DOI: 10.4274/tjcd.galenos.2021.2020-10-6
Turk J Colorectal Dis

RESEARCH ARTICLE

The Effects of Neoadjuvant and Adjuvant Treatments on Anastomotic Leakage in Rectal Cancer

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ABSTRACT

Aim: Anastomosis leakage (AL) is a major complication seen after colorectal surgery. In the present study, we aimed to investigate the effects of adjuvant (AT) and neoadjuvant treatments (NT) on AL in surgical patients with rectal cancer.

Materials and Methods: The study included 319 patients over 18 years of age who were diagnosed with rectal cancer and received AT or NT treatment with surgical operation between January 1, 2010 and December 31, 2018. Demographic data, tumor staging, metastasis status, organ and lymph node involvement, type of surgery, the presence of AT and NT, the presence of AL, mortality status, and serum carcinoembryonic antigen levels were evaluated.

Results: One hundred seventy-nine (56.1%) of the patients were male, one hundred forty (43.9%) were female, and the mean age was 58.6 ± 13.2 years. Of the patients included in the study, 48.6% (n=155) received AT and 51.4% (n=164) received NT. It was found that 13.1% (n=42) of the patients received only radiotherapy (RT), 10.6% (n=34) received only chemotherapy (CT), and 76.2% (n=243) received both RT and CT (CRT). AL was detected in 23.5% (n=75) of the patients. There was no difference in terms of AL frequency between the patients receiving AT or NT (p=0.758). In addition, it was determined that RT and CT had no effect on the development of AL (p=0.827 and p=0.1, respectively). Mortality was not higher in patients with AL.

Conclusion: There is no difference in terms of AL development between patients receiving NT or AT and using RT or CT alone or together. These treatments should not be abandoned in the treatment of rectal cancer due to better local control, overall survival and sphincter function preservation rates.

Keywords: rectum cancer; radiotherapy; chemotherapy; anastomotic leakage

Introduction

Colorectal cancer is one of the most common and life-threatening malignant tumors worldwide. The treatment of stage II and stage III colorectal cancer now involves a multidisciplinary structure that includes combined therapy rather than surgery alone. Combined chemotherapy (CT) is recommended as the main adjuvant therapy for stage III colon cancer [1]. In rectal cancer, like colon cancer, combined treatment is recommended, and the difference lies in the application of radiotherapy (RT). Historically, the combination of adjuvant RT and CT has been shown to reduce local recurrence and improve survival in locally advanced rectal cancer (LARC) [2]. Later, recurrence rates decreased with the introduction of total mesorectal excision (TME) as a surgical method [3, 4]. Neoadjuvant chemoradiotherapy (CRT) is preferred as a treatment method in all stage II and III rectal cancers, after it was shown that neoadjuvant CRT provides better outcomes compared with adjuvant CRT, is better tolerated, and enables downstaging in many cases, thus preventing permanent ostomy [5].

Anastomotic leakage (AL) is defined as a defect of the intestinal wall in the anastomosis region (including the sutures and staple lines of the neorectal reservoirs), leading to transition between the intra- and extra-luminal compartments [6]. AL is an important and potentially life-threatening postoperative complication after colorectal surgery. About one-third of deaths after colorectal surgery are due to anastomotic complications [7]. If managed well, mortality in AL can be prevented [8], but patients with AL who are treated and survive have increased perioperative morbidity and lower survival in the long term [9-11].

Numerous studies have focused on the predisposing factors for AL. However, the leak is thought to be caused by a large spectrum composed of both preventable and unavoidable factors [12]. Despite the perioperative management (Enhanced Recovery After Surgery; ERAS) and the improvement and

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Received/Geliş Tarihi: 05.01.2021 **Accepted/Kabul Tarihi:** 14.04.2021

optimization of surgical techniques (minimally invasive surgery), AL rates have remained high (8–20%) over time [12-15]. There are many local and general factors causing AL [16]. One of the local factors affecting the development of AL is that patients receive CT and / or RT. Some studies showed that neoadjuvant RT or CRT did not increase the development of AL [17, 18], whereas other studies showed that neoadjuvant RT or CRT increased the development of AL [19-22]. In a study with a five-year follow-up period in which adjuvant and neoadjuvant CRT were compared, AL was detected in 11% of the neoadjuvant CRT arm and 12% of the adjuvant CRT arm, and no difference was found between the two groups [5]. In the present study, it was aimed to investigate the effects of neoadjuvant therapy (NT) and adjuvant therapy (AT) on AL in patients who underwent surgery with a diagnosis of rectal cancer.

