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FULL PAPER

Results of re-irradiation for pelvic recurrence in anorectal cancer patients

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Objective: To evaluate outcomes and toxicity profiles after re-irradiation in patients with pelvic recurrence of anorectal cancer.

Methods: 25 anorectal cancer patients who received re-irradiation for pelvic recurrence between 2005 and 2015 were included. For initial treatment, all patients underwent surgical resection and preoperative or post-operative radiotherapy.

Results: The median follow-up duration was 21.5 months (range, 2.9–84.4). After a median of 43.3 months (range, 11.7–218.5), patients received re-irradiation with a median dose of 45 Gy (range, 36–60). The equivalent dose in 2 Gy fractions (EQD2) of re-irradiation—calculated using $\alpha/\beta = 10$ Gy—ranged from 34.5 to 84.0 Gy (median, 46.4). Surgical resection was performed for 11 patients, and 14 patients received concurrent chemotherapy with re-irradiation. The 3-year local progression-free survival was 29.7%.

The 3-year overall survival was 49.7%. Concurrent chemotherapy with re-irradiation and re-irradiation doses >50 Gy EQD2 $_{\alpha/\beta=10}$ were significant prognostic factors for local progression free survival and overall survival according to multivariate analysis. 90% (9 of 10) of patients with symptoms had improvement after re-irradiation. Among 23 patients available for evaluation of late toxicity, 12 developed late toxicities. There were no Grade 4 late toxicities, and 6 patients had Grade 3 late toxicities (small bowel obstruction, bowel perforation and fistula).

Conclusion: Re-irradiation for pelvic recurrence of anorectal cancer improved symptoms of patients but the rate of late toxicity was high. Further investigation for patient selection is required.

Advances in knowledge: Re-irradiation could be considered as a possible option for pelvic recurrence of anorectal cancer in selected patients.

INTRODUCTION

Although multimodality treatment of rectal cancer consists of total mesorectal excision (TME) and preoperative or postoperative concurrent chemoradiotherapy improves outcomes, about 5–10% of patients still experience local recurrence.^{1–3} Locally recurrent rectal cancer not only affects prognosis, but it also decreases quality of life.⁴ Although a standard treatment for locally recurrent rectal cancer is not established, surgical resection with negative margin is considered the primary curative treatment.^{5–7} However, radical resection is not possible in most patients, and it can be accompanied by substantial complications.⁸ Radiotherapy is a potential alternative local treatment modality in patients with unresectable disease.

However, with increased use of radiotherapy as a part of initial multimodality treatment, most patients with local recurrence of rectal cancer have previously undergone irradiation to the pelvis. Historically, re-irradiation has been discouraged because of concerns about late toxicity of normal tissues and because few data regarding re-irradiation were available. Recently, a few studies have tested the efficacy and safety of re-irradiation for rectal cancer. Mohiuddin et al demonstrated the feasibility of re-irradiation followed by surgical resection in selected patients with locally recurrent rectal cancer.⁹ Lingraeddy et al reported the outcomes of palliative re-irradiation for recurrent rectal cancer.¹⁰ They showed effective symptom palliation after re-irradiation and a reduced rate of late complications with

hyperfractionated treatment. In a Phase II prospective study, Valentini et al reported the outcomes of hyperfractionated re-irradiation with acceptable toxicities.¹¹

In this study, we evaluate the treatment outcomes and toxicities of re-irradiation for pelvic recurrence of anorectal cancer patients previously treated with radiotherapy.

METHODS AND MATERIALS

Between 2005 and 2015, patients with adenocarcinoma of the rectum or anus undergoing re-irradiation for pelvic recurrence were identified. The inclusion criteria were as follows: (1) histologically confirmed adenocarcinoma of anus or rectum; (2) initial pre- or post-operative radiotherapy; (3) initial curative surgical resection; (4) no initial distant metastases; (5) re-irradiation for pelvic recurrence; (6) completion of planned radiotherapy. The medical records of the patients were reviewed with approval by the institutional review board.

