines. We believe that OAMBP should become a standard preoperative bowel preparation in Japan to reduce the incidence of postoperative complications. Thus, OAMBP needs to be covered by the insurance system.

Despite these limitations, this study has two main strengths: it is the first RCT to compare MBP content, and it proved non-inferiority with a low rate of postoperative complications, even with a low patient burden preparation of only 10 mL. It may become a useful MBP for sigmoid colon and rectal surgery, reducing the preoperative patient burden and facilitating surgical manipulation for the surgeon.

5 | CONCLUSIONS

mOAMBP is safe and reduces patient burden. It not only reduces intraoperative bowel dilatation but also demonstrates non-inferiority to cOAMBP in terms of the incidence of SSI. These findings suggest that mOAMBP can be the preferred bowel preparation method for sigmoid colon and rectal cancer surgery.

AUTHOR CONTRIBUTIONS

Sodai Arai: conceptualization; investigation; methodology; formal analysis; validation; visualization; writing—original draft; writing—review and editing. Marie Hanaoka: conceptualization; methodology; supervision; writing—review and editing. Shinichi Yamauchi: supervision; writing—review and editing. Hironobu Baba: investigation, supervision; writing—review and editing. Ryoichi Hanazawa: formal analysis; supervision; writing—review and editing. Hiroyuki Sato: formal analysis; supervision; writing—review and editing. Akihiro Hirakawa: formal analysis; supervision; writing—review and editing. Masanori Tokunaga: supervision; writing—review and editing. Yusuke Kinugasa: supervision; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

DATA AVAILABILITY STATEMENT

The datasets generated during and analyzed during this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The trial protocol was approved by the Institutional Review Board of Tokyo Medical and Dental University (R2020-026), and contact was made regularly for updates. Written informed consent was obtained from all patients before randomization. The trial was registered with the UMIN Clinical Trial Registry (UMIN000043162). It was in accordance with the ethical standards of the responsible committee

for human experimentation and with the Helsinki Declaration of 1964 and later versions.

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