Original article

Metastasis-Directed Radiotherapy for Oligoprogressive or Oligopersistent Metastatic Colorectal Cancer

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Abstract

Our study explored the role of metastasis-directed radiotherapy (MRT) for oligoprogressive or oligopersistent tumor from metastatic colorectal cancer (mCRC). We observed that MRT was performed safely while continuing systemic treatment and showed postponement of the time to change to next-line systemic therapy. Prospective evaluation of this approach is warranted in patients with mCRC.

Introduction: Some patients with cancer may present with progressive or persistent disease at a limited number of sites following a period of treatment response. We evaluated the safety and effectiveness of metastasis-directed radiotherapy (MRT) for oligoprogressive or oligopersistent disease in patients receiving systemic treatment for metastatic colorectal cancer (mCRC). **Patients and methods:** Patients with mCRC who received 5-fluorouracil, leucovorin, and oxaliplatin; 5-fluorouracil, leucovorin, and irinotecan; and/or capecitabine chemotherapy between 2011 and 2020 at a single institution were identified. Then, those who underwent MRT for five or fewer lesion sites while receiving systemic treatment for other metastases were categorized. The primary endpoint was time to change to systemic therapy. Secondary endpoints included MRT-related toxicity, overall survival, and local control. **Results:** Among 4157 patients included, 91 (2%) received MRT to limited lesion sites (55 oligoprogressive and 36 oligopersistent) during systemic treatment following a period of treatment response. The median time to change to next-line systemic therapy was 5 months in the overall cohort (measured from the current chemotherapy session) and 9.5 (range, 6.0–40.6) months in the MRT group (measured from the MRT session). No severe toxicity or systemic treatment interruption was observed following MRT. The 1-year local control and overall survival rates were 69% and 99%, respectively. **Conclusion:** In patients with oligoprogressive or oligopersistent mCRC, MRT may be performed safely in conjunction with systemic treatment to maximize the benefit of systemic therapy and to prolong the time to change to systemic therapy. Further prospective studies should confirm these findings.

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Introduction

Systemic chemotherapy, including 5-fluorouracil, capecitabine, irinotecan, oxaliplatin, and molecular targeted agents, is often effective in patients with metastatic or recurrent colorectal cancer (mCRC).[1] However, drug resistance conferred by genetic alterations has been a major challenge, with most patients developing progressive disease. The genetic heterogeneity between primary tumor and metastatic lesions or among multiple metastases often results in a mixed response to systemic therapy.[2,3]

Oligoprogression—a state under the broader definition of oligometastasis—occurs when a few (eg, five or fewer) metastases progress while other disease sites respond to the current treatment.[4–6] In such cases, the next step to improve disease control might be next-line systemic therapy. However, this decision is associ-

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ated with disadvantages, such as intrinsic toxicity, added expense, different treatment compliance, and decreased efficacy. In some other cases, a limited number of metastases may persist following systemic therapy, and this is called oligopersistence.[5,6] Oligopersistent metastases may progress locally and serve as a seed for further metastases initiated by potentially proliferating treatment-resistant clones.[8]

In mCRC, because of fewer efficacious options available in later lines of therapy, there has been considerable interest in maximizing existing treatment options, including (1) the use of maintenance therapy after first-line therapies for unresectable mCRC and (2) therapy retreatment or rechallenge. A systemic review and meta-analysis showed the probable lack of benefit in overall survival (OS) following maintenance therapy.[7] Currently, the FIRE-4 study (NCT02934529) is recruiting participants to assess the efficacy of therapy rechallenge for mCRC.

In our institution, a multidisciplinary tumor board has been established since 2012 to discuss the cases of patients with potentially resectable mCRC from initial work-up through follow-up. At the same time, metastasis-directed radiotherapy (MRT) is offered to patients with unresectable mCRC with oligoprogressive or oligopersistent metastases to enhance the efficacy of systemic therapy.[9] In this study, we aimed to evaluate the safety and effectiveness of MRT in selected patients with unresectable oligoprogressive or oligopersistent mCRC.

