Short- and Long-term Outcomes of 2-Step Stapled Intracorporeal Versus Extracorporeal Anastomosis in Laparoscopic Colectomy for Colon Cancer

HAJIME KAYANO¹, EIJI NOMURA¹, YASUHIKO UEDA¹, TORU KURAMOTO², TAKASHI MACHIDA¹,
MASAYA MUKAI¹, SEIICHIRO YAMAMOTO³ and HIROYASU MAKUUCHI¹

¹Department of General and Gastroenterological Surgery, Tokai University Hachioji Hospital, Tokyo, Japan;

²Department of General and Gastroenterological Surgery, Saiseikai Suita Hospital, Osaka, Japan;

³Department of Surgery, Tokai University School of Medicine, Kanagawa, Japan

Abstract. *Background/Aim:* Intracorporeal anastomosis (IA) in laparoscopic colectomy for colon cancer is technically difficult, and there is a lack of consensus on the risk of bacterial contamination and cancer cell dissemination. In this study, short- and long-term outcomes of IA were examined. *Patients and Methods:* Short and long-term outcomes of those who underwent IA (n=44) or extracorporeal anastomosis (EA) (n=61) were compared. *Results:* IA was better than EA for blood loss, incision length, and first stool. Maximum temperature and C-reactive protein on postoperative day 1 were higher for the IA group. The rate of positive cultures from intraoperative lavage was higher for IA. The rate of positive cultures improved to an equivalent level by replacing mechanical pretreatment with chemical pretreatment. IA and EA were equivalent for the results of ascites cytology from lavage. *Conclusion:* With the use of appropriate preoperative treatment, IA takes advantage of the minimally invasive nature of laparoscopic surgery.

Extracorporeal functional end-to-end anastomosis (FEEA), in which the dissected and mobilized bowel is delivered outside the body and a linear stapler is used to form the anastomosis, is currently widely used in laparoscopic colectomy for colon cancer because of its safety and simplicity. However, in obese patients with thick abdominal walls or mesenteric fat tissue,

or in patients who have cancer of the transverse or descending colon, or cancer of the proximal sigmoid colon for which the double stapling technique cannot be used for anastomosis, it may be difficult to adequately deliver the bowel outside the body for reasons such as obstruction of the small incision by the mesentery or because of insufficient bowel length. Although intracorporeal anastomosis (IA) resolves these issues, its technical difficulty and the lack of consensus on the risk of bacterial contamination, cancer cell dissemination, and its short-term and long-term postoperative outcomes mean that it is not generally performed. In this study, outcomes of the anastomotic method of IA for colon cancer were compared with those of conventional extracorporeal anastomosis (EA). The effectiveness of and problems with IA were evaluated by investigating its postoperative outcomes in both the short and long term, and bacterial contamination in terms of postoperative biological reactions and ascites bacterial cultures, as well as cancer cell dissemination from the results of ascites cytology.

Patients and Methods

Study design. The subjects of this study were patients with colon cancer who underwent laparoscopic surgery between April 2015 and December 2018. Patients who also underwent gastric, large bowel, small bowel, or gallbladder resection at the same time were excluded. These patients were then divided into those who first underwent lymph node dissection and bowel mobilization within the peritoneal cavity, after which EA was performed by delivering the bowel outside the body through the small incision and creating an FEEA with a linear stapler under direct visual observation (EA group), and those who similarly first underwent lymph node dissection and bowel mobilization within the peritoneal cavity but in whom the mesentery was then divided within the peritoneal cavity, and IA was performed with a linear stapler under laparoscopic observation (IA group). The study subjects comprised 105 patients, 61 in the EA group and 44 in the IA group. After IA was introduced in September 2015, it was performed on patients

Correspondence to: Hajime Kayano, Department of General and Gastroenterological Surgery, Tokai University Hachioji Hospital, 1838 Ishikawa-machi, Hachioji, Tokyo 192-0032, Japan. Tel: +81 426391111, Fax: +81 426391144, e-mail: h.kayano@tsc.u-tokai.ac.jp

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who consented to undergo the procedure after having received an explanation of both methods, including the information that IA was a novel anastomotic procedure and that it entailed the risk of bacterial contamination of the peritoneal cavity. The study protocol was approved by the Institutional Review Board for Clinical Research, Tokai University (18R-304).

