Analysis of anastomotic leakage after rectal surgery: A case-control study

Junichiro Tanaka*, Takeshi Nishikawa, Toshiaki Tanaka, Tomomichi Kiyomatsu, Keisuke Hata, Kazushige Kawai, Shinsuke Kazama, Hiroaki Nozawa, Hironori Yamaguchi, Soichiro Ishihara, Eiji Sunami, Joji Kitayama, Toshiaki Watanabe

Department of Surgical Oncology, The University of Tokyo, Tokyo, Japan

HIGHLIGHTS

- Frequency of anastomotic leakage was rather low in our institute.
- Male sex was the only risk factor for anastomotic leakage in rectal surgery.
- Tumor histological type was added in this revision.
- Attentive surgical procedure seems to have lead to less frequent anastomotic leakage.

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ABSTRACT

Background: The incidence of anastomotic leakage in rectal surgery is around 10 percent. Poor blood supply to the anastomosis, high anastomotic pressure and tension, increased operative blood loss, long operative time, and male sex are risk factors of anastomotic leakage. In the present study, we examined anastomotic leakage cases in rectal surgery at our institute and tried to ascertain the risk factors.

Methods: Three hundred fifty-seven consecutive patients who underwent rectal resection with anastomosis between January 2008 and October 2013 were included in the study. Patients were divided into two groups according to the existence of anastomotic leakage. Clinicopathological features, operative procedures, and intraoperative outcomes were compared between the two groups. Regarding intraoperative procedure, we focused on the ligation level of the inferior mesenteric artery, installing a transanal drainage tube in the rectum, and constructing a diverting stoma.

Results: Anastomotic leakage occurred in eight patients. All of them were male (p = 0.0284). There were no statistical differences in other characteristics of the patients or tumors, in operative procedures, or in intraoperative outcomes.

Conclusions: In the present study, no statistically significant risk factors for anastomotic leakage in rectal surgery were detected, except for male sex. However, the rate of anastomotic leakage at our institute was revealed to be rather low. Our exertion to preserve good blood flow and to prevent high tension and pressure on the anastomosis in operation may have led to this result.

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1. Introduction

The incidence of anastomotic leakage (AL) in rectal surgery is reported to be around 10 percent [1,2]. Male sex, poor blood supply to the anastomosis, high anastomotic tension, high pressure of the bowel, increased operative blood loss, long operative time, and preoperative radiation therapy are the risk factors for anastomotic leakage [3–9]. Regarding short-term operative outcomes, AL is significantly associated with 30-day mortality rate. As for long-
term outcomes, AL is related to worse disease-free or overall survival [2,10–12]. Therefore, reduction of AL is crucial for good operative outcomes. For that purpose, each institution aims to maintain good anastomotic blood flow and reduce anastomotic tension and pressure. Practically, at our institution, we usually ligate the inferior mesenteric artery (IMA) under the level of the bifurcation of the left colic artery (LCA) to maintain good blood flow, put a transanal drainage tube in the rectum to reduce intra-rectal pressure, and mobilize splenic flexure to reduce anastomotic tension, if necessary. Here, we retrospectively reviewed our rectal surgery cases, investigated frequency of AL, surgical procedures, and perioperative outcomes, and explored measures to reduce AL in rectal surgery.

2. Patients and methods

The study was conducted with the approval of the Ethics Committee of our hospital.

All patients who underwent high anterior resection, low anterior resection, and intersphincteric resection (ISR) between January 2008 and October 2013 were included in the study. Patients without anastomosis, such as Hartmann’s operation or Miles’ operation, were excluded. Finally, three hundred fifty-seven patients were the objects of this study. The operations were performed by thirty-eight surgeons; sixteen of them were residents who were six to eight years of experience as a surgeon, and others are surgeons with more years of experience. Patients who suffered from AL were identified and the patients were divided into two groups: anastomotic leakage group (LG) and no anastomotic leakage group (NLG). Characteristics of patients and tumors, presence or absence of preoperative radiotherapy, operative procedures, intraoperative outcomes, and the experience of surgeons were retrospectively investigated and compared between the two groups. The numbers of patients with factors influencing anastomotic leakage, such as LCA preservation, transanal drainage tube, and diverting stoma, were compared between the two groups.