Acute and late toxicities were graded using the Common Terminology Criteria for Adverse Events v. 4.0. Local progression was defined as any recurrence or progression in the re-irradiation field. Local progression free survival (LPFS) and overall survival (OS) were calculated from the first day of re-irradiation. The actuarial survival rates were estimated using the Kaplan–Meier method, and the difference of survival curves were verified with the log-rank test. Variables found to be statistically significant or marginally significant on univariate analysis were analyzed by multivariate analysis with the Cox proportional-hazards model. All statistical analyses were performed with SPSS, v. 18.0.1 (SPSS Inc. Chicago, IL).

RESULTS

Among 27 patients referred for re-irradiation during the accrual period, 2 patients were excluded from the analysis. One patient was off re-irradiation after one fraction due to the bleeding from the pre-existing rectovaginal fistula. The other patient initially refused planned surgical resection after pre-operative concurrent chemoradiotherapy (CCRT). Patient underwent palliative surgical resection after tumor regrowth. Thus, 25 patients were analyzed in this study.

Patient characteristics and initial treatment

The patient and treatment characteristics at initial treatment are summarized in Table 1. Among the 25 patients included, 24 had rectal cancer and 1 had anal cancer. The median age at diagnosis was 50 years (range, 31–75) and 15 patients (60.0%) were male. The median radiation dose was 50.4 Gy (range, 50.4–59.4). 21 patients (84.0%) received concurrent chemotherapy during radiotherapy.

Re-irradiation

The patient and treatment characteristics at re-irradiation are summarized in Table 2. The median age was 57 years (range, 34–81), and seven patients had synchronous extrapelvic metastases at re-irradiation. The locations of recurrent tumors were as follows: anastomosis site or tumor bed in nine patients, pelvic side-wall in five patients, regional lymph node in five patients

Table 1. Patient and treatment characteristics at initial treatment

Characteristics		n	%
Age, year	Median (range)	50 (31–75)	
Gender	Male	15	60.0
	Female	10	40.0
Types of surgery	Low anterior resection	16	64.0
	Abdominoperineal resection	9	36.0
Resection margin status	Negative	20	80.0
	Positive	4	16.0
	N/A	1	4.0
Aim of RT	Preoperative	12	48.0
	Postoperative	13	52.0
RT dose, Gy	Median (range)	50.4 (50.4–59.4)	
CCRT	Yes	21	84.0
	No	4	16.0
CCRT regimen	5-fluorouracil	11	52.4
	Capecitabine	8	38.1
	5-fluorouracil + leucovorin	2	9.5

CCRT, concurrent chemoradiotherapy; N/A, not available; RT, radiotherapy.

and presacral area in five patients. Two patients had recurrences in anastomosis site with regional lymph node or abdominal wall involvement. Surgical resection was performed in 11 patients, and of these patients, pelvic exenteration was performed in 4 patients, Hartmann's operation in 1, and abdominoperineal resection in 1 patient. The median interval between two courses of radiotherapy was 43.3 months (range, 11.7–218.5). The aim of re-irradiation was salvage in 6 patients, pre- or postoperative in 9 patients, and palliative in 10 patients. Four patients received pre-operative radiotherapy, five received post-operative adjuvant radiotherapy, and two patients received re-radiotherapy after surgery as salvage or palliative therapy, respectively. 18 patients were treated with three-dimensional conformal radiotherapy (3D-CRT), 5 with intensity-modulated radiotherapy (IMRT), 1 with stereotactic body radiotherapy (SBRT), and 1 patient received initial 3D-CRT followed by an IMRT boost. The radiation doses ranged from 36 to 60 Gy, with a median of 45 Gy. Because patients received re-irradiation at diverse fractionation schedules, the radiation dose was converted to the equivalent dose in 2 Gy fractions (EQD2) using α/β of 10 Gy. The median $\text{EQD2}_{\alpha/\beta=10}$ of re-irradiation was 46.4 Gy (range, 34.5–84.0). The total summated dose of initial and re-irradiation EQD2 with α/β of 3 Gy had a median of 92.5 Gy (range, 80.1–199.8). The target volume of re-irradiation was the recurrent tumor or tumor bed plus a 5–10 mm margin in 22 patients, the whole pelvis followed by boost to the gross tumor in two patients, and lymphatic chains in two patients. The median clinical target volume was 191.1 cc