Data collection. Information on patient factors, tumour-related factors, surgery-related factors, surgical data, long-term and short-term postoperative outcomes, and postoperative complications was held in a database. Patient factors included age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS) classification, and previous abdominal surgery. Tumour-related factors included tumour location, maximum tumour diameter, and histopathological TNM classification (American Joint Committee on Cancer/Union for International Cancer Control) (1). Surgery-related factors included surgical procedure, extent of lymph node dissection (2), and mobilization of the left and right colonic flexures. The surgical procedure was classified by the Japanese Society for Cancer of the Colon and Rectum (2018) Japanese classification of colorectal, appendiceal, and anal carcinoma (ninth edition) (2). Surgical data included operating time, blood loss, incision length, and the results of ascites bacterial cultures and cytology after post-anastomosis peritoneal lavage with 3,000 ml of physiological saline. Ascites bacterial cultures were performed for obligate aerobic bacteria, facultative anaerobic bacteria, and obligatory anaerobic bacteria, and if one of the bacteria grew, the case was considered positive. Ascites bacterial cultures and cytology were performed for 73 patients (36 in the EA group and 37 in the IA group) who underwent surgery from April 2016. Postoperative outcomes included time to first passage of gas and first stool, time to resumption of oral ingestion, and duration of postoperative hospitalization. Postoperative complications included surgical site infection (SSI), postoperative ileus, anastomotic leakage, intraperitoneal abscess, lymphorrhea, ischemic enteritis, infectious enteritis, haemorrhage at the anastomosis site, cholecystitis, and port site hernia. Postoperative ileus was defined as cases requiring fasting, intravenous fluids, and decompression, and it was diagnosed by abdominal signs, abdominal computed tomography (CT), plain abdominal X-ray, or abdominal ultrasound. Anastomotic leakage was diagnosed on the basis of fluid retention around the site of anastomosis on abdominal CT, the presence of free air, and clinical signs comprising peritoneal irritation signs, and fever, and blood test results. Postoperative complications were classified according to the timing of their occurrence as short-term if they occurred between the completion of surgery and initial postoperative discharge or long-term if they occurred after initial postoperative discharge. Short-term postoperative complications were classified using the Clavien–Dindo classification (3).

Surgical procedure. Five ports were used to perform EA of the right colon, with a 12-mm port inserted in the umbilicus and 5-mm ports in the left hypochondrium, the left and right lower abdomen, and the suprapubic region. For IA, the 5-mm port in the left lower abdomen was replaced with a 12-mm port through which the linear stapler was inserted. For both EA and IA, until central lymph node dissection and main vasculature resection *via* the medial approach and mobilization of the ileocecal region from the caudal side, the operator stood between the patient's legs, while the assistant and the endoscopist were positioned to the patient's left. While mobilizing

