Impact of Early Postoperative Diarrhea on Anastomotic Leakage after Laparoscopic Low Anterior Resection for Rectal Cancer

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Abstract

Introduction: Despite the remarkable improvements in surgical techniques and technological advancements in the medical instruments used, anastomotic leakage (AL) still remains a serious complication after laparoscopic low anterior resection (Lap-LAR) of the rectum. The definitive mechanism underlying the occurrence of AL remains unclear, and the relationship between postoperative diarrhea and AL is still unknown.

Methods: This study was a retrospective study performed at a single institution in 65 consecutive patients with rectal cancer who underwent Lap-LAR by the double-stapling technique (DST) for anastomosis between January 2011 and April 2015. Various candidate factors associated with symptomatic AL were examined by univariate analyses. Furthermore, an additional analysis was also conducted to investigate the relation between diarrhea developing in the early phase after operation and the occurrence of AL.

Results: The rate of occurrence of symptomatic AL was 7.7% (5/65 cases). Univariate analysis only identified undoing of a diverting ileostomy creation as tending to be associated with the risk of development of AL (p = 0.07). Further analysis revealed a strong association between early postoperative diarrhea and the risk of AL in patients without a diverting stoma (p < 0.01).

Conclusions: Postoperative diarrhea occurring in the early phase after Lap-LAR may be a notable risk factor for symptomatic AL, especially in patients without a diverting stoma.

Key words: anastomotic leakage, diarrhea, laparoscopic low anterior resection, rectal cancer

Introduction

In spite of the technical difficulties involved with the delicate procedure within a narrow pelvic cavity, laparoscopic surgery for rectal cancer has recently been demonstrated to be feasible and also begun to be performed often for colon cancer①-③. Low anterior resection (LAR) by the double-stapling technique (DST) has been the most frequently performed anus-preserving operation for rectal cancer for about 30 years④-⑤. Nevertheless, anastomotic leakage (AL) after LAR remains a serious complication which could cause not only peritonitis and prove fatal, but also increase the risk of local recurrence and consequently, a poor prognosis⑥-⑦. Despite the remarkable improvements in the techniques of surgery and technological advancements in the medical instruments used, AL after laparoscopic LAR (Lap-LAR) still occurs in 2.6%-12.3% of cases (median, 8%), according to recent reports②,⑧,⑨. Numerous studies have been conducted to identify the risk factors for AL and various clinical attempts have been made to prevent AL, including diverting ileostomy and transanal insertion of a drainage tube, nationwide⑩-⑬. However, the precise mechanism of development of AL remains unclear and un-
under debate due to its complexity. On the other hand, the relationship between postoperative diarrhea and the risk of AL after LAR has scarcely been reported. Herein, we examined the correlation between postoperative diarrhea and the risk of AL after Lap-LAR.

Materials and Methods

Study population

A total of 65 consecutive rectal cancer patients who had undergone elective Lap-LAR by DST between January 2011 and April 2015 at the Shiga University of Medical Science Hospital were included in this retrospective analysis. The clinicopathological data were collected from the hospital medical records. The location of the tumor was diagnosed by colonoscopy and barium enema preoperatively and confirmed during the operation. Tumors located between the inferior border of the second sacral vertebra and the peritoneal reflection were recorded as being located in the upper rectum, while tumors located below the peritoneal reflection were recorded as being located in the lower rectum. Patients took regular meals until the day before the surgery and underwent mechanical bowel preparation (without chemical bowel preparation) on the day prior to the surgery. In general, patients started to take sips of clear water on the day after the surgery and to eat solid foods around two or three days later, after passage of the first flatus. We do not routinely prescribe drugs for controlling the intestinal function. Perioperative prophylactic antibiotics were administered immediately before the operation and periodically until postoperative day 2.

