



Surgical Recurrence at Anastomotic Site After Bowel Resection in Crohn's Disease: Comparison of Kono-S and End-to-end Anastomosis

Norimitsu Shimada¹ · Hiroki Ohge¹ · Toru Kono² · Ayumu Sugitani² · Raita Yano¹ · Yusuke Watadani¹ · Kenichiro Uemura¹ · Yoshiaki Murakami¹ · Taijiro Sueda¹

Received: 7 May 2018 / Accepted: 10 October 2018 / Published online: 23 October 2018
© 2018 The Society for Surgery of the Alimentary Tract

Abstract

Background Anastomotic surgical recurrence after bowel resection in Crohn's disease patients is problematic. This study was performed to evaluate the increased risk of anastomotic surgical recurrence.

Methods From 2006 to 2016, we performed anastomoses in 215 consecutive Crohn's disease patients. The cohort was divided into two groups: Kono-S anastomosis ($n = 117$) and end-to-end anastomosis ($n = 98$). Multivariate analysis of predictors of anastomotic surgical recurrence and Kaplan–Meier analysis for the 5-year anastomotic surgical recurrence rate were evaluated.

Results The two groups showed no statistically significant differences in patient backgrounds. During a median follow-up of 54 months, 28 patients required anastomotic surgical recurrence [4 (3.4%) in the Kono-S group and 24 (24.4%) in the end-to-end group]. Six leaks (5.1%) were detected in the Kono-S group and 17 leaks (17.3%) in the end-to-end group; all were successfully treated conservatively. End-to-end anastomosis, leakage, age < 45 years, and body mass index of $\geq 18 \text{ kg/m}^2$ at the first surgery had a higher risk of anastomotic surgical recurrence. Kono-S anastomosis significantly reduced the risk of anastomotic surgical recurrence after 1 year (odds ratio, 0.14). Anastomotic leakage influenced anastomotic surgical recurrence within 1 year (odds ratio, 4.84). The 5-year surgery-free survival rate at the anastomosis site with Kono-S anastomosis (95.0%) was significantly higher than that with end-to-end anastomosis (81.3%; $P < 0.001$).

Conclusions Anastomotic leakage after bowel resection in Crohn's disease patients increased anastomotic surgical recurrence within 1 year, and Kono-S anastomosis is associated with a low risk of anastomotic surgical recurrence after > 1 year.

Keywords Crohn's disease · Surgical recurrence · Anastomosis · End-to-end · Kono-S anastomosis

Introduction

Surgical recurrence at the anastomotic site (SRA) after bowel resection still occurs with considerable frequency in patients with Crohn's disease (CD). Despite the advances in medical therapy, up to 80% of patients with CD

have a lifetime risk of intestinal resection.^{1,2} After resection, endoscopic recurrence occurs at the anastomosis site in 80 to 90% of patients within 3 years of surgery, and 30 to 40% of patients require recurrent surgery following primary bowel resection.^{2–5} The terminal ileum and ileocolic anastomotic site are the most common sites of recurrence.^{6,7} Stapled side-to-side anastomosis with a wide lumen was expected to reduce the surgical recurrence rate, but comparison of this technique with handsewn end-to-end anastomosis (EEA) did not provide consistent results in some meta-analyses.^{8,9}

To prevent SRA, Kono et al.¹⁰ created a new anti-mesenteric functional EEA technique called Kono-S anastomosis (KSA) in 2003. This technique is characterised by an anti-mesenteric longitudinal enterotomy and supporting column that maintain the three-dimensional structure. The endoscopic recurrence rate is reportedly lower with KSA than with conventional EEA, and two studies showed that

Conference presentation: This study was presented as a poster at the 2017 meeting of The American Society of Colon and Rectal Surgeons in Seattle, Washington (10–14 June 2017).

✉ Norimitsu Shimada
shimada@hiroshima-u.ac.jp

¹ Department of Surgery, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima City, Hiroshima 734-8551, Japan

² Center for Clinical and Biomedical Research, Sapporo Higashi Tokushukai Hospital, 3-1, Kita 33-jo Higashi, 14-chome, Higashi-ku, Sapporo, Hokkaido 065-0033, Japan

the 5-year surgical anastomotic recurrence rate was 1.8% during a median follow-up of 65 months (range, 43–138 months).^{10,11} No anastomotic configuration has been established to reduce SRA in patients with CD. Some reports have described good results of KSA, but their sample sizes were small and follow-up periods were short.^{10,12–14}

In our institution, KSA has been performed in patients with CD since 2009 and appears to have reduced the SRA rate.

In this study, we evaluated the risk factors for SRA as the primary outcome and the 5-year surgical recurrence-free survival rate at the anastomosis site and complications according to anastomotic configurations as the secondary outcomes.

Materials and Methods

In total, 216 patients undergoing bowel resection with anastomosis for CD in Hiroshima University Hospital from January 2006 to July 2016 were retrospectively enrolled. The diagnosis of CD was established by clinical symptoms, endoscopic findings, and pathologic data.