the right colonic flexure, the operator and endoscopist both stood on the left side of the patient, and the assistant moved to a position between the patient's legs. For IA, the operator returned to a position between the patient's legs, with the assistant and endoscopist to the left side of the patient. For the left colon, the procedure was carried out as usual using five ports, a 12-mm port in the umbilicus, 5-mm ports in the left upper and lower abdomen and the right upper abdomen, and a 12-mm port in the right lower abdomen. The operator and endoscopist stood on the right side of the patient, with the assistant on the patient's left. While mobilizing the left colonic flexure, the assistant moved to a position between the patient's legs. Left colonic flexure mobilization was only carried out if the anastomosis was under strain, and it was not performed in all cases. For both EA and IA, the bowel was mobilized after central lymph node dissection and main vasculature resection *via* the medial approach. For EA, the method of anastomosis used for both the right and left colon was to deliver the bowel outside the body *via* the port incision in the umbilicus, which was extended into a small laparotomy, and to use four linear staplers to create a FEEA. IA was performed by isoperistaltic side to side anastomosis. The mesentery was divided, after which a linear stapler was used to transect the bowel. An ECHELON FLEX™ Powered ENDOPATH Stapler® 60 mm (blue cartridge) (Ethicon Endo-Surgery Inc, Cincinnati, OH, USA) was then used to create the anastomosis. Because the linear stapler was approximately 7 cm in length and 1.5 cm in width, insertion openings were made at points 7 cm from the anal stump and 3 cm from the oral stump of the bowel for side-to-side anastomosis formation. The insertion opening for the oral stump was made at a point 3 cm from this stump to keep the stump from becoming involved when closing the insertion opening and ensure that the blind end was no longer than necessary. The linear stapler was inserted *via* the insertion opening, and a side-to-side anastomosis was created, after which the insertion opening was first temporarily sutured and then closed with the linear stapler. The port incision in the umbilicus was extended into a small laparotomy, and the specimen was extracted. After both EA and IA, peritoneal lavage was carried out with 3,000 ml of physiological saline, peritoneal fluid samples were taken for ascites bacterial cultures and cytology, and the operation was concluded without drain insertion. Pretreatment was initially carried out mechanically (MAGCOROL P® Magnesium citrate; Horii Pharmaceutical Ind., Ltd, Osaka, Japan) 25 g plus Laxoberon solution 0.75%® sodium picosulfate hydrate (Teijin Pharma, Tokyo, Japan) 5 ml on the day before surgery), but this mechanical pretreatment has now been replaced by chemical pretreatment alone (2,000 mg/day kanamycin monosulfate plus 1500 mg/day metronidazole on the day before surgery). In both groups, patients were permitted to eat until the evening meal on the day before surgery.

Statistical analysis. Comparisons between the two groups were made using the Mann–Whitney test for continuous variables and either a chi-squared test or Fisher's exact test (for small samples) for categorical variables, with $p < 0.05$ regarded as significant. The software used for this statistical analysis was JMP for Windows, version 13.0 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics. Table I shows a comparison of the characteristics of all patients in the IA and EA groups. There

Table I. Patient characteristics.

	IA (n=44)	EA (n=61)	p-Value
Gender, n (%)			
Male	22 (50.0%)	31 (50.8%)	0.9339
Female	22 (50.0%)	30 (49.1%)	
Age, years			
Median (range)	68.1 (38-91)	70.6 (38-92)	0.2473
BMI, kg/m ²			
Median (range)	22.4 (17.7-28.3)	22.5 (16.7-31.3)	0.9250
ASA-PS, n (%)			
1	3 (6.8%)	7 (11.4%)	0.3769
2	35 (79.5%)	41 (67.2%)	
3	6 (13.6%)	13 (21.3%)	
Previous abdominal surgery, n (%)			
Yes	14 (31.8%)	20 (32.7%)	0.9166
No	30 (68.1%)	41 (67.2%)	
Tumour location, n (%)			
Vermiform process	0 (0%)	1 (1.6%)	0.2849
Cecum	10 (22.7%)	12 (19.6%)	
Ascending colon	16 (36.3%)	26 (42.6%)	
Transverse colon	6 (13.6%)	13 (21.3%)	
Descending colon	8 (18.1%)	3 (4.9%)	
Sigmoid colon	4 (9.0%)	6 (9.8%)	
Maximum tumour size, mm			
Median (range)	32.0 (0-75)	39.2 (0-110)	0.2022
Pathological T stage, n (%)			
Tis	2 (4.5%)	5 (8.2%)	0.3113
T1	6 (13.6%)	12 (19.6%)	
T2	12 (27.2%)	10 (16.3%)	
T3	22 (50.0%)	26 (42.6%)	
T4	2 (4.5%)	8 (13.1%)	
Pathological N stage, n (%)			
N0	30 (68.1%)	42 (68.8%)	0.0663
N1	14 (31.8%)	13 (21.3%)	
N2	0 (0%)	6 (9.8%)	
Pathological M stage, n (%)			
M0	43 (97.7%)	57 (93.4)	0.3090
M1	1 (2.2%)	4 (6.5%)	

BMI: Body mass index; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ASA-PS: American Society of Anesthesiologists physical status classification.

were no differences between the two groups in the patient factors of sex, age, BMI, ASA-PS, or previous abdominal surgery. There were also no differences between the groups in the tumour-related factors of tumour location, maximum tumour diameter, pathological invasion depth, lymph node metastasis, or clinical distant metastasis.