Surgical procedures

Anastomosis by DST was executed using a circular stapler after tumor-specific mesorectal excision and removal of the tumor, as described previously. The criteria adopted for creation of a diverting ileostomy at our institution, in principle, are as follows: three or more cartridges of the linear stapler needed during rectal transection, distance of less than 5 cm from the anastomosis to the anal verge, and serious preoperative comorbidities. Actually, the clinical decisions about stoma creation and transanal tube placement were left to the discretion of the operating surgeons.

Definition of anastomotic leakage

Symptomatic AL was defined as AL associated with abdominal pain, pyrexia, purulent or fecal discharge from the pelvic drainage tube, and peritonitis within 30 days of surgery. These signs of AL were confirmed by radiographic enema using a liquid contrast medium and abdominal computed tomography. According to the proposed grading system, AL was classified into three grades: Grade A, requiring no active therapeutic intervention, Grade B, requiring active therapeutic intervention, and Grade C, requiring re-operation. For this analysis, we defined Grade B and Grade C AL as “symptomatic” AL.

Candidate risk factors

The following three categories of candidate risk factors for symptomatic AL were examined in this analysis: patient-, tumor-, and surgery-associated factors. Patient-associated factors included age, sex, body mass index (BMI), preoperative serum albumin and hemoglobin values, physical status according to the American Society of Anesthesiologists (ASA) classification, presence/absence of diabetes mellitus, and history of preoperative chemotherapy. Tumor-associated factors included tumor location, UICC-TNM stage (8th edition), maximum tumor diameter, and preoperative CEA value. Surgery-associated factors included the operation time, intraoperative bleeding, level of inferior mesenteric artery (IMA) ligation, lateral lymph node dissection (yes/no), simultaneous resection of other organs (yes/no), number of cartridges of the linear stapler used during rectal transection, distance of the anastomosis from the anal verge, diverting stoma creation (yes/no) and transanal tube placement (yes/no).

Early postoperative diarrhea

Finally, we conducted an additional analysis to determine the relationship between early postoperative watery diarrhea and the risk of AL in patients who did not have a diverting ileostomy. Early postoperative diarrhea was defined as frequent watery bowel movements (more than three times per day) until postoperative day 2. If a transanal tube was placed, early diarrhea was defined as watery defecation of more than 200 g weight or frequent diaper exchange (more than three times per day) until postoperative day 2.

Ethical considerations

This study was performed in accordance with the principles laid down in the Declaration of Helsinki, and with the approval of the Ethics Committee of the Shiga University of Medical Science (approved
Early postoperative diarrhea leads to AL.

Table 1 Clinicopathological characteristics of patients (n = 65)

| Characteristics                  | No. of patients |
|----------------------------------|-----------------|
| Sex                              |                 |
| Male                             | 37              |
| Female                           | 28              |
| Age (years)                      |                 |
| Median (range)                   | 69 (34-82)      |
| BMI (kg/m²)                      |                 |
| Median (range)                   | 22.0 (14.5-31.1) |
| Location                         |                 |
| Upper (RS, Ra)                   | 49              |
| Lower (Rb)                       | 16              |
| TNM Stage                        |                 |
| 0                                | 3               |
| I                                | 24              |
| II                               | 9               |
| III                              | 25              |
| IV                               | 4               |
| T category                       |                 |
| Tis                              | 3               |
| T1                               | 22              |
| T2                               | 7               |
| T3                               | 31              |
| T4                               | 2               |
| N category                       |                 |
| N0                               | 36              |
| N1                               | 19              |
| N2, N3                           | 10              |
| M category                       |                 |
| M0                               | 61              |
| M1                               | 4               |
| Tumor size (mm)                  |                 |
| Median (range)                   | 40 (5-110)      |
| Preoperative chemotherapy        | 2               |
| Anastomotic leakage              | 5               |

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Statistical analysis

All statistical calculations were performed using the statistical software program R (http://cran.r-project.org). Fisher’s exact test was used for comparison of categorical variables. A p-value of less than 0.05 was considered as being indicative of statistical significance.