Since 2009, all patients with CD have undergone KSA for resection of small and large bowel disease. Conventional EEA with layer-to-layer suturing was performed for all patients before the introduction of KSA as well as for all patients who did not have a sufficient anastomotic margin for KSA, such as those with CD involving the upper rectum in the pelvic space. Patients with low rectal anastomosis below the peritoneum were not included. Stapled side-to-side anastomosis was not performed at our institution. The patients' medical records were reviewed to obtain information on demographics and clinical history. The type of CD was classified according to the affected regions: small bowel type, large bowel type, or small and large bowel type; these types did not always correspond to the surgical site. A laparoscopic surgical technique was applied only for the first surgery and excluded the penetrating type of CD with abdominal abscesses. With respect to preoperative medications, patients taking anti-tumour necrosis factor alpha (infliximab or adalimumab) within 12 weeks prior to the operation and those taking other medications within 3 days before the operation were included. Anastomotic leakage was defined as detection of a fluid or air bubble around the anastomosis site with computed tomography or abdominal ultrasound and included both symptomatic and asymptomatic cases. Small bowel obstruction was defined as ileus showing multiple hydroaeric levels (niveau) on abdominal X-ray examination within the hospitalisation period for surgery.

The KSA technique has been described in detail in previous literature.^{10,11} We slightly modified the original method; a running 4-0 absorbable suture was placed in a single layer in the posterior wall, and the anterior wall was sutured in two

layers with a running 4-0 absorbable suture in the inner layer and interrupted 4-0 absorbable sutures in the outer layer (Fig. 1). Layer-to-layer EEA was performed using 4-0 absorbable sutures, with a running suture in the inner layer and interrupted sutures in the outer layer.

In this study, we retrospectively analysed the risk factors for SRA. Surgical recurrence was defined as a stricture or penetrating lesion requiring surgical repair at the anastomotic site as detected by endoscopy, intestinal contrast examination, and computed tomography and pathological finding of CD with resected specimens. The study protocol and informed consent form were consistent with the recommendations of the Declaration of Helsinki and approved by the Institutional Review Board of Hiroshima University (E-556).

Statistical Analysis

The statistical analysis was conducted with SAS Studio Release 3.6 (SAS Institute Inc., Cary, NC, USA). Normally distributed continuous variables were analysed using a *t* test, and non-normally distributed continuous variables were analysed by the nonparametric Wilcoxon rank-sum test. Fisher's exact test was performed for categorical variables. Multivariable logistic regression analysis was performed to detect predictive risk factors for surgical recurrence at the anastomosis site. Surgical recurrence-free survival was analysed by Kaplan–Meier analysis, and the log-rank test was performed. Each analysis was performed with the use of a two-sided, 5% significance level and 95% confidence interval.