Materials and Methods

Patients

The study was approved by the institutional review board (4-2021-0866) of our institute and was conducted according to the Declaration of Helsinki. We identified patients with mCRC who received systemic chemotherapy from a prospective institutional registry between January 2011 and October 2020. Chemotherapy regimens included 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX); 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI); and capecitabine (accepted as third-line chemotherapy for advanced colorectal cancer in the Republic of Korea). Patients were excluded if they were younger than 18 years of age, had non-adenocarcinoma histology, or received other treatment regimens (due to the small number of patients). We also identified patients with mCRC who underwent MRT without surgical resection of oligoprogressive or oligopersistent metastases (five or fewer lesion sites) while receiving systemic treatment for other metastases. Patients with de novo oligometastatic disease or those who received palliative RT were excluded.

Treatment

Data of all mCRC patients were thoroughly reviewed and discussed among the multidisciplinary colorectal cancer team to decide on the next treatment step. The team comprised specialists from the Departments of Gastroenterology, Medical Oncology, Radiation Oncology, Surgical Oncology, Radiology, and Pathology.

For patients who were to undergo MRT, we performed a computed tomography (CT)-based simulation with immobilization devices suitable for the respective treatment site, such as abdominal compression, active breathing control, and continuous positive airway pressure. CT images and structure sets were imported into the Treatment Planning System. The clinical target volume (CTV) was generated by adding a 0–1 cm expansion upon the gross target volume (GTV), to encompass microscopic disease extension, according to the physician's discretion. When treating lymph nodes, the CTV included an elective nodal area adjacent to the GTV. MRT was typically delivered with intensity-modulated RT (IMRT), volumetric modulated arc therapy, stereotactic body RT (SBRT), and stereotactic radiosurgery (SRS). If the distance between the GTV and organ at risk was greater than 1 cm or the GTV was less than 5–6 cm, hypofractionated RT or SBRT was preferred. The radiation dose scheme was determined considering the toxicity of normal organs. The total irradiated dose was aimed to be a biological equivalent dose with an α/β 10 Gy of 60 or higher generally in long-course fractionation, and tried to increase dose as high as reasonably achievable (at least BED 100 Gy) in hypofractionated SBRT. In all cases, daily image-guided RT using cone beam CT was performed.

The median biological effective dose of MRT was 76.2 (range, 38.4–187.5) Gy, corresponding to a median total dose of 50 (range, 20.0–76.0) Gy and a median fractional dose of 7.5 (range, 1.8–30.0) Gy. Although there were several different dose-fraction schemes, the most common were as follows: 45 Gy in three fractions (9.9%); 50 and 60 Gy in 25 fractions (7.7% and 6.6%, respectively); 20, 25, and 30 Gy in a single fraction (4.4%, 2.2%, and 5.5%, respectively); and 60, 48, and 40 Gy in four fractions (4.4%, 4.4%, and 3.3%, respectively).

Outcomes

Generally, patients with mCRC underwent follow-up at 3 month intervals, wherein the following are evaluated: clinical assessment of patient symptoms, physical examination, laboratory examination, such as tumor marker levels, and chest and abdominal CT. The primary endpoint was the cumulative incidence of change to next-line systemic therapy. We used an in-house Chemotherapy Assistant Program to extract data on chemotherapy regimens, duration, cycles, start and completion dates, and reason for completion.[10] Accordingly, we assessed the time interval from the initiation of systemic therapy to the requirement for and initiation of next-line systemic therapy. Secondary endpoints were both infield tumor control, defined as the time of progression of irradiated lesions from the initiation of MRT, and OS, defined as the time from initiation of current systemic therapy to the date of death or last follow-up. Additionally, we assessed MRT-related toxicity and the interruption of systemic chemotherapy due to MRT-induced toxicity.

To determine the outcomes of all patients with mCRC treated with systemic therapy during the same period at the same institution, the cumulative incidence of change to next-line systemic therapy and OS were calculated in the general mCRC population treated with systemic therapy without MRT during the study period. These control patients were a reference group, not a comparator group.