Surgery-related factors. Table II shows a comparison of surgery-related factors for patients in the IA and EA groups. There were no differences between the two groups in terms of surgical procedure, mobilization of the right or left colonic flexure, or the extent of lymph node dissection.

Table II. Surgery-related factors.

	IA (n=44), n (%)	EA (n=61), n (%)	p-Value
Procedure			
Ileocecal resection	19 (43.1%)	30 (49.1)	0.0970
Right hemicolectomy	7 (15.9%)	14 (22.9)	
Left hemicolectomy	5 (11.3%)	0 (0%)	
Sigmoidectomy	4 (9.0%)	6 (9.8%)	
Partial resection	9 (20.4%)	11 (18%)	
Right flexure mobilization			
Yes	27 (61.3%)	48 (78.6%)	0.0790
No	17 (38.6%)	13 (21.3%)	
Left flexure mobilization			
Yes	8 (18.1%)	5 (8.2%)	0.1253
No	36 (81.8%)	56 (91.8%)	
Lymph node dissection area			
D1	0 (0%)	1 (1.6%)	0.0970
D2	1 (2.2%)	8 (13.1%)	
D3	43 (97.7%)	52 (85.2%)	

IA: Intracorporeal anastomosis; EA: extracorporeal anastomosis.

Comparisons of outcomes and complications. Table III shows comparisons of the short-and long-term postoperative outcomes and complications of patients in the IA and EA groups.

Short-term outcomes: A comparison of surgical outcomes showed that operative time was significantly longer in the IA group (236 *vs.* 206 min, $p=0.0136$) than in the EA group, and the learning curve for operative time in IA using the moving average method was 27 patients (Figure 1). Blood loss was significantly lower in the IA group (33.3 *vs.* 76.8 ml, $p=0.0010$), and the incision length was significantly shorter (3.0 *vs.* 4.3 cm, $p=0.0001$). There was no difference in the number of lymph nodes dissected between the two groups. There was also no difference between them in the length of the proximal margin, but the distal margin was significantly longer in the IA group (103 *vs.* 85 mm, $p=0.0015$). A comparison of postoperative recovery of intestinal motility found that, although there was no difference in the time to resumption of oral ingestion, in the IA group, the time to first passage of gas tended to be shorter, and the time to first stool was significantly shorter than in the EA group (2.1 *vs.* 2.6 days, $p=0.0321$). There was no difference in the duration of postoperative hospitalization between the two groups. There was also no difference in the overall incidence of postoperative complications, and there were no differences in Clavien–Dindo grade or the types of complications that occurred.

Long-term outcomes: There were no differences between the two groups in either the types of long-term postoperative complications that occurred or the re-admission rate. There