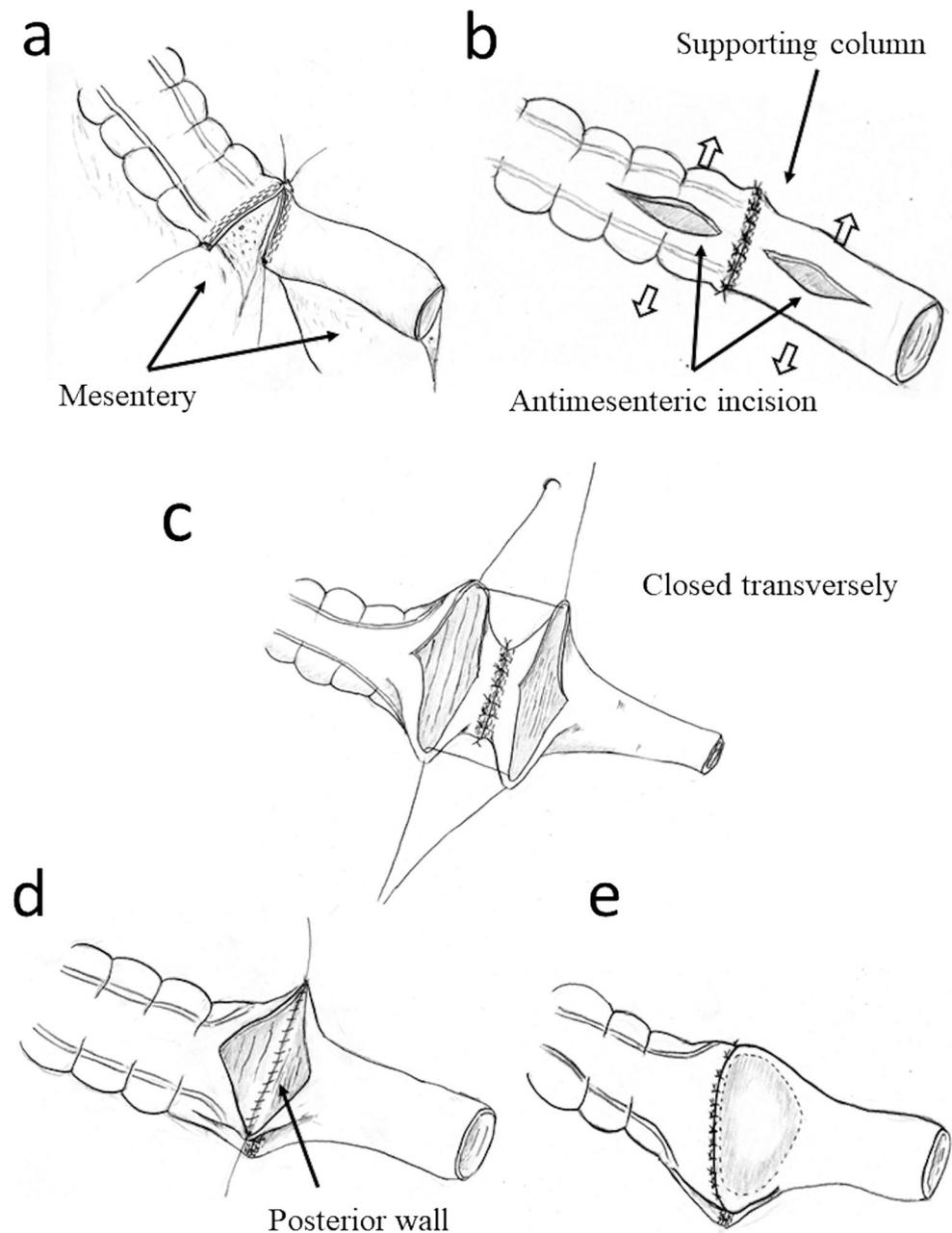
Results

In total, 215 patients (158 male) with CD underwent surgical operations for small and large intestinal disease with a median age at surgery of 37 years (Table 1). KSA was performed in 117 patients, and EEA was performed in 98 patients. In terms of the surgical indications, 132 (58.0%) patients had the stricture type of CD and 80 (35.6%) had the penetration type. A total of 117 (54.0%) patients had the small bowel type, 11 (5.1%) had the large bowel type, and 86 (40.0%) had the small and large bowel type. During the median follow-up of 54 months (interquartile range (IQR), 29.7–86), 28 patients required reoperation because of SRA.

Risk Factors for Surgical Recurrence at the Anastomotic Site

The univariate analysis showed five factors that might affect the risk of surgical recurrence at the anastomosis site (Table 2): age (< 45 years), body mass index (BMI) (≥ 18 kg/m²), small

Fig. 1 Kono-S anastomosis. (a) The bowel was divided with a linear stapler perpendicular to the mesentery. Each stapled line was connected and reinforced (supporting column). (b) Antimesenteric longitudinal incisions (7 to 8 cm) were performed on each stump, starting within 0.5 to 1 cm away from staple line. (c) Anti-mesenteric orifice was closed transversely. (d) Single-layer running suture was used at posterior wall. (e) Anterior wall was closed in two layers with running and interrupted sutures



and large bowel type, anastomosis method, and anastomosis leakage. Multivariate logistic regression analysis showed that age, BMI, the anastomotic configuration, and anastomotic leakage were statistically significant. Patients aged < 45 years and those with a BMI of $\geq 18 \text{ kg/m}^2$ at the first surgery were found to have a higher risk of SRA. In patients who underwent KSA as the anastomotic configuration, the SRA rate was significantly lower than that in patients who underwent EEA (odds ratio (OR), 0.014; 95% confidence interval (CI), 0.04–0.44; $P < 0.001$). Anastomotic leakage after bowel resection in patients with CD was associated with an increased rate of SRA (OR, 4.84; 95% CI, 1.09–21.5; $P < 0.001$).

Short- and Long-term Outcomes According to Anastomosis Technique

Patient characteristics, preoperative medications, and the rate of postoperative anti-TNF were similar in the KSA group and the EEA group (Table 3). Infliximab was administered for 35 patients in KSA, and 27 patients in EEA. Adalimumab was administered for 23 patients and 17 patients, respectively. Two patients in EEA was received both biological agents. The KSA and EEA showed no significant difference in the median operative time, estimated blood loss, or rate of patients requiring blood transfusions. In terms of postoperative complications,

Table 1 Patient characteristics, preoperative medications, and postoperative anti-TNF administration

Age, median (IQR)	37 (30–45)
Sex (male:female)	158:57
BMI (kg/m ²)	18.7 (16.9–20.2)
Type (SB:LB:SLB)	117:11:86
Stricture disease:penetration disease:others	132:80:3
Open:laparoscopic	183:32
Anastomosis KSA:EEA	117:98
Transfusion in operation	24 (11.1%)
Preoperative medication	
5ASA	154 (71.6%)
Azathioprine	33 (15.3%)
Steroid	46 (21.4%)
anti-TNF	49 (22.7%)
Postoperative anti-TNF	100
Anastomosis leakage	23 (10.6%)
Ileus	25 (11.6%)
Superficial incisional SSI	21 (9.7%)
Deep incisional SSI	34 (15.8%)
Organ/space SSI	30 (13.9%)
Second surgery at anastomosis site	28 (13%)
Observation period (month), median (IQR)	54 (29.7–86.3)