Materials and Methods

Patient selection

Our study was conducted on retrospective file scans of patients who underwent surgery with a diagnosis of rectal cancer between January 1st, 2010, and December 31st, 2018, in XXX University General Surgery Department. Patients who were older than 18 years, diagnosed as having rectal cancer, underwent surgery in our clinic, and were given AT or NT by the radiation oncology and medical oncology clinics were included. Patient data were obtained from the central archive and archives of the oncology clinics. Two groups were formed according to patients' AT or NT status. Demographic data, tumor staging, metastasis status, organ and lymph node involvement, type of surgery, AT and NT, presence of AL, mortality, and serum carcinoembryonic antigen (CEA) levels were recorded from the patient files. The patients had a minimum of two and a maximum of eight years of follow-up.

Chemotherapy and radiotherapy protocols

Surgery was performed according to TME principles. Generally, RT and CT were applied together as AT or NT, but in some patients, RT or CT was administered alone. According to the protocol [23], a total of 50.4 Gy (single dose of 1.8 Gy) RT was applied to the tumor and pelvic lymph nodes for five weeks. As CT, 5-fluorouracil (5-FU) was administered in the first and fifth weeks of RT as a 120-hour continuous infusion at a dose of 1000 mg/m^2/day. Apart from these, four cycles of 5-FU were administered in 4 weeks, in 5 consecutive days, as bolus injection at a dose of 500 mg/m^2/day. Unlike in NT, an additional 5.4 Gy of RT was administered to the tumor bed for three days in AT. Surgical treatment was performed 4-6 weeks after the concurrent use of neoadjuvant CT and RT was completed, and the remaining four cycles of 5-FU were started 3-4 weeks after surgery. Alternatively, surgical treatment was performed first and AT started 1-2 weeks after surgery.

Approach to anastomotic leaks

The AL grading recommended by Rahbari et al. [6] was used. Accordingly, grade A does not require a therapeutic intervention, grade B requires active intervention without laparotomy, and grade C requires laparotomy. As stated in the literature, when a leak was suspected, CT was performed for diagnosis, followed by contrast enema and endoscopy, and a reoperation was performed [24]. After the reoperation, the anastomosis was usually removed, and a permanent stoma was created. If possible, anastomosis was rescued in grade A and B leaks, with or without drainage and/or antibiotic treatments [25, 26].

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) package program version 22 was used for data analysis. The normality of the distribution of the data was investigated using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Mean ± standard deviation or median (minimum–maximum) was used for continuous variables, and frequency and percentage (%) were used for categorical variables. The Mann–Whitney U test was used to compare categorical variables that were not normally distributed, as well as in the comparison of continuous variables obtained in laboratory measurements. Pearson's Chi-square test was used for comparisons between categorical variables. The McNemar test was used for comparisons between dependent categorical variables. The level of statistical significance was accepted as $p \leq 0.05$.

Results

The average age of the patients was 58.6 ± 13.2 (range, 27–85) years. One hundred seventy-nine (56.1%) of the patients were male. The mean body weight of the patients was 74.52 ± 13.7 kg.

It was found that 48.6% (n=155) of the patients received AT and 51.4% (n=164) received NT; 13.2% (n=42) received only RT, 10.7% (n=34) received CT, and 76.2% (n=243) received both RT and CT. Of the patients who were treated with NT (n=164), 18 (11.0%) received only RT, 21 (12.8%) received only CT, and 125 (76.2%) received both RT and CT. Of the patients who were treated with AT (n=155), 25 (16.1%) received only RT, 12 (7.7%) received only CT and 118 (76.1%) received both RT and CT (Table 1).

It was found that 16.3% (n=52) of the patients underwent anterior resection, 73.0% (n=233) had low anterior resection and 10.7% (n=34) received a very low anterior resection.

Perineural invasion was investigated in 83.1% (n=265) of the patients, and was detected in 16.6% (n=44). Lymphatic

Table 1: The applied treatment options as adjuvant and neoadjuvant therapy.