Table 2. Patient and treatment characteristics at re-irradiation

Characteristics		n	%
Age, year	Median (range)	57 (34–81)	
Extrapelvic metastasis	Yes	7	28.0
	No	18	72.0
Surgery	Yes	11	44.0
	No	14	56.0
Types of surgery	Debulking/excision	4	36.4
	Pelvic exenteration	4	36.4
	Hartmann's operation	1	9.1
	Abdominoperineal resection	1	9.1
	Lymph node dissection	1	9.1
Interval between RT, month	Median (range)	43.3 (11.7–218.5)	
Aim of RT	Salvage	6	24.0
	Preoperative	4	16.0
	Postoperative	5	20.0
	Palliative	10	40.0
RT modality	3D-CRT	18	72.0
	IMRT	5	20.0
	SBRT	1	4.0
	3D + IMRT	1	4.0
RT dose, Gy	Median (range)	45.0 (36.0–60.0)	
RT dose, EQD2, Gy ($\alpha/\beta = 10$ Gy)	Median (range)	46.4 (34.5–84.0)	
Total cumulative dose, EQD2, Gy ($\alpha/\beta = 3$ Gy)	Median (range)	92.5 (80.1–199.8)	
RT schedule	QD	19	76.0
	BID	6	24.0
Chemotherapy	Before re-RT	10	40.0
	CCRT	14	56.0
	After re-RT	16	36.0
	CCRT regimen		
	Capecitabine	9	64.3
	5-fluorouracil	2	14.3
	XELOX	1	7.1
	FOLFOX	1	7.1
	5-fluorouracil + leucovorin	1	7.1

BID, twice a day fractionation; CCRT, concurrent chemoradiotherapy; 3D-CRT, three dimensional conformal radiotherapy; EQD2, equivalent dose in 2 Gy fractions; FOLFOX, leucovorin + 5-FU + oxaliplatin; IMRT, intensity modulated radiotherapy; QD, once-daily fractionation; RT, radiotherapy; Re-RT, re-irradiation; SBRT, stereotactic body radiotherapy; XELOX, capecitabine + oxaliplatin.

Figure 1. Local progression-free survival (A) and overall survival (B)

(range, 8.6–777.3). 19 patients were irradiated in once-daily fractionation (QD), and 6 in twice a day fractionation (BID). Concurrent chemotherapy was administered in 15 patients and all received 5-fluorouracil-based chemotherapy.

Pelvic control

The median follow-up was 21.5 months (range, 2.9–84.4). One patient was lost to follow-up after re-irradiation, and the treatment outcome could not be evaluated. Among 24 patients with available follow-up data, 13 patients (54.2%) developed local recurrence with 2-year and 3-year LPFS of 44.6 and 29.7%, respectively (Figure 1A). The results of the univariate and multivariate analyses for local control are summarized in Table 3. Surgical resection for recurrent lesions was not associated with LPFS ($p = 0.717$). The time interval between two courses of radiotherapy and concurrent chemotherapy with re-irradiation showed marginally significant associations with LPFS ($p = 0.050$ and $p = 0.057$, respectively). Re-irradiation doses >50 Gy EQD2 $_{\alpha/\beta=10}$ were associated with improved LPFS (3-year LPFS 58.3% vs 0.00%, $p = 0.007$). Most patients with re-irradiation intervals ≤ 36 months (6 of 8, 75.0%) received less than 50 Gy EQD2 $_{\alpha/\beta=10}$, while more patients with re-irradiation intervals > 36 months (10

Table 3. Univariate and multivariate analysis for local progression-free survival