IQR, interquartile range; *BMI*, body mass index; *SB*, small bowel type; *LB*, large bowel type; *SLB*, small and large bowel type; *KSA*, Kono-S anastomosis; *EEA*, end-to-end anastomosis; *anti-TNF*, anti-tumour necrosis factor alpha; *SSI*, surgical site infection

anastomotic leakage occurred in 6 (5.1%) patients in the KSA group versus 17 (17.3%) in the EEA group ($P=0.067$), respectively. All patients who had leakage were treated conservatively with or without drainage, but reoperation was not performed. Other postoperative complications were not significantly different between the groups (Table 4).

With respect to long-term outcomes, Kaplan–Meier analysis showed a lower probability of a second surgery at the anastomosis site in KSA than in EEA (Fig. 2). The 5-year surgery-free survival rate at the anastomosis site with KSA was 95.0% (95% CI, 0.90–1.00), which was significantly higher than that with EEA 81.3% (95% CI, 0.73–0.89). Four (3.4%) patients in the KSA group underwent a second surgery at the anastomosis site after a mean of 47.3 months (IQR, 31–66), and 24 (24.4%) patients in the EEA group underwent such a second surgery after a mean of 99 months (IQR, 64–115).

Risk Factors for Surgical Recurrence at the Anastomosis Site Within 1 Year

Seven patients required a second surgery within 1 year, and 5 of those had anastomotic leakage at the first surgery. Logistic

regression analysis showed that anastomotic leakage was a higher risk factor for SRA within 1 year (OR, 23.6; 95% CI, 3.9–14; $P<0.001$), but the anastomotic configuration was not statistically associated (Fig. 3).

More than 1 year after surgery, 21 patients developed surgical recurrence at the anastomosis site. During this period, use of KSA reduced the risk of SRA (OR, 0.08; 95% CI, 0.02–0.33; $P<0.001$), and anastomotic leakage was not a significant factor in the multivariate analysis.

Anastomotic leakage could be associated with early surgical recurrence within 1 year.

Discussion

Many studies have focused on the effect of the anastomotic configuration on SRA rates. These data have raised concerns among surgeons regarding what type of anastomosis could restore intestinal continuity in a more “anatomical” way, minimising faecal stasis, ileocolonic reflux, ischaemia, and bacterial overgrowth in the non-terminal ileum.^{15,16} To date, none of the anastomotic configurations have been considered a risk factor for SRA. A recent multi-centre observational study showed no correlation between the type of anastomotic configuration and early postoperative endoscopic recurrence.¹⁷ The present study showed that the new anastomotic configuration, KSA, reduced the risk of SRA (OR, 0.012) compared with EEA, and the 5-year surgery-free survival rate at the anastomosis site with KSA was significantly high at 95% (95% CI, 0.90–1.00). New data are needed, especially from randomised studies evaluating all types of anastomotic configurations, including KSA.^{3,14}

KSA, which is an anti-mesenteric functional handsewn EEA technique, was devised by Kono et al.¹⁰ to reduce SRA in patients with CD. The defining characteristic of KSA is the creation of a widely patent anastomotic hole on the opposite side of the mesentery and establishment of a supporting column. To reduce the risk of SRA, both the wide lumen at the anastomotic site and the supporting column are important to maintain a three-dimensional structure. The supporting column prevents distortion and keeps the intestinal tract in the anastomosis region straight.¹⁰ This straight structure also makes endoscopic examination after surgery easy to perform. In contrast, the stapled functional EEA structure is hairpin-like, making endoscopy difficult to observe and balloon dilatation difficult to perform.

An additional advantage of KSA is that the lumen of the mesenteric side does not need to be sutured. The mesenteric-side intestinal wall suturing is a major factor involved in anastomosis leakage in EEA. Especially in patients with CD, the thickened fat pad hinders the view required for suturing in this region. Avoidance of suturing in this area helps to reduce anastomotic leakage. In this study, the rate of anastomotic

Table 2 Predictive risk factors for second surgery at anastomosis site in patients with Crohn's disease