All statistical analyses were performed using SPSS v25.0 (IBM SPSS Inc., Chicago, IL, USA). Cumulative incidence rates of change

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Table 1 Patient and Treatment Characteristics in mCRC Patients Treated With Metastasis-Directed RT and Systemic Chemotherapy (MRT Group, n = 91)

Variables	n		%
Age (year)	median (range)	60 (35-82)	
Sex	Male	51	56.0%
	Female	40	44.0%
Primary site	Colon	50	54.9%
	Rectum	41	45.1%
Tumor type	Metastatic	77	84.6%
	Recurrent	14	15.4%
Chemotherapy regimen	FOLFOX	45	49.5%
	FOLIFRI	29	31.9%
	Capecitabine	17	18.7%
Lines of chemotherapy	first-line	26	28.6%
	second-line	45	49.5%
	third-line	15	16.5%
	fourth-line or more	5	5.5%
Number of involved organs	1	60	65.9%
	2	19	20.9%
	3	9	9.9%
	4	3	3.3%
Number of metastatic lesions	1	28	30.8%
	2	27	29.7%
	3	15	16.5%
	4	7	7.7%
	5	3	3.3%
	> 6	11	12.1%
Oligometastasis type treated with RT	Oligopersistent	36	39.6%
	Oligoprogressive	55	60.4%
Number of oligopersistent/oligoprogressive lesions treated with RT	1	46	50.5%
	2	26	28.6%
	3	11	12.1%
	4	3	3.3%
	5	5	5.5%
Site of lesions treated with RT	Lung	29	31.9%
	Liver	19	20.9%
	LN	30	33.0%
	Soft tissue	8	8.8%
	Lung+LN	2	2.2%
	Liver+LN	1	1.1%
	Soft tissue+LN	2	2.2%
RT modality	IMRT	42	46.2%
	SBRT/SRS	49	53.8%

Abbreviations: BED, biological equivalent dose with α/β 10 Gy; FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin; FOLFIRI, 5-fluorouracil, leucovorin, and irinotecan; Gy, Gray; LN, lymph node; IMRT, intensity modulated RT; mCRC, metastatic or recurrent colorectal cancer; RT, radiotherapy; SBRT, stereotactic body RT; SRS, stereotactic radiosurgery.

to next-line systemic therapy, infield tumor control of irradiated lesions, and OS were determined using the Kaplan–Meier method. The log-rank test was used for intergroup comparisons according to various tumor and treatment variables. Infield tumor control was measured from the time of the first MRT session to the progression of the irradiated lesions. OS was calculated from the initiation of

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Table 2 Patient and Treatment Characteristics in mCRC Patients Treated With Systemic Chemotherapy Alone (Non-MRT Group, n = 4066)

Variables	n		%
Age (year)	median (range)	65 (19-97)	
Sex	Male	2432	59.8%
	Female	1634	40.2%
Primary site	Colon	2555	62.8%
	Rectum	1511	37.2%
Tumor type	Metastatic	3613	88.9%
	Recurrent	453	11.1%
Chemotherapy regimen	FOLFOX	1720	42.3%
	FOLIFRI	1601	39.4%
	Capecitabine	745	18.3%
Sequence of current chemotherapy	First line	1849	45.5%
	Second line	1389	34.2%
	Third line	633	15.6%
	Fourth line or more	195	4.8%

Abbreviations: FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin; FOLFIRI, 5-fluorouracil, leucovorin, and irinotecan; mCRC, metastatic or recurrent colorectal cancer.

ongoing systemic chemotherapy to death by any cause. A P value < .05 was considered statistically significant.