Table III. *Outcomes and complications*

	IA (n=44)	EA (n=61)	p-Value
Short-term outcomes, median (range)			
Operative time, min	236 (151-345)	208 (121-406)	0.0136
Blood loss, ml	33.3 (3-200)	76.8 (4-405)	0.0010
Incision length, cm	3.0 (2.0-4.5)	4.3 (3.0-6.0)	0.0001
Number of dissected lymph nodes	21 (5-54)	21 (2-60)	0.9120
Proximal margin, mm	90 (30-250)	93 (30-250)	0.5645
Distal margin, mm	103 (40-180)	85 (35-270)	0.0015
Time to first pass gas, days	1.4 (1-5)	1.6 (1-5)	0.0546
Time to first stool, days	2.1 (1-6)	2.6 (1-8)	0.0321
Time to resumption of soft diet, days	5.3 (2-28)	4.0 (2-15)	0.8801
Postoperative hospital stay, days	10.7 (7-44)	9.3 (6-23)	0.6775
Complications, n (%)			
Overall	12 (27.2%)	14 (22.9%)	0.0617
CD Grade			
1	3 (6.8%)	7 (11.4%)	0.4225
2	5 (11.3%)	7 (11.4%)	0.9858
3a	2 (4.5%)	0 (0%)	0.0927
3b	2 (4.5%)	0 (0%)	0.0927
SSI	4 (9.0%)	5 (8.2%)	0.8717
Anastomotic leakage	1 (2.2%)	3 (4.9%)	0.4848
Anastomotic bleeding	1 (2.2%)	1 (1.6%)	0.8148
Postoperative ileus	1 (2.2%)	2 (3.2%)	0.7601
Lymphorrhea	1 (2.2%)	0 (0%)	0.2368
Infectious enteritis	1 (2.2%)	1 (1.6%)	0.8148
Ischemic enteritis	1 (2.2%)	0 (0%)	0.2368
Cholecystitis	1 (2.2%)	0 (0%)	0.2368
Orchitis	0 (0%)	1 (1.6%)	0.3935
Hyponatremia	0 (0%)	1 (1.6%)	0.3935
Port site hernia	1 (2.2%)	0 (0%)	0.2368
Long-term outcomes, n (%)			
Overall complications	5 (11.3%)	11 (18.0)	0.3481
Incisional hernia	3 (6.8%)	10 (16.3%)	0.1416
Ischemic colitis	0 (0%)	1 (1.6%)	0.3935
Intraabdominal abscess	1 (2.2%)	0 (0%)	0.2368
Mesenteric panniculitis	1 (2.2%)	0 (0%)	0.2368
Re-admission	2 (4.5%)	1 (1.6%)	0.3778
Recurrence	3 (6.8%)	4 (6.5%)	0.9578
Non-regional lymph node	2 (4.5%)	0 (0%)	0.0927
Liver	1 (2.2%)	3 (4.9%)	0.4848
Peritoneal metastasis	0 (0%)	1 (1.6%)	0.3935
Period of observation, days			
Median, range	481 (7-1111)	703 (110-1326)	0.0035

CD: Clavien–Dindo classification; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis.

were also no differences in the rate or type of recurrence. The follow-up period was longer for those treated with EA, the conventional procedure, compared with IA, which was introduced more recently (481 vs. 703 days, $p=0.0035$).

Comparison of the postoperative biological reaction. A comparison of postoperative biological reactions showed that the maximum patient temperature on postoperative day 1 was significantly higher in the IA group (37.8 vs. 37.4°C, $p=0.0008$), as was the C-reactive protein level (5.95 vs. 4.71 mg/dl,

$p=0.00172$); the white blood cell count also tended to be higher. There were no subsequent differences on postoperative day 4 or 7 (Table IV).

Intraoperative peritoneal washing bacteriological examination. A comparison of ascites bacterial cultures from peritoneal lavage after anastomosis completion found that the positive rate was significantly higher in the IA group (64.8% vs. 36.1%, $p=0.00140$) but there was no significant difference between the two groups in the incidence of superficial/deep incisional nor

Figure 1. Time taken to perform intracorporeal anastomosis as a function of the number of cases. The moving average method was used to determine changes in operative time.

Table IV. Postoperative biological reactions. Data are median values (range).

	POD	IA (n=44)	EA (n=61)	p-Value
WBC count, n/mm ³	1	10247.7 (5600-21700)	8965.6 (3200-14300)	0.0579
	4	6081.8 (3100-11800)	6100.0 (2400-16000)	0.7874
	7	6193.0 (3200-13400)	6135.0 (2800-14300)	0.4112
CRP, mg/dl	1	5.95 (1.80-12.39)	4.71 (0.39-12.13)	0.0172
	4	8.35 (0.95-27.37)	6.51 (0.65-29.81)	0.0778
	7	3.59 (0.19-22.29)	2.50 (0.21-14.80)	0.4458
Temperature, °C	1	37.8 (36.9-39.9)	37.4 (36.4-38.5)	0.0008
	4	36.7 (35.7-38.5)	36.7 (36.0-38.7)	0.2330
	7	36.5 (35.3-38.8)	36.4 (35.8-37.2)	0.6737