	Univariate analysis			Multivariable analysis		
	OR	95% CI	P value	OR	CI	P value
Age (< 45)	11.2	1.49–84.85	0.019*	10.7	1.2–92	0.003*
Sex (male)	1.12	0.45–2.8	0.80			
BMI (≥ 18)	0.30	0.13–0.71	0.006*	0.19	0.07–0.53	0.001*
Type (SLB)	3.08	1.35–7.05	0.008*	1.89	0.72–5.0	0.19
Stricture disease/others	0.87	0.38–1.9	0.74			
Laparoscopic	< 0.01	< 0.01–> 99	0.95			
Anastomosis (KSA)	0.11	0.036–0.33	< 0.001*	0.14	0.04–0.44	0.001*
Transfusion	1.92	0.66–5.6	0.23			
Preoperative medication						
5ASA	0.68	0.29–1.5	0.36			
Azathioprine	0.91	0.29–2.8	0.87			
Steroid	0.99	0.38–2.6	0.99			
anti-TNF	0.37	0.08–1.6	0.19			
Postoperative anti-TNF	0.98	0.41–2.3	0.96			
Ileus	1.82	0.62–5.3	0.28			
Anastomosis leakage	5.85	2.2–15.3	< 0.001*	4.84	1.09–21.5	0.038*
Superficial incisional SSI	0.68	0.15–3.0	0.62			
Deep incisional SSI	1.98	0.77–5.1	0.16			
Organ/space SSI	2.38	0.91–6.2	0.07	1.22	0.28–5.29	0.78

SLB, small and large bowel type compared with either small bowel type or large bowel type

leakage with KSA (5.1%) was significantly lower than that with EEA.

Multivariate logistic regression analysis showed in this study that anastomotic leakage is associated with an increase rate of SRA within 1 year. To the best of our

knowledge, no other reports have explored anastomotic leakage as an independent risk factor for SRA. Patients with postoperative intra-abdominal septic complications, including anastomotic leakage, had significantly higher 1-, 2-, 5-, and 10-year SRA rates (25%, 29%, 50%, and

Table 3 Patient characteristics, preoperative medications, and postoperative anti-TNF administration in the KSA group and the EEA group

	Kono-S N = 117	EEA N = 98	P value
Age (median, IQR)	39 (31–47)	34 (28–43)	0.038
Sex (male:female)	84:33	74:24	0.642
BMI (kg/m ²)	18.9 (16.9–20.3)	18.6 (17.0–20.3)	0.733
Smoking	7 (6.0%)	4 (4.1%)	0.758
Type (SB:LB:SLB)	69:5:42	48:6:44	0.285
Stricture disease:penetration disease:others	68:48:1	64:32:2	0.403
Preoperative medication			
5ASA	87 (74.3%)	67 (68.3%)	0.364
Azathioprine	20 (17.0%)	13 (13.2%)	0.455
Steroid	21 (18.1%)	25 (25.5%)	0.242
anti-TNF	36 (30.2%)	14 (14.3%)	0.009
Postoperative anti-TNF	58 (49.6%)	42 (43.3%)	0.410
Observation period (month), median (IQR)	38 (24–56)	89 (58–104)	< 0.001

IQR, interquartile range; BMI, body mass index; SB, small bowel type; LB, large bowel type; SLB, small and large bowel type; KSA, Kono-S anastomosis; EEA, end-to-end anastomosis; anti-TNF, anti-tumour necrosis factor alpha; SSI, surgical site infection

Table 4 Clinical outcomes of patients with Crohn’s disease according to anastomosis methods

	Kono-S N= 117	EEA N= 98	P value
Operative outcome			
Operative time (min), median (IQR)	215 (180–277)	239 (180–300)	0.585
Estimated blood loss (ml), median (IQR)	239 (105–450)	245 (130–460)	0.537
Blood transfusion	12 (10.2%)	12 (12.2%)	0.669
Postoperative complications			
Anastomosis leakage	6 (5.1%)	17 (17.4%)	0.007*
Superficial SSI	15 (12.8%)	6 (6.1%)	0.112
Deep SSI	17 (14.5%)	17 (17.4%)	0.579
Organ space SSI	13 (11.1%)	17 (17.4%)	0.236
Small bowel obstruction	13 (11.1%)	11 (12.2%)	0.833
Surgical recurrence of anastomosis site	4 (3.4%)	24 (24.5%)	< 0.001*

IQR, interquartile range; SSI, surgical site infection; EEA, end-to-end anastomosis

57%, respectively) than patients without intra-abdominal septic complications (4%, 7%, 19%, and 38%, respectively; $P = 0.0003$).¹⁸ These findings support our data.

Many studies have compared anastomotic configurations in patients with CD. Kono et al.¹¹ reported that the rate of anastomotic leakage in patients who underwent KSA was 1.1%. Resegotti et al.¹⁹ found that the rate of anastomotic leakage after stapled side-to-side anastomosis was significantly lower than that after handsewn EEA (2.0% vs. 14.1%, respectively). Windmar et al.²⁰ reported that over-sewing the staple line in functional EEA reduced anastomotic complications, and no leakage occurred among 120 patients. In contrast, some authors have found no difference in the anastomosis leakage rate between stapled and sutured methods.^{21–23} McLeod et al.⁹ reported

that the anastomotic type did not affect recurrence in patients with CD after ileocolic resection. There are no optimal anastomotic configurations in patients with CD to prevent anastomotic leakage and SRA. KSA is a slightly complicated procedure involving creation of a supporting column and a long handsewn suturing technique. However, it does not extend the operation time, and in the present study, it was associated with low rates of SRA and anastomotic leakage. KSA is a feasible technique for CD, but a follow-up period of ≥ 10 years is essential to validate its superiority.