AL was defined as leakage of bowel content from the anastomotic site. AL was diagnosed when there was fecal discharge from the anastomotic site, and when fluid collection or fistula at the anastomotic site was detected radiologically in patients with symptoms, such as peritonitis.

All collected data were entered into the database and analyzed with JMP® Pro 10.0.2 (2012 SAS Institute Inc.). Univariate analysis was performed using the chi-square test or Fisher’s exact test for categorical values, and the Student’s t-test for numerical values. A value of p < 0.05 was considered statistically significant.

3. Results

AL occurred in eight patients. All of them were male patients (p = 0.0284). There were no statistical differences in other characteristics of the patients (Table 1). Original illness for surgery was rectal or advanced lower sigmoid colon cancer in all patients, except for one rectal carcinoid case. There was no emergency operation that comes from perforation of the bowel. Cases that showed stenosis due to advanced cancer were treated with transanal ileus tube or colonic stent before surgery in our institute. Perioperative outcomes are shown in the Table 3. LCA was preserved in all patients in the LG. Two of the eight patients showed ileus and two patients without ileus had severe stenosis caused by rectal tumor before surgery. A transanal drainage tube was placed in 150 patients. Though the percentage of patients with a transanal drainage tube in the LG was higher than that in the NLG, there was no statistical significance. Diverting ileostomy or colostomy was performed during the first operation in two patients in the LG. In the other six patients with AL, four recovered from leakage without undergoing additional surgery for intraperitoneal drainage or constructing a diverting stoma.

There was no statistical difference in the rate of laparoscopic surgery between the two groups. There were no statistical differences in tumor histology, tumor diameter, tumor stage, amount of intraoperative blood loss, or operative time (Tables 2 and 3). All of the cases with anastomotic leakage did not underwent preoperative radiotherapy. The rate of residents as the operator of the surgery in the two groups did not also show statistical difference (Table 3).

4. Discussion

The incidence of AL is reported to be around 10 percent [1,2]. AL is associated with subsequent local recurrence and distant metastasis as well as operative mortality [1,2,11–13]. Therefore, various contrivances are employed to prevent AL at each institution. At our institution, LCA is preserved in all patients except for those who have lymph node (LN) metastasis at the root of IMA. In the present study, no significant association was detected between the rate of AL and the ligation level of IMA. According to the previous study, correlation between the ligation level of IMA and AL is still controversial. Trencheva et al. reported that ligating IMA below LCA significantly decreased the rate of AL using univariate and multivariate analysis (p = 0.0281 and 0.0165 respectively) [6]. Komen et al. detected increased blood flow in patients with preserved LCA using laser Doppler flowmetry [14]. Cirocchi et al. conducted meta-analysis including 8666 patients and showed no statistically significant difference in AL rate between the high tie and low tie groups [15].

Regarding the transanal drainage tube, the present study showed no significant difference in AL rate between the patients with and without one. However, Zhao et al. conducted a non-randomized prospective study and showed that AL was less frequent in patients with one (7.8% in the group with one and 2.5% in the other group), though no statistically significant difference was detected (p = 0.160) [16]. Nishigori et al. retrospectively reviewed rectal cancer surgery cases and showed a similar result with statistical significance (p = 0.04) [17].

A diverting stoma is constructed to protect the distal colorectal anastomosis. In the present study, no significant difference was identified in AL rate between patients who had one constructed and those who had not. However, some studies have shown the effectiveness of stoma in reducing AL. In a retrospective study by Peeters et al., diverting stoma was significantly associated with lower anastomotic failure rate (p = 0.003) [17]. Thoker et al. conducted a randomized controlled trial including 78 rectal cancer patients and showed less frequent anastomotic leakage in cases with diverting stoma without statistical significance [18]. Multivariate analysis in a case-control study conducted by Jestin et al. showed that a diverting stoma significantly reduces AL [3].
We also investigated the association between laparoscopic surgery and AL. Though there was no statistical significance, leakage rate was rather low in laparoscopic surgery. We referred to a study regarding perioperative outcome and accomplishment of LN dissection in laparoscopic surgery. Sekimoto et al. reported that equivalent LN dissection to a high-tie technique could be achieved in a low-tie operation without excessive operative time or bleeding [19]. It is expected that a safe and adequate operation can be achieved in laparoscopic as well as open surgery.