CRP: C-Reactive protein; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; POD: postoperative day; WBC: white blood cell.

organ/space SSIs (Table V). An investigation of the effect of the type of preoperative pretreatment on positivity of bacterial culture of ascites found that when patients underwent mechanical pretreatment, those in the IA group had a significantly higher positive culture rate (90.0% vs. 44.4%, $p=0.0329$) but that there was no difference in the positive culture rates between the two groups when patients underwent chemical pretreatment (Table VI).

Intraoperative peritoneal washing cytology and recurrence. A comparison of the results of ascites cytology from peritoneal lavage after anastomosis completion found no positive results for patients in either group, and no

significant difference in class between the two groups (Table VII).

Discussion

Since it was first reported, laparoscopic colectomy has rapidly become widely used. The noninferiority of laparoscopic colectomy to open surgery was established in large-scale clinical studies including the COST study (4-6), COLOR study (7, 8), and CLASICC study (9, 10). Several studies have also found that because laparoscopic surgery is less invasive than open surgery, postoperative recovery is faster (7, 11). Laparoscopic surgery for colon cancer is more

Table V. Intraoperative peritoneal washing bacteriological examinations and surgical site infection (SSI).

	IA (n=37)	EA (n=36)	p-Value
Culture result			
Positive	24 (64.8%)	13 (36.1%)	0.0140
SSI			
Superficial/deep incisional	1 (2.7%)	1 (2.7%)	0.9843
Organ/space	1 (2.7%)	1 (2.7%)	0.9343

IA: Intracorporeal anastomosis; EA: extracorporeal anastomosis.

difficult than open surgery but remarkable recent advances in endoscopic surgical instruments and improved surgical techniques mean that it has now become virtually standardized. However, even under these circumstances, it may prove difficult to deliver the bowel outside the body *via* a small incision during laparoscopic surgery for colon cancer, making it difficult to complete the procedure properly. In colon cancer surgery, many hospitals usually carry out lymph node dissection and dissection and mobilization of the bowel laparoscopically before delivering the bowel outside the body to transect it and create the anastomosis. However, in obese patients with thick abdominal walls or mesenteric fat tissue, it may be difficult to deliver the bowel outside the body *via* a small incision, and this may sometimes damage the mesentery, causing unnecessary haemorrhage. If the operations involved in anastomosis formation must be conducted with the bowel insufficiently delivered outside the body, this can hinder the creation of an accurate, reliable anastomosis, increasing the risk of subsequent anastomotic leakage. In patients with cancer of the transverse, descending, or sigmoid colon, additional mobilization of the left colonic flexure may also be necessary simply to deliver the bowel outside the body. Not only does IA in laparoscopic colectomy reduce the extent of bowel mobilization and avoid the risk of damaging the bowel or mesentery during delivery of the bowel outside the body, but adequate laparoscopic anastomosis operations may also reduce the occurrence of anastomotic leakage.

Recently, the number of reports of the performance of IA in hospitals where EA had been the first choice in laparoscopic colectomy has gradually been increasing, although this involves only a proportion of hospitals. IA for laparoscopic colectomy was first described in 2003 (12), but although over a decade has elapsed since that report, comparisons of IA and EA have yet to reach a conclusion as to which procedure is best. Some comparative studies of IA and EA have found that IA reduces operative time (13), others have found that it prolongs it (14, 15), and still others reported that the two are equivalent (16, 17). In the present study, operative time was longer in the IA group but this may

Table VI. Bacterial culture-positive cases by preparation.

Preparation	IA		IE		p-Value
Mechanical	n=10	9 (90%)	n=9	4 (44.4%)	0.0329
Oral antibiotic	n=27	15 (55.5%)	n=27	9 (33.3%)	0.1003

IA: Intracorporeal anastomosis; EA: extracorporeal anastomosis.