Anastomotic leakage was the independent risk factor for SRA in this study. According to this finding, we speculate that an additional inflammatory response caused by the leakage disturbs the mucosal healing and healing process at the anastomotic site. A previous study showed that a histopathological inflammatory change proximal to the anastomosis may be detected within 1 week after surgery.²⁴ The leakage might promote the inflammation of CD at the proximal site. The healing process at the anastomotic leakage site leads to overgrowth of fibrosis, which may contribute to stricture formation at the anastomotic site and cause faecal stasis. Faecal stasis was suspected to influence mucosal healing by modifying the microbial–mucosal interaction.²⁵ However, we have no data regarding this issue, and the number of affected patients was small, making it difficult to draw conclusions. Further studies are needed to clarify these results.

Age (< 40 years) and BMI ($< 18 \text{ kg/m}^2$) were the independent risk factors for SRA in our multivariate logistic analysis. A younger age at diagnosis is considered to be a major factor for a more aggressive and disabling course.²⁶ However, its effect on SRA is less clear, and data extracted from the literature do not consistently indicate age as a predictive factor.²⁷ BMI has not been established as a risk

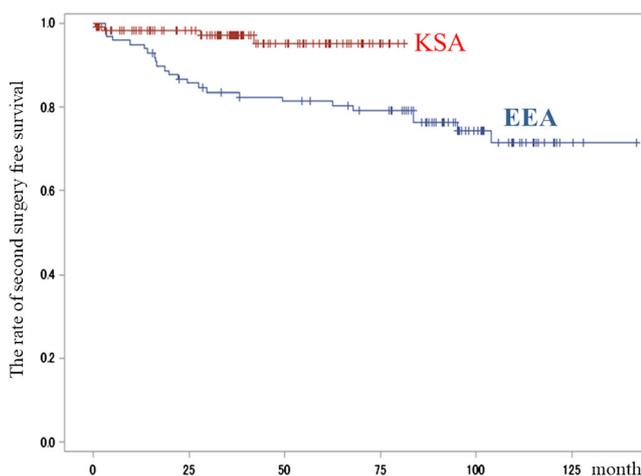


Fig. 2 Surgery-free survival at anastomosis site. The Kaplan–Meyer survival curve shows the 5-year second surgery-free rate at the anastomosis site. This rate was 95% in the KSA group and 81% in the EEA group. KSA, Kono-S anastomosis group; EEA, end-to-end anastomosis group

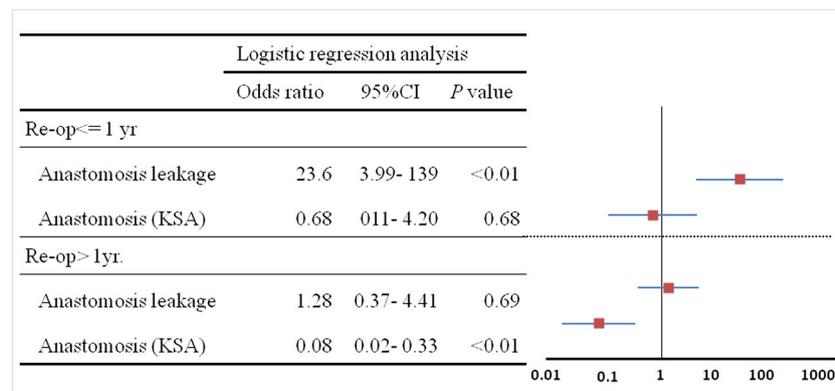


Fig. 3 Predictive risk factors for second surgery at anastomosis site within 1 year after first surgery and > 1 year after surgery. The forest plot shows that anastomosis leakage increased the risk for surgical recurrence at the anastomosis site within 1 year after surgery. More than

1 year later, KSA was associated with a reduced risk. Re-op ≤ 1 yr., second surgery at anastomosis site within 1 year; Re-op > 1 yr., second surgery > 1 year later

factor. Thus, further data are required to clarify the relation of BMI to recurrence rates.

Previously reported risk factors for postoperative recurrence include smoking, perforating disease, and a history of intestinal resection.^{9,28,29} These risk factors were not detected in the present study. Recent multi-centre observational studies failed to recognise smoking as a risk factor for postoperative recurrence after ileocolic resection,^{17,30} although smoking is a well-established modifiable risk factor for the postoperative course of CD.²⁷ Our results regarding smoking could be explained by the small number of patients recruited ($n = 215$), including only 5.1% smokers.

In this study, the rate of infectious complications and anastomosis leakage was higher than that in previous studies. We cannot explain the reason for these results clearly. The anastomosis leakage 17% in EEA was higher than previous study; this may be the cause of difference in the accuracy for complication evaluation between facilities, although it is clear that the leakage of KSA was significantly lower.