Results

Patients

We identified a total of 4157 patients with mCRC who received first-line to fifth-line systemic chemotherapy (one or more patient duplicates). Among them, 91 patients (median age, 60 years) were treated with MRT to oligometastases during systemic chemotherapy. Oligoprogressive and oligopersistent cases accounted for 55 (60.4%) and 36 (39.6%) of the total, respectively. Forty-five (49.5%) patients were on FOLFOX, 29 (31.9%) on FOLFIRI, and 17 (18.7%) on capecitabine. At the time of MRT, 26 (28.6%) patients were on first-line therapy, 45 (49.5%) were on second-line therapy, and 20 (22%) were on third- or later-line chemotherapy. The median time interval between current chemotherapy and MRT was 5.0 (range, 0.5–36.7) months. Commonly irradiated sites were the lungs (31.9%), liver (20.9%), and lymph nodes (33.0%). MRT was delivered using IMRT (46.2%) and SBRT/SRS (53.8%). The baseline characteristics of the patients and treatment are presented in Table 1.

In the remaining 4066 patients with mCRC who received systemic chemotherapy but not MRT, the median age was 65 (range, 19–97) years. There were 2555 (62.9%) patients with colon cancer and 1511 (37.2%) with rectal cancer. Among them, 1720 (42.3%) patients were on FOLFOX, 1601 (39.4%) on FOLFIRI, and 745 (18.3%) on capecitabine. The characteristics of the patients and treatment are summarized in Table 2.

Change to next-line systemic therapy

In patients treated with MRT, the median follow-up duration after the initiation of current chemotherapy was 19.9 (range, 5.8–90.5) months. The cumulative incidence of change to next-line systemic therapy from the initiation of current systemic therapy was 68.0% and 83.6% at 1 and 2 years, respectively. The median time to change to next-line systemic therapy was 9.5 (range, 6.0–40.6; 95% confidence interval [CI], 8.5–10.5) months (Figure 1, Table 3). According to oligometastatic type, the median time to change to next-line systemic therapy was 9.5 (95% CI, 7.6–11.4) months for patients with oligoprogressive disease and 8.9 (95% CI, 7.3–10.5) months for patients with oligopersistent disease (P = .155) (Figure 2, Table 3). No factors, including age, primary site, or chemotherapy regimen, were associated with time to change to next-line systemic therapy (Table 3, Supplementary Table 1).

In the patients with mCRC who received systemic chemotherapy but not MRT, the cumulative incidence of change to next-line systemic therapy was 90.8% and 97.3% at 1 and 2 years, respectively. The median time to change to next-line systemic therapy was 5.0 (95% CI, 4.8–5.2) months (Table 4, Figure 1).

Infield tumor control, OS, and toxicity

The median follow-up duration after MRT was 13.8 (range, 2.6–85.0) months in the patients treated with MRT. The 1 and 2 year infield tumor control rates of irradiated lesions were 69.2% and 47.5%, respectively (Figure 3A). Infield tumor control was not significantly different between those with oligoprogressive and oligopersistent diseases (P = .434) (Figure 3B, Supplementary Table 1). No MRT-related factors, including radiation dose and modality, affected infield tumor control (Supplementary Table 1). In addition, at the time of the last follow-up, 83 (91.2%) of the patients were still alive. During the median follow-up period of 19.9 months from initiation of current chemotherapy, the 1 and 2 year OS rates were 98.7% and 95.1%, respectively. No grade 3 or higher MRT-related toxicities were observed. No systemic treatment interruption occurred because of MRT-related toxicity.

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Figure 1 Cumulative incidence of change to next-line systemic chemotherapy in 91 patients treated with systemic chemotherapy and metastasis-directed radiotherapy (MRT group) and in 4066 patients with metastatic or recurrent colorectal cancer treated with systemic chemotherapy without MRT (non-MRT group).

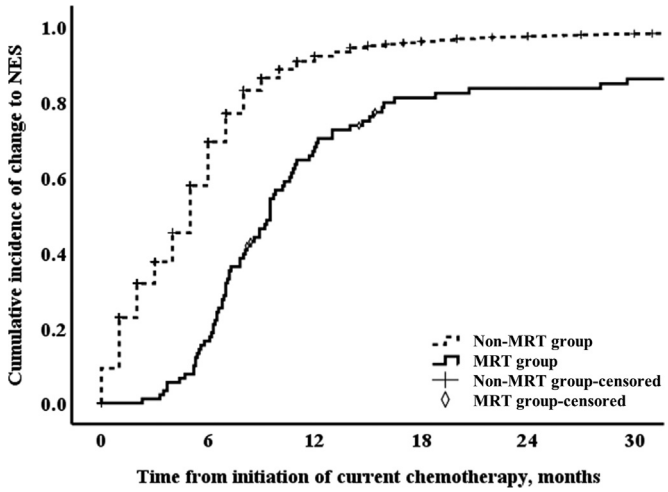

Table 3 Cumulative Incidence of Changing Next Line Systemic Chemotherapy (NES) (MRT Group, n = 91)