Table VII. Intraoperative peritoneal washing cytology.

	IA (n=37)	EA (n=36)	p-Value
Class			0.1967
I	12 (32.4%)	17 (47.2%)	
II	25 (67.5%)	19 (52.7%)	

IA: Intracorporeal anastomosis; EA: extracorporeal anastomosis.

have been because IA requires more coordination with the assistant than does EA, and a somewhat higher level of surgical skill is required than for EA. Laparoscopic surgery entails a learning curve (18), and, in this study, it was found that it was possible to complete the procedure in an operative time almost the same as that for EA after 27 cases. Even after the 27th patient, however, the operative time remained unstable, and since this study included only 44 cases, the possibility must be taken into account that the stable phase may not have been achieved. Associated intraoperative blood loss was significantly lower for IA than for EA. Previous studies have also reported lower volumes of haemorrhage (19-21). In EA, haemorrhage may occur due to damage to the mesentery when the bowel is delivered outside the body, and unnecessary haemorrhage may also occur if the mesentery must be divided in a position in which it is not directly visible, but in IA, the use of magnified imaging and of devices with improved haemostatic function may contribute to reducing haemorrhage from the mesentery.

Several studies have reported that incision length is shorter for IA (13, 17, 20, 21). In the present study, it was also significantly shorter. In IA, the resected bowel is straightened to remove it from the body, enabling the use of a smaller incision for tumours of the same diameter. By reducing the length of the incision, IA provides superior cosmetic results to those of EA. Attempts have also been made to combine IA with specimen extraction through a natural orifice, extracting specimens *via* the vagina or rectum to minimize destruction of the abdominal wall and achieve less invasiveness and better cosmetic results in a concept different from that of reduced port surgery (22, 23).

Some comparative studies of postoperative recovery time have found that it is equivalent for IA and EA (13, 20), while

others have found that recovery is faster after IA (15-17, 21). In the present study, bowel movements resumed significantly earlier after IA, and the first passage of gas also tended to be earlier. Because IA does not require the bowel to be delivered outside the body, there is no need to perform bowel mobilization that is not oncologically necessary but is carried out solely to enable bowel delivery for EA, and this reduces the extent of mobilization. It is also conceivable that the bowel may recover faster because it is neither touched directly by hand nor exposed to the outside air at any point in the procedure.

Numerous studies have reported that postoperative complication rates are equivalent (24-28). In the present study, the results of IA were also equivalent to those of EA. The rates of suture failure, a complication that is one focus of concern in gastrointestinal surgery, were also equivalent. Different studies have reported different types of anastomosis created in IA but side-to-side anastomosis is basically the most common. A randomized, clinical trial found no difference between isoperistaltic and anti-peristaltic anastomosis formation (29). In the present study, isoperistaltic side-to-side anastomoses were created because they provide physiological bowel motility, require a smaller extent of bowel mobilization, are a simple procedure, have a large anastomotic orifice with little risk of stenosis, and have a low risk of anastomotic leakage. The insertion opening may be closed by hand suturing or mechanical suturing, but practice varies between hospitals, and since there has been no comparative study of the two techniques, it is unclear at this point which is better. We use mechanical suture closure because of the simplicity and reliability of the procedure. Technical issues with side-to-side anastomoses created entirely with linear staplers mean that if the staplers are inserted *via* the same 12-mm port, the axis of the linear stapler used to create the side-to-side anastomosis is different from that of the linear stapler used to close the insertion opening, making the procedure somewhat complicated. In the right colon, the procedure is ileocolostomy, and the good mobility of the small intestine means that problems are unlikely, but in the left colon, this difficulty becomes more pronounced the closer the anastomosis site is to the promontory angle. This problem can be resolved by inserting the stapler *via* the 12-mm port in the umbilicus during side-to-side anastomosis creation and through the 12-mm port in the left lower abdomen when closing the insertion opening.