Examining the eight cases with anastomotic leakage, only two patients had a diverting stoma constructed during the first surgery. Two of the other six patients underwent secondary operation for diverting stoma and peritoneal drainage. The remaining four patients showed minor leakage that could be cured with fasting and antibiotics without additional surgery. This low frequency of major leakage might be due to good blood flow of the anastomosis induced by LCA preservation.

In the present study, a statistical difference in the rate of AL was found only in sex between the two groups. None of the other factors such as tumor histology, diameter, stage, amount of intraoperative blood loss, or operative time showed statistical difference in the rate of AL. This may be due to the very low occurrence of AL. Though risk factors could not be elucidated in the present study, the rate of AL at our institute was rather low. Our low occurrence rate of AL should be seriously considered. There was nothing unique about our surgical procedure. However, we have made diverting stomas in those cases whose anastomoses are close to anus, which may have masked the minor leakage. Positively interpreting our result, our exertion to preserve good blood flow and to prevent high tension and pressure on the anastomosis in operation may have led to this result. Further investigation with more cases is needed to determine a way to reduce AL after rectal surgery.

**Conflicts of interest**

No disclosure to report.

**Sources of funding**

No disclosure to report.

**Ethical approval**

The study was conducted with the approval of the Ethics Committee of our hospital.

**Research registration unique identifying number (UIN)**

Researchregistry169.

**ISRCTN**

Not applicable.

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**Table 2**

Characteristics of tumors.

|                  | LG       | NLG      | Total    | P         |
|------------------|----------|----------|----------|-----------|
| Tumor diameter   | 47.7 ± 15.0 | 38.6 ± 19.1 | 329      | NS (P = 0.2129) |
| Histological type| tub1, tub2, pap | muc, por | muc, por | NS (P = 0.4833) |
|                  | 7        | 11       | 11       |           |
|                  | 0        | 4        | 4        |           |
|                  | 1        | 10       | 11       |           |
|                  | 0        | 1        | 1        |           |
|                  | 0        | 1        | 1        |           |
| LN metastasis    | Yes      | 5        | 145      | 150 NS (P = 0.1410) |
|                  | No       | 2        | 200      | 202       |
| Stage            | 0 – II   | 2        | 179      | 181 NS (P = 0.2570) |
|                  | IIIa – IV| 5        | 152      | 157       |

LG, anastomotic leakage group; NLG, no anastomotic leakage group. tub1, well differentiated tubular adenocarcinoma; tub2, moderately differentiated tubular adenocarcinoma. pap, papillary adenocarcinoma; por, poorly differentiated adenocarcinoma; muc, mucinous adenocarcinoma. LN, lymph node; LCA, left colic artery.

**Table 3**

Operative procedures and intraoperative outcomes.

|                  | LG       | NLG      | Total    | P         |
|------------------|----------|----------|----------|-----------|
| Operative time   | 341.6 ± 94.1 | 332.7 ± 163.5 | NS (P = 0.8783) | 341.6 ± 94.1 |
| Intraoperative blood loss | 652.0 ± 521.2 | 394.9 ± 628.0 | NS (P = 0.2516) | 652.0 ± 521.2 |
| Surgeon          | Resident | 1        | 24       | NS (P = 0.4439) |
|                  | More experienced | 7 | 325     |           |
| LCA preservation | Yes      | 8 (100.0) | 333 (95.4) | 341       |
|                  | No       | 0 (0.0) | 16 (4.6) | 16       |
| Transanal drainage tube | Yes | 4 (50.0) | 146 (41.8) | 150 NS (P = 0.7250) |
|                  | No       | 4 (50.0) | 203 (58.2) | 207       |
| Diverting stoma  | Yes      | 2 (25.0) | 63 (18.1) | 65       |
|                  | No       | 6 (75.0) | 286 (81.9) | 292       |
| Laparoscopic surgery | Yes | 2 (25.0) | 159 (45.6) | 161 NS (P = 0.3026) |
|                  | Open surgery | 6 (75.0) | 190 (54.4) | 196       |

LG, anastomotic leakage group; NLG, no anastomotic leakage group. LN, lymph node; LCA, left colic artery. Values in parentheses are percentages.
Author contribution
Junichiro Tanaka: study design, data collections, data analysis, writing.
Takeshi Nishikawa: data collection.
Toshiaki Tanaka: data collection.
Tomomichi Kiyomatsu: data collection.
Keisuke Hata: data collection, data analysis, writing.
Kazushige Kawai: data collection.
Shinsuke Kazama: data collection.
Hiroaki Nozawa: data collection.
Hironori Yamaguchi: data collection.
Soichiro Ishihara: data collection, writing.
Eiji Sunami: data collection.
Joji Kitayama: data collection.
Toshiaki Watanabe: writing.