This study has several limitations. First, it was a nonrandomised retrospective study, which limits the availability of certain data. Endoscopic recurrence was also not evaluated. Second, potential bias cannot be ruled out; for example, the follow-up period was shorter in the KSA group than in the EEA group because of the single-institution nature of the study. The preoperative status and postoperative medications were not fully evaluated in both groups, which might have affected the final outcomes.

Conclusions

In conclusion, anastomotic leakage after bowel resection in patients with CD is a predictor of early recurrence within 1 year. KSA was associated with a low risk of SRA after > 1 year. KSA was superior with respect to a lower rate of SRA

at 5 years using Kaplan–Meyer analysis as well as a lower rate of anastomotic leakage compared with EEA.

Authors' Contributions Study conception: Norimitsu Shimada, Hiroki Ohge, Toru Kono, Taijiro Sueda

Study design: Norimitsu Shimada, Hiroki Ohge, Toru Kono

Data acquisition: Norimitsu Shimada, Raita Yano, Yusuke Watadani

Quality control of data and algorithms: Yusuke Watadani, Kenichiro Uemura, Yoshiaki Murakami

Data analysis and interpretation: Norimitsu Shimada, Ayumu Sugitani, Raita Yano

Statistical analysis: Ayumu Sugitani

Manuscript preparation: Norimitsu Shimada

Manuscript editing: Hiroki Ohge, Yoshiaki Murakami, Kenichiro Uemura

Manuscript review: Toru Kono, Taijiro Sueda

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest

References

- Bernell O, Lapidus A, Hellers G. Risk factors for surgery and postoperative recurrence in Crohn's disease. *Annals of surgery*. 2000;231(1):38–45.
- Lewis RT, Maron DJ. Efficacy and complications of surgery for Crohn's disease. *Gastroenterology & hepatology*. 2010;6(9):587–96.
- Michelassi F. Crohn's recurrence after intestinal resection and anastomosis. *Digestive diseases and sciences*. 2014;59(7):1352–3. <https://doi.org/10.1007/s10620-014-3096-4>.
- Olaison G, Smedh K, Sjudahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualised ileal ulcers preceding symptoms. *Gut*. 1992;33(3):331–5.
- Peyrin-Biroulet L, Harmsen WS, Tremaine WJ, Zinsmeister AR, Sandborn WJ, Loftus EV, Jr. Surgery in a population-based cohort of Crohn's disease from Olmsted County, Minnesota (1970–2004). *Am J Gastroenterol*. 2012;107(11):1693–701. <https://doi.org/10.1038/ajg.2012.298>.