Problems with IA include (i) bacterial contamination of the peritoneum as a result of faecal leakage, and (ii) the possibility of cancer cell dissemination. IA has been widely performed in laparoscopic gastric cancer surgery for some time, but in colorectal disease, any intestinal fluid that leaks contains stool, increasing the risk of the occurrence of SSIs such as peritoneal abscess; for this reason, IA has not become generally used despite its technical feasibility. In the

present study, ascites bacterial cultures from peritoneal lavage after anastomosis completion were positive in a significantly higher proportion of patients who underwent IA. The effect was evident in postoperative biological reactions, with maximum temperature and blood test results indicating an inflammatory reaction on postoperative day 1 both higher in patients who underwent IA, although the incidence of SSIs was similar. This is because the bacterial species constituting the human normal flora cannot be judged clinically even if the isolated bacteria are identified, there are many bacterial species that are difficult to isolate and identify, obligatory anaerobic bacteria rarely cause infection alone, and it seems to be affected by the fact that there are many cases of multiple bacterial infections with aerobic bacteria and other anaerobic bacteria.

We had initially carried out the procedure after solely mechanical pretreatment of the bowel. Because leakage of watery mushy stool had also been noted during EA before the introduction of IA, and we had also seen postoperative intraperitoneal abscess formation due to leakage of watery mushy stool into the peritoneal cavity in patients who underwent IA when it was first introduced, we considered that mechanical pretreatment of the bowel made the stool more watery, increasing the risk of leakage during anastomosis creation and the extent of bacterial contamination. The surgical site infection guidelines issued jointly by the American College of Surgeons and the Surgical Infection Society (30) recommend the combined use of mechanical pretreatment and oral antibiotics for elective colorectal surgery. However, since mechanical pretreatment of the bowel is not recommended for the Enhanced Recovery After Surgery program, which aims to promote postoperative recovery, we replaced mechanical pretreatment with chemical pretreatment using oral antibiotics. The results of the present study clearly demonstrated that the use of this pretreatment may significantly reduce the rate of positive bacterial cultures in IA. This suggests that although the surgical procedure of IA entails a high risk of intraperitoneal contamination, carrying out preoperative pretreatment by chemical rather than mechanical means may limit such contamination to the same level as in EA.

No cancer cells were detected in ascites cytology after peritoneal lavage in either group. Many patients with gastric cancer with positive peritoneal lavage cytology go on to develop peritoneal recurrence, and this is regarded as a poor prognostic factor (31), but the clinical significance of peritoneal lavage cytology in colorectal cancer has yet to be established (32, 33). Because the sensitivity of peritoneal lavage cytology for detection is not very high (34), the argument for oncological safety is somewhat difficult to make on the basis of cytology alone. However, comparisons of recurrence rates have found that they are equivalent, and the type of recurrence is not peritoneal recurrence due to

cancer cell dissemination or recurrence at the anastomosis site. In the present study, thus, no oncological problems were identified.

This study was limited by its nature as a non-randomized, single-centre study. Despite the equivalence of the IA and EA groups in terms of patient characteristics, surgery-related factors, and tumour-related factors, it is possible that bias may still have occurred. The results of the comparisons between the two groups must therefore be interpreted with caution. Although the present study included a large number of patients overall, the number in each group may still have been too small to permit proper analysis. Despite all these limitations, however, the present study clearly identified a number of advantages of IA, as well as its problems and methods for dealing with them. However, further randomized trials are required to compare IA and EA properly.

Conclusion

After appropriate preoperative pretreatment, IA may provide an effective approach making the best use of the minimal invasiveness that is the advantage of laparoscopic surgery, by enabling faster bowel recovery and shorter incision length than in EA.

Conflicts of Interest

Hajime Kayano, Eiji Nomura, Yasuhiro Ueda, Toru Kuramoto, Takashi Machida, Masaya Mukai, Seiichiro Yamamoto and Hiroyasu Makuuchi have no conflicts of interest or financial ties to disclose.

Authors' Contributions

HK and EN drafted this study. HK, YU, TK, and TM collected the patient data. HK, EN, MM, SY, and YM analysed and interpreted data. HK was a major contributor in writing the article. All Authors read and approved the final article.

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