Variables		n ^a (%)	Univariate		Multivariate	
			3-year LPFS (%)	<i>p</i>	<i>p</i>	HR (95% CI)
Initial surgery	Sphincter saving surgery	16 (66.7)	24.9	0.468		
	Abdominoperineal resection	8 (33.3)	40.0			
Initial RT dose	≤50.4 Gy	15 (62.5)	32.3	0.434		
	>50.4 Gy	9 (37.5)	31.7			
Initial CCRT	No	4 (16.7)	0.00	0.948		
	Yes	20 (83.3)	33.6			
Aim of initial RT	Preoperative	11 (45.8)	30.3	0.532		
	Postoperative	13 (54.2)	33.0			
Surgery at recurrence	No	13 (54.2)	30.0	0.717		
	Yes	11 (45.8)	32.7			
Interval between RT	≤36 mo	8 (33.3)	0.00	0.050	0.317	
	>36 mo	16 (66.7)	53.3			
Extrapelvic metastases at re-RT	No	18 (75.0)	35.2	0.489		
	Yes	6 (25.0)	0.00			
CCRT at re-RT	No	10 (41.7)	0.00	0.057	0.001	5.802 (1.434–23.474)
	Yes	14 (58.3)	42.1			
Re-RT aim	Salvage, adjuvant ^b	15 (62.5)	37.7	0.681		
	Palliative	9 (37.5)	20.8			
Re-RT dose, EQD2 ($\alpha/\beta = 10$)	≤50 Gy	12 (50.0)	0.00	0.007	0.001	8.422 (1.955–36.282)
	>50 Gy	12 (50.0)	58.3			
Re-RT modality	3D-CRT ^c	18 (75.0)	42.5	0.186		
	IMRT, SBRT	6 (25.0)	0.00			
Re-RT schedule	QD	18 (75.0)	50.2	0.091		
	BID	6 (25.0)	0.00			

LPFS, local progression-free survival; HR, hazard ratio; CI, confidence interval; RT, radiotherapy; Re-RT, re-irradiation; CCRT, concurrent chemoradiotherapy; EQD2, equivalent dose in 2 Gy fractions; 3D-CRT, three dimensional conformal radiotherapy; IMRT, intensity modulated radiotherapy; SBRT, stereotactic body radiotherapy; QD, once-daily fractionation; BID, twice a day fractionation.

^aOne patient lost to follow-up after re-irradiation was excluded.

^bPreoperative and postoperative.

^cOne patient received 3-D CRT followed by IMRT boost.

of 17, 58.8%) received more than 50 Gy EQD2 $_{\alpha/\beta=10}$, although this difference was not statistically significant. On multivariate analysis, CCRT at recurrence and re-irradiation dose remained significant predictors of LPFS ($p = 0.001$, [Figure 2](#)).

Overall survival

Among 25 patients, there were 18 deaths and 2-year and 3-year OS rates were 54.6 and 49.7%, respectively ([Figure 1B](#)). For OS, extrapelvic metastases at recurrence, CCRT at recurrence, the aim of re-irradiation, and the dose of re-irradiation showed significant associations in univariate analysis ([Table 4](#)). Patients with extrapelvic metastasis had poorer survival than those without metastasis (3-year OS 14.3% vs 63.5%, $p < 0.001$), and patients treated with CCRT showed better survival than those who did not (3-year OS 82.5% vs 9.1%, $p < 0.001$). The 3-year OS was 62.0% in patients treated with aim of neoadjuvant or

adjuvant (pre- or postoperative) salvage and 30.0% for patients who received palliative re-irradiation ($p = 0.018$). There was a tendency toward improved survival with re-irradiation doses >50 Gy EQD2 $_{\alpha/\beta=10}$ compared with ≤50 Gy EQD2 $_{\alpha/\beta=10}$ (3-year OS 58.3% vs 42.2%, $p = 0.044$). On multivariate analysis, CCRT at recurrence and re-irradiation dose were independent prognostic factors for OS ([Figure 3A and B](#)). Most patients without extrapelvic metastasis received concurrent chemotherapy (14 of 18, 77.8%), while none of the patients with extrapelvic metastasis received concurrent chemotherapy (0 of 7, 0%). 12 of 14 patients who received CCRT were treated with salvage, preoperative, or postoperative aims.