6. Cho SM, Cho SW, Regueiro M. Postoperative management of Crohn disease. *Gastroenterol Clin North Am*. 2009;38(4):753–62.
7. Peyrin-Biroulet L, Loftus EV, Jr., Colombel JF, Sandborn WJ. The natural history of adult Crohn's disease in population-based cohorts. *The American journal of gastroenterology*. 2010;105(2):289–97. <https://doi.org/10.1038/ajg.2009.579>.
8. He X, Chen Z, Huang J, Lian L, Rouniyar S, Wu X et al. Stapled side-to-side anastomosis might be better than handsewn end-to-end anastomosis in ileocolic resection for Crohn's disease: a meta-analysis. *Digestive diseases and sciences*. 2014;59(7):1544–51. <https://doi.org/10.1007/s10620-014-3039-0>.
9. McLeod RS, Wolff BG, Ross S, Parkes R, McKenzie M. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. *Dis Colon Rectum*. 2009;52(5):919–27.
10. Kono T, Ashida T, Ebisawa Y, Chisato N, Okamoto K, Katsuno H et al. A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease. *Dis Colon Rectum*. 2011;54(5):586–92. <https://doi.org/10.1007/DCR.0b013e318208b90f>.
11. Kono T, Fichera A, Maeda K, Sakai Y, Ohge H, Krane M et al. Kono-S Anastomosis for Surgical Prophylaxis of Anastomotic Recurrence in Crohn's Disease: an International Multicenter Study. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2016;20(4):783–90. <https://doi.org/10.1007/s11605-015-3061-3>.
12. Fichera A, Zoccali M, Kono T. Antimesenteric functional end-to-end handsewn (Kono-S) anastomosis. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2012;16(7):1412–6. <https://doi.org/10.1007/s11605-012-1905-7>.
13. Katsuno H, Maeda K, Hanai T, Masumori K, Koide Y, Kono T. Novel antimesenteric functional end-to-end handsewn (Kono-S) anastomoses for Crohn's disease: a report of surgical procedure and short-term outcomes. *Digestive surgery*. 2015;32(1):39–44. <https://doi.org/10.1159/000371857>.
14. Luglio G, Rispo A, Castiglione F, Imperatore N, Giglio MC, De Palma GD et al. Kono-type anastomosis in a patient with severe multi-recurrent Crohn's disease. *Int J Colorectal Dis*. 2016;31(8):1565–6. <https://doi.org/10.1007/s00384-016-2567-9>.
15. Fornaro R, Caratto E, Caratto M, Fornaro F, Caristo G, Frascio M et al. Post-operative recurrence in Crohn's disease. Critical analysis of potential risk factors. An update. *The surgeon : journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*. 2015;13(6):330–47. <https://doi.org/10.1016/j.surge.2015.04.002>.
16. De Cruz P, Kamm MA, Prideaux L, Allen PB, Desmond PV. Postoperative recurrent luminal Crohn's disease: a systematic review. *Inflammatory bowel diseases*. 2012;18(4):758–77. <https://doi.org/10.1002/ibd.21825>.
17. de Barcelos IF, Kotze PG, Spinelli A, Suzuki Y, Teixeira FV, de Albuquerque IC et al. Factors affecting the incidence of early endoscopic recurrence after ileocolonic resection for Crohn's disease: a multicentre observational study. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2017;19(1):O39–O45. <https://doi.org/10.1111/codi.13581>.
18. Iesalnieks I, Kilger A, Glass H, Muller-Wille R, Klebl F, Ott C et al. Intraabdominal septic complications following bowel resection for Crohn's disease: detrimental influence on long-term outcome. *International journal of colorectal disease*. 2008;23(12):1167–74. <https://doi.org/10.1007/s00384-008-0534-9>.
19. Resegotti A, Astegiano M, Farina EC, Ciccone G, Avagnina G, Giustetto A et al. Side-to-side stapled anastomosis strongly reduces anastomotic leak rates in Crohn's disease surgery. *Dis Colon Rectum*. 2005;48(3):464–8. <https://doi.org/10.1007/s10350-004-0786-6>.
20. Widmar M, Cummings DR, Steinhagen E, Samson A, Barth AR, Greenstein AJ et al. Oversewing staple lines to prevent anastomotic complications in primary ileocolic resections for Crohn's disease. *J Gastrointest Surg*. 2015;19(5):911–6. <https://doi.org/10.1007/s11605-015-2792-5>.
21. Kusunoki M, Ikeuchi H, Yanagi H, Shoji Y, Yamamura T. A comparison of stapled and hand-sewn anastomoses in Crohn's disease. *Digestive surgery*. 1998;15(6):679–82.
22. Smedh K, Andersson M, Johansson H, Hagberg T. Preoperative management is more important than choice of sutured or stapled anastomosis in Crohn's disease. *The European journal of surgery = Acta chirurgica*. 2002;168(3):154–7. <https://doi.org/10.1080/110241502320127766>.
23. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum*. 2000;43(8):1141–5.
24. D'Haens GR, Geboes K, Peeters M, Baert F, Penninckx F, Rutgeerts P. Early lesions of recurrent Crohn's disease caused by infusion of intestinal contents in excluded ileum. *Gastroenterology*. 1998;114(2):262–7.
25. de Buck van Overstraeten A, Vermeire S, Vanbeckevoort D, Rimola J, Ferrante M, Van Assche G et al. Modified Side-To-Side Isoperistaltic Strictureplasty over the Ileocaecal Valve: An Alternative to Ileocaecal Resection in Extensive Terminal Ileal Crohn's Disease. *Journal of Crohn's & colitis*. 2016;10(4):437–42. <https://doi.org/10.1093/ecco-jcc/jjv230>.
26. Blonski W, Buchner AM, Lichtenstein GR. Clinical predictors of aggressive/disabling disease: ulcerative colitis and Crohn disease. *Gastroenterol Clin North Am*. 2012;41(2):443–62. <https://doi.org/10.1016/j.gtc.2012.01.008>.
27. Gklavas A, Dellaportas D, Papaconstantinou I. Risk factors for postoperative recurrence of Crohn's disease with emphasis on surgical predictors. *Annals of gastroenterology*. 2017;30(6):598–612. <https://doi.org/10.20524/aog.2017.0195>.
28. De Cruz P, Kamm MA, Hamilton AL, Ritchie KJ, Krejany EO, Gorelik A et al. Crohn's disease management after intestinal resection: a randomised trial. *Lancet (London, England)*. 2015;385(9976):1406–17. [https://doi.org/10.1016/s0140-6736\(14\)61908-5](https://doi.org/10.1016/s0140-6736(14)61908-5).
29. Reese GE, Nanidis T, Borysiewicz C, Yamamoto T, Orchard T, Tekkis PP. The effect of smoking after surgery for Crohn's disease: a meta-analysis of observational studies. *Int J Colorectal Dis*. 2008;23(12):1213–21. <https://doi.org/10.1007/s00384-008-0542-9>.
30. Manser CN, Frei P, Grandinetti T, Biedermann L, Mwinyi J, Vavricka SR et al. Risk factors for repetitive ileocolic resection in patients with Crohn's disease: results of an observational cohort study. *Inflammatory bowel diseases*. 2014;20(9):1548–54. <https://doi.org/10.1097/MIB.0000000000000123>.