	AT (n=155)	NT (n=164)
Only Chemotherapy	7.7% (n=12)	12.8% (n=21)
Only Radiotherapy	16.1% (n=25)	10.9% (n=18)
Chemotherapy + Radiotherapy	76.1% (n=118)	76.2% (n=125)

AT, Adjuvant therapy; **NT,** Neoadjuvant therapy

invasion was investigated in 84.9% (n=271), and was found in 16.6% (n=44). AL was detected in 23.5% (n=75) of the patients. Ninety (28.2%) patients died.

The average age of the deceased patients was 58.68 ± 0.87 years, and the average age of the living patients was 58.4 ± 1.39 years; there was not a significant difference between the ages of survivors and those who died (p=0.871). While the mean body weight of the patients was 74.38 ± 0.89 kg, no statistically significant difference was found in terms of body weight between the survivors and those who died (p=0.822). Fifty (55.6%) of the male patients and 40 (44.4%) of the female patients died; there was not a significant difference between the sexes of the survivors and those who died (p=0.900).

Among the survivors and deceased patients, there were no differences in terms of TNM staging, type of surgery, preoperative and postoperative CEA levels, anastomosis leaks, RT and / or CT, perineural invasion, and lymphatic invasion (Table 2).

Among patients receiving AT or NT, there were no differences in terms TNM staging, type of surgery, preoperative and postoperative CEA levels, anastomosis leak, mortality, perineural invasion, and lymphatic invasion (Table 3).

When the average age and body weight of the patients were compared according to the presence of AL, there was not a significant difference between those with and without AL in terms of age (p=0.227), but the average body weight of patients with AL was lower than that of patients without AL (p=0.042). When the sex distribution of the patients was compared according to the presence of AL, there was not a significant difference in terms of sex between those with and without AL.

Table 4 shows the factors those predictors to AL development. In univariate analysis, the relationship between gender, age, weight, type of surgery, laparoscopic surgery, tumor size, lymph node involvement, NT or AT, perineural involvement, lymphatic invasion, RT or CT, and AL were examined. There was a relationship (p=0.021) between N2 lymph node involvement and AL. Also, it was observed that RT, CT, or CRT did not have statistically significant effects on the development of AL.

Table 2: The comparison between patients who survived and patients who died in terms of TNM staging, type of surgery, preoperative and postoperative CEA levels, anastomosis leak, radiotherapy and/or chemotherapy, perineural invasion, and lymphatic invasion.

Variables	Survival (n=229)	Mortality (n=90)	p
AL No (n=244) Yes (n=75)	76.0% (n=174) 24.0% (n=55)	77.8% (n=70) 22.2% (n=20)	0.734
CEA *Preoperative >10 (n=238)* *Preoperative <10 (n=81)*	73.8% (n=169) 26.2% (n=60)	76.7% (n=69) 23.3% (n=21)	0.045
Postoperative >10 (n=133) *Postoperative<10 (n=186)*	41.9% (n=96) 58.1% (n=133)	41.1% (n=37) 58.9% (n=53)	0.946
T1 (n=22) **T2 (n=16)** **T3 (n=112)** **T4 (n=169)**	7.4% (n=17) 5.7% (n=13) 33.2% (n=76) 53.7% (n=123)	5.6% (n=5) 3.3% (n=3) 40.0% (n=36) 51.1% (n=46)	0.578
N0 (n=120) **N1 (n=93)** **N2 (n=60)** **Nx (n=46)**	37.6% (n=86) 29.3% (n=67) 19.7% (n=45) 13.5% (n=31)	37.8% (n=34) 28.9% (n=26) 16.7% (n=15) 16.7% (n=15)	0.862
M0 (n=289) **M1 (n=30)**	90.8% (n=208) 9.2% (n=21)	90% (n=81) 10% (n=9)	0.819
Anterior resection (n=52) *Low Anterior resection (n=233)* *Very Low Anterior Resection (n=34)*	15.7% (n=36) 73.8% (n=169) 10.5% (n=24)	17.8% (n=16) 71.1% (n=64) 11.1% (n=10)	0.880
Perineural invasion (n=44)	14.4% (n=33)	12.2% (n=11)	0.679
Lymphatic invasion (n=72)	23.6% (n=54)	20.0% (n=18)	0.655
Radiotherapy Yes (n=285) No (n=34)	89.1% (n=204) 10.9% (n=25)	90% (n=81) 10% (n=9)	0.811
Chemotherapy Yes (n=86) No (n=14)	85.6% (n=196) 14.4% (n=33)	90% (n=81) 10% (n=9)	0.294

CEA, Carcinoembryonic antigen; **AL,** Anastomosis leakage

There were no significant differences between the postoperative and preoperative serum CEA levels in patients receiving AT and NT in patients who survived and died, nor in patients with and without AL (p>0.001) (Table 5).