		Cumulative incidence of changing NES at 1 year/2 years, %	Period to changing NES, median (95% CI), months
Total		68.0/83.6	9.5 (8.5-10.5)
Oligometastasis type	Oligoprogression (n = 55)	60.6/78.1	9.5 (7.6-11.4)
	Oligopersistance (n = 36)	79.6/92.2	8.9 (7.3-10.5)
Chemotherapy regimen	FOLFOX (n = 45)	73.3/88.9	7.2 (6.1-8.3)
	FOLIFRI (n = 29)	75.9/90.8	9.5 (8.4-10.6)
	Capecitabine (n = 17)	37.4/51.3	14.0 (0.0-40.6)

Abbreviations: FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin; FOLFIRI, 5-fluorouracil, leucovorin, and irinotecan

Figure 2 Cumulative incidence of change to next-line systemic chemotherapy in patients treated with metastasis-directed radiotherapy according to oligometastatic type.

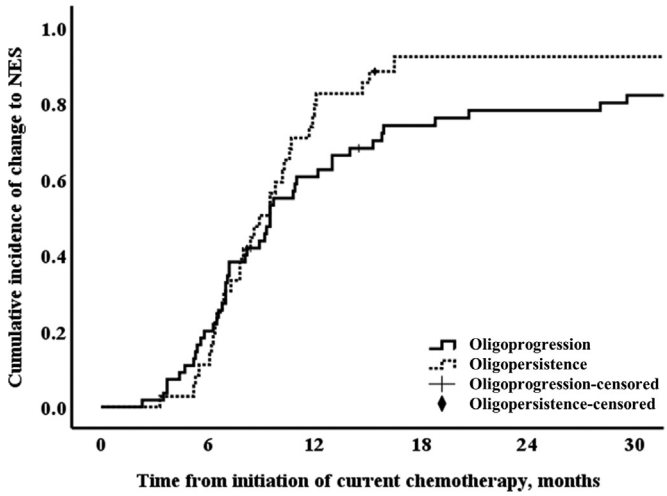

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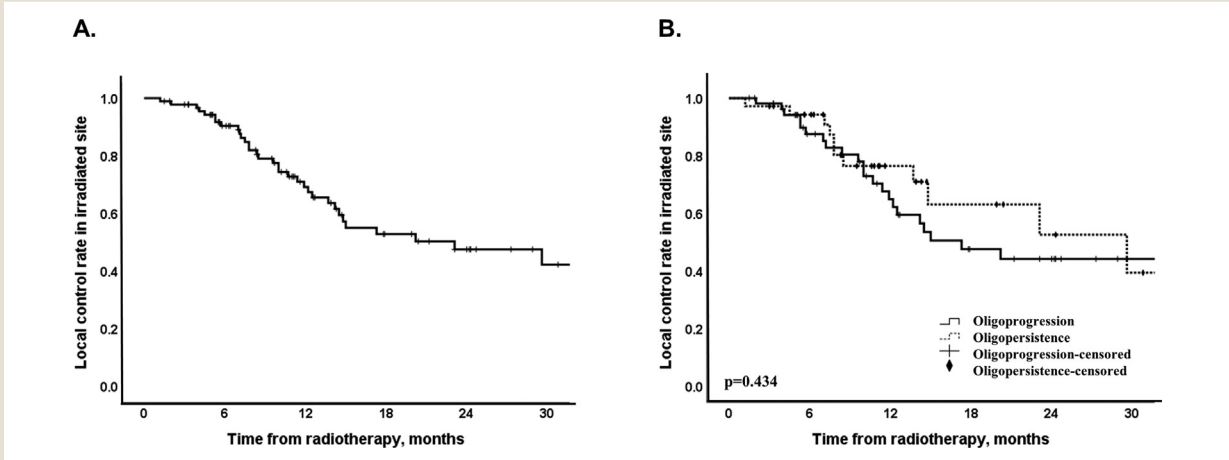
Table 4 Cumulative Incidence of Changing Next Line Systemic Chemotherapy (NES) in Control Group (Non-MRT Group, n = 4066)