Symptoms and toxicity

Of the 25 patients, 10 had clinical symptoms related to recurrent lesions before re-irradiation. Nine patients had pelvic or lower

Figure 2. Local progression-free survival according to re-irradiation dose. reRT, re-irradiation; CCRT, concurrent chemoradiotherapy; EQD2, equivalent dose in 2 Gy fractions.

extremity pain, and one patient had lower extremity paresthesia. The symptoms improved in 9 of 10 patients (90.0%) and stayed stable in one patient (10.0%) during or after re-irradiation.

All 25 patients completed re-irradiation as planned, and no patients had any acute complications. Late complications could not be evaluated in 2 patients because one was lost to follow-up after re-irradiation, and 1 died within 3 months after re-irradiation. Among 23 patients with available data, 12 patients (52.2%) experienced late toxicities (Table 5). Grade 3 toxicities developed in six patients, and the actuarial 3-year rate of Grade 3 toxicity was 52.5%. Among the Grade 3 fistula cases, there were two enterovaginal fistulas, two enterocutaneous fistulas, one vesicocutaneous fistula, and for one patient the fistula location was not specified. No clinical or treatment factor was associated with Grade 3 late toxicities.

DISCUSSION

In this study, we evaluated the treatment outcomes of re-irradiation to the pelvis in patients with recurrent rectal cancer who were previously treated with radiotherapy. The actuarial 3-year LPFS and OS were 29.7 and 49.7%, respectively. Concurrent chemotherapy with re-irradiation and re-irradiation dose were

significant prognostic factors for LPFS and OS in multivariate analysis.

After initial studies, which reported acceptable toxicities with low re-irradiation doses of about 30 Gy in hyperfractionations,^{9,10} most studies then used radiation doses of 30–40 Gy using hyperfractionation schedules.^{11–15} In those studies, re-irradiation dose did not affect the local control rate of recurrent lesions, while they reported improved local control with surgical resection.^{13–15} In our study, re-irradiation dose exceeding 50 Gy EQD2 $_{\alpha/\beta=10}$ was a significant prognostic factor, and surgical resection did not improve LPFS. These results might suggest the possibility that the re-irradiation doses of 30–40 Gy in previous studies were not sufficient to control recurrent lesions. In a recent study by Koom et al, infield progression-free survival was significantly increased with re-irradiation doses exceeding 50 Gy EQD2 $_{\alpha/\beta=10}$, which was compatible with our results.¹⁶ Additionally, re-irradiation dose was a significant predictor of OS in our study. In a study by Mohiuddin et al, re-irradiation dose was not associated with local control but significantly associated with overall survival, and they recommended 50–55 Gy of re-irradiation in patients whose intervals to re-irradiation were more than 36 months.¹² Susko et al also found a longer overall survival in patients who received more than 32 Gy than those who received less than 32 Gy, although the difference was not statistically significant.¹⁵ In rectal cancer, improved local control often translates into improved survival, and multimodality treatment with TME has been a standard treatment to improve local control.^{2,17,18} Although there are little data regarding the association of local control and overall survival in patients with recurrent disease, there are possibilities that improved local control by sufficient doses of re-irradiation prolonged the survival of patients in our study. Therefore, higher dose of re-irradiation, more than 50 Gy EQD2 $_{\alpha/\beta=10}$ in current analysis, might provide more durable local control of recurred rectal cancer and consequently, improve overall survival. Further studies to evaluate the efficacy of high-dose re-irradiation in large numbers of patients are needed.