Table 3: The comparison between patients who were treated with adjuvant therapy and patients who were treated with neoadjuvant therapy in terms of TNM staging, type of surgery, preoperative and postoperative CEA levels, anastomosis leak, mortality, perineural invasion, and lymphatic invasion.

Variables	AT (n=155)	NT (n=164)	p
AL (n=70)	42.8% (n=30)	57.2% (n=40)	0.758
CEA			
Preoperative >10 (n=238)	76.8% (n=119)	72.5% (n=119)	0.999
Preoperative <10 (n=81)	23.2% (n=36)	27.4% (n=45)	
Postoperative >10 (n=133)	36.8% (n=57)	46.3% (n=76)	
Postoperative <10 (n=186)	63.2% (n=98)	53.6% (n=88)	0.206
T1 (n=22)	54.5% (n=12)	45.5% (n=10)	
T2 (n=16)	56.3% (n=9)	43.8% (n=7)	0.758
T3 (n=112)	50% (n=56)	50% (n=56)	
T4 (n=169)	46.2% (n=78)	53.8% (n=91)	
N0 (n=120)	48.3% (n=58)	51.7% (n=62)	
N1 (n=93)	45.2% (n=42)	54.8% (n=51)	0.208
N2 (n=60)	60.0% (n=36)	40.0% (n=24)	
Nx (n=46)	41.3% (n=19)	58.7% (n=27)	
M0 (n=289)	47.8% (n=138)	52.2% (n=151)	0.352
M1 (n=30)	56.7% (n=17)	43.3% (n=13)	
Anterior resection (n=52)	51.9% (n=27)	48.1% (n=25)	
Low anterior resection(n=233)	48.1% (n=112)	51.9% (n=121)	0.866
Very low anterior resection (n=34)	47.1% (n=16)	52.9% (n=18)	
Perineural invasion (n=44)	18% (n=28)	9.7% (n=16)	0.758
Lymphatic invasion (n=72)	51.4% (n=37)	48.6% (n=35)	0.700
Survival (n=229)	48.9% (n=112)	51.1% (n=117)	0.856
Mortality (n=90)	47.8% (n=43)	52.2% (n=47)	

CEA, Carcinoembryonic antigen; **AL**, Anastomosis leakage; **AT**, Adjuvant therapy; **NT**, Neoadjuvant therapy

Discussion

According to our findings, there was no difference in terms of the development of AL between patients receiving NT and AT. Also, there was no difference between use of CRT and either RT or CT alone as NT or AT in terms of development of AL. However, in patients with AL, N2 lymph node involvement and lower body weight were observed more frequently. Development of AL did not affect mortality in patients.

Colorectal cancer now accounts for approximately 10% of cancer-related mortality in Western countries [27]. There are new treatments for primary and metastatic colorectal cancer, including laparoscopic surgery, radiotherapy, and neoadjuvant and palliative chemotherapy. Every method

Table 4: The comparison between patients who had anastomosis leakage and those who did not have in terms of TNM staging, laparoscopic surgery, tumor size, lymph node involvement, type of surgery, RT and/or CT, NT or AT, perineural invasion, and lymphatic invasion.