Results

The 65 patients who underwent Lap-LAR are listed in Table 1. The subject population consisted of 37 (56.9%) male and 28 (43.1%) female patients. The median age was 69 years (range 34-82). The median BMI was 22.0 (range, 14.5-31.1). Of the 65, 49 patients (75.4%) had upper rectal cancer, while the remaining 16 (24.6%) had lower rectal cancer. There were no cases of conversion to open surgery during the study period.

The overall incidence of clinical AL was 7.7% (5/65 cases), and none of the patients received a diverting stoma. Among the 5 patients, 2 had Grade B AL, while the remaining 3 patients had Grade C AL, needing emergency re-laparotomy. There were no cases of asymptomatic AL (Grade A). There was also no case of postoperative mortality. The results of univariate analyses performed using patient- and tumor-associated factors are summarized in Table 2 and Table 3, respectively. None of the factors showed any statistically significant relationship with the risk of development of AL. Among the surgery-associated factors, on the other hand, creation of a diverting ileostomy was identified as tending to have a statistically significant preventive effect against the development of symptomatic AL (p = 0.07) (Table 4).

None of the five patients who developed AL had received a diverting ileostomy and all had early postoperative diarrhea before the onset of the AL (Table 5). Therefore, further subgroup analysis focusing on postoperative diarrhea was performed in the 38 patients who did not have a diverting ileostomy. The results showed that early diarrhea occurred in 11 out of the 38 patients (28.9%), and that the rate of development of AL in the early postoperative diarrhea group (45.5%, 5/11 cases) was significantly higher than that in the non-early diarrhea group (0%, 0/27 cases) (p < 0.01) (Table 6).
Discussion
AL still remains a devastating complication after LAR for rectal cancer, despite the remarkable advancements in the surgical techniques and medical devices used. Various risk factors for the development of AL have been reported previously: male
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gender, obesity, tumor location in the lower rectum, large size of the tumor, intraoperative bleeding, ≥3 stapler firings during resection, and a shorter distance from the anastomosis to the anal verge. Laparoscopic surgery appears to be a comparable alternative to open surgery for rectal cancer, with no additional perioperative complications.

Meanwhile, the usefulness of protective diverting ileostomy to avoid AL is controversial. Several causes of postoperative diarrhea have been reported, including preoperative mechanical bowel preparation, obstructive colitis caused by a large tumor, and prophylactic antibiotic-induced Clostridium difficile infection. Diarrhea is generally defined as frequent (≥3 times) watery stools per day, according to Bristol stool chart’s type 6 and 7; respectively mushy consistency with ragged edges and liquid consistency with no solid pieces. However, clinical judgment of postoperative diarrhea is often oblique and inaccurate, and in addition, it is usually not a clinically serious symptom, and therefore, tends to be disregarded. Recently, a retrospective study reported that postoperative diarrhea may be associated with superficial surgical site infection (SSI).

Furthermore, another retrospective study revealed that a total fecal volume of >118 mL for 3 consecutive days after surgery may be a reliable predictor of the development of AL. A transanal drainage tube is often used for the purpose of decreasing the intraluminal pressure at the site of anastomosis and preventing the occurrence of AL. In our study, a transanal tube was inserted in four of the five symptomatic AL patients, however, it did not work effectively as expected, probably due to obstruction by feces or excessive anal pressure.

This retrospective study had several limitations, including the small number of patients from a single institution, a low incidence of symptomatic AL, absence of use of definitive criteria for diverting stoma creation and the multifactorial causation of AL. Further clinical studies, including a large multicenter randomized controlled study, are required to clarify the impact of postoperative early diarrhea on the risk of development of AL in patients with rectal cancer treated by Lap-LAR.

In conclusion, our findings suggest that early postoperative diarrhea might be a predictor of the development of symptomatic AL in patients undergoing Lap-LAR for rectal cancer.

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Conflict of interest: None.

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