The time interval between the two courses of radiotherapy was associated with LPFS with marginal statistical significance in univariate analysis, but this was not significant in multivariate analysis. In general, because of concerns about toxicity, patients with short re-treatment intervals tend to receive lower doses of re-irradiation than those with longer intervals. In our study, although this finding was not statistically significant, patients with longer re-irradiation intervals tended to receive higher doses of re-irradiation than those with short intervals. Mohiuddin et al reported the long-term results of re-irradiation with concurrent chemotherapy in 103 patients with recurrent rectal cancer.¹² They used different radiation doses and fractionation schedules depending on the interval between initial treatment and recurrence, and they made dose recommendations based on the interval to re-irradiation. Therefore, the time interval might be an important consideration when determining re-irradiation doses.

Concurrent chemotherapy with re-irradiation was another significant predictor for local control and overall survival. CCRT at

Table 4. Univariate and multivariate analysis for overall survival

Variables		n (%)	Univariate		Multivariate	
			3-year OS (%)	<i>p</i>	<i>p</i>	HR (95% CI)
Initial surgery	Sphincter saving surgery	16 (64.0)	45.1	0.623		
	Abdominoperineal resection	9 (36.0)	55.6			
Initial RT dose	≤50.4 Gy	16 (64.0)	45.1	0.623		
	>50.4 Gy	9 (36.0)	55.6			
Initial CCRT	No	4 (16.0)	25.0	0.102		
	Yes	21 (84.0)	55.4			
Aim of initial RT	Preoperative	12 (48.0)	36.5	0.605		
	Postoperative	13 (52.0)	60.6			
Surgery at recurrence	No	14 (56.0)	41.7	0.129		
	Yes	11 (44.0)	58.9			
Interval between RT	≤36 mo	8 (32.0)	72.9	0.734		
	>36 mo	17 (68.0)	39.2			
Extrapelvic metastases at re-RT	No	18 (72.0)	63.5	<0.001	0.543	
	Yes	7 (28.0)	14.3			
CCRT at re-RT	No	11 (44.0)	9.1	<0.001	<0.001	41.278 (7.015–242.878)
	Yes	14 (56.0)	82.5			
Re-RT aim	Salvage, adjuvant ^a	15 (60.0)	62.0	0.018	0.158	
	Palliative	10 (40.0)	30.0			
Re-RT dose, EQD2 ($\alpha/\beta = 10$)	≤50 Gy	13 (52.0)	42.2	0.061	0.010	4.757 (1.452–15.588)
	>50 Gy	12 (48.0)	58.3			
Re-RT modality	3D-CRT ^b	19 (76.0)	56.0	0.156		
	IMRT, SBRT	6 (24.0)	33.3			
Re-RT schedule	QD	19 (76.0)	40.5	0.779		
	BID	6 (24.0)	80.0			

OS, overall survival; HR, hazard ratio; CI, confidence interval; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; Re-RT, re-irradiation; EQD2, equivalent dose in 2 Gy fractions; 3D-CRT, three dimensional conformal radiotherapy; IMRT, intensity modulated radiotherapy; SBRT, stereotactic body radiotherapy; QD, once-daily fractionation; BID, twice a day fractionation.

^aPreoperative and postoperative.

^bOne patient received 3-D CRT followed by IMRT boost.

recurrence was a marginally significant factor in univariate analysis for LPFS, but in multivariate analysis, it remained a statistically significant factor. In univariate analysis for OS, synchronous extrapelvic metastasis and aim of re-irradiation were significant factors, but lost their significance in multivariate analysis, while CCRT was a strong prognostic factor in both univariate and multivariate analysis. In our study, most patients with extrapelvic metastasis were treated with a palliative aim and did not receive CCRT. Because treatment decisions were made based on the patients' general condition and disease status, CCRT itself might have reflected all of the other clinical factors considered in the analysis.