Variables	No AL (n=244)	AL (n=75)	p
CEA			
Preoperative >10 (n=238)	77.7% (n=185)	22.3% (n=53)	0.111
Preoperative <10 (n=81)	72.8% (n=59)	27.2% (n=22)	
Postoperative >10 (n=133)	84.2% (n=112)	15.8% (n=21)	0.589
Postoperative <10 (n=186)	71.0% (n=132)	29.0% (n=54)	
T1 (n=22)	86.4% (n=19)	13.6% (n=3)	
T2 (n=16)	81.2% (n=13)	18.8% (n=3)	0.057
T3 (n=112)	83.0% (n=93)	17.0% (n=19)	
T4 (n=169)	70.4% (n=119)	29.6% (n=50)	
N0 (n=120)	84.2% (n=101)	15.8% (n=19)	
N1 (n=93)	72.0% (n=67)	28.0% (n=26)	0.021
N2 (n=60)	65.0% (n=39)	35.0% (n=21)	
Nx (n=46)	80.4% (n=37)	19.6% (n=9)	
M0 (n=289)	77.2% (n=223)	22.8% (n=66)	0.379
M1 (n=30)	70.0% (n=21)	30.0% (n=9)	
Anterior resection (n=52)	73.1% (n=38)	26.9% (n=14)	
Low anterior resection (n=233)	76.8% (n=179)	23.2% (n=54)	0.774
Very low anterior resection (n=34)	79.4% (n=27)	20.6% (n=7)	
Laparoscopic surgery			
Yes (282)	75.5% (n=213)	24.5% (n=69)	0.266
No (37)	83.8% (n=31)	16.2% (n=6)	
Perineural invasion (n=44)	75.0% (n=33)	25.0% (n=11)	0.633
Lymphatic invasion (n=72)	75.0% (n=54)	25.0% (n=18)	0.555
Radiotherapy			
Yes (n=285)	77.2% (n=220)	22.8% (n=65)	0.391
No (n=34)	70.6% (n=24)	29.4% (n=10)	
Chemotherapy			
Yes (n=277)	87.3% (n=213)	85.3% (n=64)	0.660
No (n=42)	12.7% (n=31)	14.7% (n=11)	
NT with RT and CT (n=125)	75.8% (n=94)	77.5% (n=31)	0.827
NT with either RT or CT(n=39)	24.2% (n=30)	22.5% (n=9)	
AT with RT and CT (n=118)	79.2% (n=95)	65.7% (n=23)	0.1
AT with either RT or CT (n=37)	20.8% (n=25)	34.3% (n=12)	

CEA, Carcinoembryonic antigen; **AL**, Anastomosis leakage; **AT**, Adjuvant therapy; **NT**, Neoadjuvant therapy

Table 5: Change in serum CEA levels in the postoperative period compared to the preoperative period in patients with and without anastomosis leakage, in patients who survived and who died, and in patients receiving adjuvant therapy and patients receiving neoadjuvant therapy.

		Postoperative CEA <10	Postoperative CEA >10	P
AL	**Preoperative CEA <10 (n=59)**	54.2% (n=32)	45.8% (n=27)	0.111
Yes	**Preoperative CEA >10 (n=185)**	54.0% (n=100)	46.0% (n=85)	
No	**Preoperative CEA <10 (n=22)**	63.6% (n=14)	36.4% (n=8)	0.589
	Preoperative CEA >10 (n=53)	75.5% (n=40)	24.5% (n=13)	
Survival	**Preoperative CEA <10 (n=60)**	10.0% (n=6)	90.0% (n=54)	0.045
	Preoperative CEA >10 (n=169)	53.2% (n=90)	46.7% (n=79)	
Mortality	**Preoperative CEA <10 (n=69)**	65.2% (n=45)	34.8% (n=24)	0.946
	Preoperative CEA >10 (n=21)	38.1% (n=8)	61.9%(n=13)	
AT	**Preoperative CEA <10 (n=36)**	27.8% (n=10)	72.2% (n=26)	0.999
	Preoperative CEA >10 (n=119)	73.9% (n=88)	26.0% (n=31)	
NT	**Preoperative CEA <10 (n=45)**	17.8% (n=8)	82.2% (n=37)	0.206
	Preoperative CEA >10 (n=119)	57.1% (n=68)	42.9% (n=51)	

CEA, Carcinoembryonic antigen; **AL,** Anastomosis leakage; **AT,** Adjuvant therapy; **NT,** Neoadjuvant therapy

used in cancer treatments is associated with its own side effects and complications, and these are additive in combined therapy. The appearance of AL at the suture line of the bowel folds after tumor removal is one of the most feared surgical complications. The incidence of AL is 1-19%, and the postoperative mortality rate due to anastomotic complications is 6-22% [28-32]. About one-third of deaths after colorectal surgery are due to anastomotic complications [7]. In rectal cancers, the risk of developing AL is higher. Eriksson et al. [33] reported that the AL rate was 10% in patients operated on for colorectal cancer and 18.8% in rectal resections. Additionally, mortality is higher in AL after rectal resection, and mortality rates of up to 22-50% have been observed [7, 34, 35]. Therefore, the risk factors causing AL should be well defined, and, if AL develops, it should be treated effectively.