Guarantor
Junichiro Tanaka.

References
[1] N. Matsubara, H. Miyata, M. Gotoh, et al., Mortality after common rectal surgery in Japan: a study on low anterior resection from a newly established nationwide large-scale clinical database, Dis. Colon Rectum 57 (2014) 1075–1081.
[2] M. den Dulk, C.A. Marijnen, L. Collette, et al., Multicentre analysis of oncological and survival outcomes following anastomotic leakage after rectal cancer surgery, Br. J. Surg. 96 (2009) 1066–1075.
[3] P. Jestin, L. Pahlman, U. Gunnarsson, Risk factors for anastomotic leakage after rectal cancer surgery: a case-control study, Colorectal Dis. 10 (2008) 715–721.
[4] P. Matthiessen, O. Hallbök, M. Andersson, Risk factors for anastomotic leakage after anterior resection of the rectum, Colorectal Dis. 6 (2004) 462–469.
[5] E.L. Bokey, P.H. Chapuis, C. Fung, et al., Postoperative morbidity and mortality following resection of the colon and rectum for cancer, Dis. Colon Rectum 38 (1995) 480–486 discussion 486–487.
[6] K. Trencheva, K.P. Morrissy, M. Wells, et al., Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients, Ann. Surg. 257 (2013) 108–113.
[7] K.C. Peeters, R.A. Tollenaar, C.A. Marijnen, et al., Risk factors for anastomotic failure after total mesorectal excision of rectal cancer, Br. J. Surg. 92 (2005) 211–216.
[8] M. Nano, H. Dal Corso, M. Ferronato, et al., Ligation of the inferior mesenteric artery in the surgery of rectal cancer: anatomical considerations, Dig. Surg. 21 (2004) 123–126 discussion 126–127.
[9] H.P. Bruch, O. Schwandner, T.H. Schiedek, U.J. Roblick, Actual standards and controversies on operative technique and lymph-node dissection in colorectal cancer, Langenbecks Arch. Surg. 384 (1999) 167–175.
[10] W.L. Law, H.K. Choi, Y.M. Lee, et al., Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy, J. Gastrointest. Surg. 11 (2007) 8–15.
[11] C.S. McArdle, D.C. McMillan, D.J. Hole, Impact of anastomotic leakage on long-term survival of patients undergoing curative resection for colorectal cancer, Br. J. Surg. 92 (2005) 1150–1154.
[12] K.G. Walker, S.W. Bell, M.J. Rickard, et al., Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer, Ann. Surg. 240 (2004) 255–259.
[13] R.M. Abeeg, W. Brekelman, LP. van Bebber, et al., Results of construction of protective loop ileostomies and reversal surgery for colorectal surgery, Eur. Surg. Res. 52 (2014) 63–72.
[14] N. Komen, J. Sleker, P. de Kort, et al., High tie versus low tie in rectal surgery: comparison of anastomotic perfusion, Int. J. Colorectal Dis. 26 (2011) 1075–1078.
[15] R. Ciocchi, S. Trastulli, E. Farinella, et al., High tie versus low tie of the inferior mesenteric artery in colorectal cancer: a RCT is needed, Surg. Oncol. 21 (2012) e111–123.
[16] W.T. Zhao, F.L. Hu, Y.Y. Li, et al., Use of a transanal drainage tube for prevention of anastomotic leakage and bleeding after anterior resection for rectal cancer, World J. Surg. 37 (2013) 227–232.
[17] H. Nishigori, M. Ito, Y. Nishizawa, et al., Effectiveness of a transanal tube for the prevention of anastomotic leakage after rectal cancer surgery, World J. Surg. 38 (2014) 1843–1851.
[18] M. Thoker, I. Wani, F.Q. Parry, et al., Role of diversion ileostomy in low rectal cancer: a randomised controlled trial, Int. J. Surg. 12 (9) (2014) 945–951.
[19] M. Sekimoto, I. Takemasa, T. Mizushima, et al., Laparoscopic lymph node dissection around the inferior mesenteric artery with preservation of the left colic artery, Surg. Endosc. 25 (2011) 861–866.