In our study, late toxicities were frequent relative to previous studies, which have reported 10–20% incidence rates for Grade three late toxicities.^{10,12,13} However, these previous studies used much lower re-irradiation doses than our study. A study by Koom et al, which used similar radiation doses to our study—with a median dose of 50 Gy (range, 30–66 Gy)—reported a Grade three late toxicity rate

of 36%, which is comparable to our study¹⁶. They also found that the location of recurrent tumors was associated with late toxicity. Therefore, increased re-irradiation dose is associated with higher rates of late toxicity, and careful patient selection depending tumor location could reduce the rate of late toxicity.

Two studies have reported outcomes of re-irradiation using IMRT. Cai et al¹⁹ treated 22 patients with 39 Gy in 30 fractionations, twice a day, and reported a low late toxicity rate, with 2 cases of chronic severe diarrhea (9.1%), one small bowel obstruction (4.5%), and 2 cases of dysuria (9.1%). Youssef et al reported an even lower frequency of late toxicity²⁰. They prescribed 39 Gy in 26 fractionations, BID, or 27–40 Gy in 15–22 fractionations, QD, and reported only one patient (3.2%) with Grade 3 late toxicity (sacral insufficiency fracture). Although these two studies with IMRT also used low doses of re-irradiation similar to previous studies, the toxicity rates were much lower than those studies.^{10,12,13} In a study by Abusaris et al²¹, 27 patients were retreated with SBRT for

Figure 3. Overall survival rate according to re-irradiation dose (A) and CCRT at re-irradiation (B). reRT, re-irradiation; CCRT, concurrent chemoradiotherapy; EQD2, equivalent dose in 2 Gy fractions.

Table 5. Late toxicities after re-irradiation ($n = 23$) by CTCAE criteria v. 4.0

Adverse effect	n (%)			
	Grade 1	Grade 2	Grade 3	Grade 4
Small bowel obstruction	2 (8.3)	0	1 ^a (4.2)	0
Bowel perforation	0	0	2 ^b (8.3)	0
Rectal bleeding	1 (4.2)	0	0	0
Ileus	1 (4.2)	0	0	0
Fistula	2 (8.3)	0	6 (25.0)	0

CTCAE, common terminology criteria for adverse events.

^aOne patient had both Grade 3 small bowel obstruction and fistula.

^bTwo patients had both Grade 3 bowel perforation and fistula.

abdominal or pelvic lesions; their prescribed doses were higher than those of other studies, ranging from 24 to 150 Gy EQD2_{α/β=10}, and they reported favorable outcomes. The toxicity rate was low and no grade ≥3 acute or late toxicity was observed. In a recent systematic review by Murray et al ²², SBRT was suggested as a feasible treatment option for previously irradiated patients with recurrent pelvic disease. Although the treatment modality did not affect the treatment outcome or toxicity rate in our study, using more precise radiation techniques, such as IMRT or SBRT, can be beneficial for re-irradiation by delivering higher radiation doses while minimizing the radiation exposure to adjacent normal tissues. Further studies involving larger sample sizes and using diverse radiation doses are needed to validate this.

There were some limitations in our study. Our sample was small and heterogeneous, with a diversity of systemic disease statuses and tumor locations. Therefore, the treatments for recurrent pelvic lesions were also heterogeneous, consisting of surgery, chemotherapy, and radiotherapy, and the contribution of each treatment modality to the outcome and toxicity could not be disentangled. Additionally, as this was a retrospective study, the toxicities could have been underestimated due to incomplete medical records. Higher re-irradiation dose was related with improved result in current analysis. Because the radiation doses and schedules were decided depending on the disease extent and patient performance, the improved outcome may have resulted from patient selection rather than the employed dose. However, despite these limitations, current analysis suggested the possible role of re-irradiation to improve the prognosis of patients with recurrent rectal cancer and the needs for further investigations to find the subset of patients who may benefit from re-irradiation without late toxicities.

CONCLUSIONS

Re-irradiation could be considered as a treatment option for patients with recurrent anorectal cancer, and improved the related symptoms effectively. The late toxicity rate is high, so patients should be well informed about the risks, and all appropriate measures should be undertaken to minimize re-irradiation toxicity.

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