In the literature, male sex, advanced age, lower anastomosis, malignant disease, high American Society of Anesthesiologists (ASA) score, long surgical time, emergency surgery, preoperative RT, perioperative blood loss, and transfusion have been associated with AL [30, 36-43]. In one study, male sex and rectal cancer were shown as independent risk factors for both early and late AL. Younger age, increased body mass index (BMI), laparoscopic surgery, emergency surgery, and lack of guiding ileostomy have been shown as risk factors for early AL, and the Charlson Comorbidity Index, high ASA scores, additional resection due to tumor growth, and preoperative RT have been shown as risk factors for late AL. In several studies, the frequency of AL was higher in males than in females, probably due to differences in pelvic anatomy [29, 44, 45], while in other studies, no difference was found between the sexes in terms of AL [46-48]. Many of the risk factors for early AL are surgical-related factors that reflect surgical difficulty. In one study, laparoscopic surgery was shown to be an independent risk factor for early AL [22]. In other studies, no difference was found in terms of AL between laparoscopic surgery and open surgery [49, 50]. In two separate studies, the rates of AL in patients with low anterior resection were 10% [8] and 11% [51]. Patients who underwent anterior resection, low anterior resection, or very low anterior resection were included in our study. There was no difference between these types of surgeries in terms of the development of AL. AL was detected in 23.5% of our patients, which was slightly higher than the rates in the literature. Mortality rate in AL patients was 28.2%, and it was observed that the development of AL did not increase mortality. In addition, in univariate analysis, it was observed that sex, age, tumor size, perineural involvement, and lymphatic invasion did not have significant effects on AL development. Although in one study, stage 3-4 rectal cancer and poorly differentiated or mucinous adenocarcinoma were shown as independent risk factors for early AL [21], this was not the case in another study [22]. In our study, we observed a relationship between N2 lymph node involvement (stage 3C and 4 rectal cancer) and AL, similar to the study by Shin et al. [21].

The effects of neoadjuvant RT or CRT on the development of AL are controversial. In a prospective study, it was shown that short-term neoadjuvant RT does not increase the risk of AL [17]. In another prospective study, neoadjuvant CRT therapy was shown to be a risk factor for AL in patients undergoing laparoscopic surgery with change in the direction of stoma. However, in the same study, neoadjuvant CRT therapy could not be demonstrated to be a risk factor for AL in all

patients undergoing low anterior resection due to cancer [18]. Similarly, there are studies showing that preoperative RT or CRT is a risk factor for late AL [19-22]. In a study comparing adjuvant and neoadjuvant CRT, no difference was found between the two groups in terms of AL development [5]. In our study, there was no difference in AL between patients who received CRT and patients who received CT or RT as NT. We also found no difference in AL between patients who received CT and RT as CRT and AT.

Serum CEA increases in 17-47% of patients with colorectal cancer [52, 53], but its sensitivity is not high enough to be used as a screening test. However, serum CEA levels may have prognostic value for rectal cancer. The prognosis is worse in patients with the same stage of the disease but with CEA values higher than 5 ng / mL [54]. In our study, because the reference values of our hospital's biochemistry laboratory were different, the CEA cut-off value was accepted as 10 ng / mL. The high mortality rate in patients with higher CEA levels in our study is consistent with the literature. The absence of relationships between preoperative and postoperative CEA levels as well as postoperative CEA levels and survival confirms that serum CEA levels are not sensitive enough to be used as a screening test.

Our study has some limitations. Our study was a single-center and retrospective study. Patients undergoing abdominopelvic resection and those undergoing emergency surgery were excluded from the study. Early and late AL discrimination was not performed in patients with AL. In addition, we had no data on which interventions were performed on patients who developed AL. On the other hand, our study is valuable in terms of having a high number of patients (n=319), reflecting 10 years' data from a clinic, and having 2-8 years of follow-up.

In conclusion, there was no difference in terms of the development of AL between patients receiving NT and patients receiving AT. The use of either RT or CT as NT or AT, or the use of CRT as NT or AT did not increase the risk of AL. Mortality did not increase in patients with AL. These treatments should not be abandoned in the treatment of rectal cancer due to the better local control, overall survival, and sphincter function protection rates.

Acknowledgements

We would like to acknowledge the www.makaletercume.com for their outstanding scientific proofreading and editing services that was provided for this manuscript.

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