		Cumulative incidence of changing NES at 1 year/2 years, %	Period to changing NES, median (95% CI), months
Total		90.8/97.3	5.0 (4.8-5.2)
Chemotherapy regimen	FOLFOX (n = 1720)	91.6/97.5	5.0 (4.8-5.2)
	FOLIFRI (n = 1601)	88.4/96.7	5.0 (4.8-5.2)
	Capecitabine (n = 745)	94.2/98.7	2.0 (1.9-2.2)

Abbreviations: FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin; FOLFIRI, 5-fluorouracil, leucovorin, and irinotecan

Figure 3 Local control rate in metastasis-directed radiotherapy irradiated sites (A) in all 91 patients and (B) according to oligometastatic type.



In patients who did not undergo MRT, survival data were available for 4021 patients. Among them, the 1 and 2 year OS rates were 80.4% and 64.1%, respectively, during a median follow-up duration of 17.7 (range, 0-127.3) months from the initiation of current chemotherapy (Figure 4).

Discussion

This study of patients with stage IV mCRC showed that the time to change to next-line systemic therapy could be prolonged in patients receiving MRT to oligoprogressive or oligopersistent metastases in conjunction with systemic therapy (median 9.5 months) compared with the general cohort of patients receiving systemic therapy alone (median 5 months). Furthermore, approximately one-third of patients were maintained on the same-line therapy for 1 year from when they were supposed to switch the therapy. However, caution is needed in interpreting these results, not only because they were derived from heterogeneous and disproportionate cohorts, but also because there was no head-to-head comparison.

The concept of treating oligoprogressive or oligopersistent disease while continuing systemic therapy beyond progression or after completion of systemic therapy is increasingly being recognized. These clinical scenarios are not a part of the classic state of the disease as initially proposed by Weichselbaum and Hellman[11] but an expansion in terms of genuine oligometastatic disease. Pembroke et al. reported that the survival outcomes of patients receiving SBRT for oligoprogression were inferior to that of those receiving SBRT for oligometastasis (median OS, 21.7 vs. 37 months).[12] The idea stemmed from the observation that (1) MDT (primarily SBRT) provided promising results with low toxicity in genuine oligometastatic disease; (2) later lines of chemotherapy are characterized by worse treatment outcomes; and (3) subpopulations of metastatic clones can spread through parallel evolution. Therefore, eradication of lesions that are not responding to systemic therapy could maximize the therapeutic benefit. Literature on the concept of treating oligoprogressive or oligopersistent disease is still limited.

The 5-year results of the STOMP randomized phase II trial on primary oligometastatic disease from prostate cancer have been presented recently. Metastasis-directed therapies using metastasectomy or SBRT significantly prolonged the time to initiation of systemic therapy (androgen deprivation therapy) from 8% to 34% at 5 years.[13,14] In oligoprogressive prostate cancer, a small retrospective study reported that metastasis-directed therapies (metastasectomy and MRT) delayed the need to change the systemic therapy (median survival without change in systemic therapy, 16 months).[15] In non-small-cell lung cancer, Kroeze et al. reported that 58% and 39% of patients with oligoprogressive and polyprogressive disease, respectively, under targeted therapy or immunotherapy, remained on the same drug at 1 year after MRT.[16] In metastatic renal cell carcinoma, early results of a phase II multi-center study showed that MRT with SBRT to oligoprogressive tumors during tyrosine kinase

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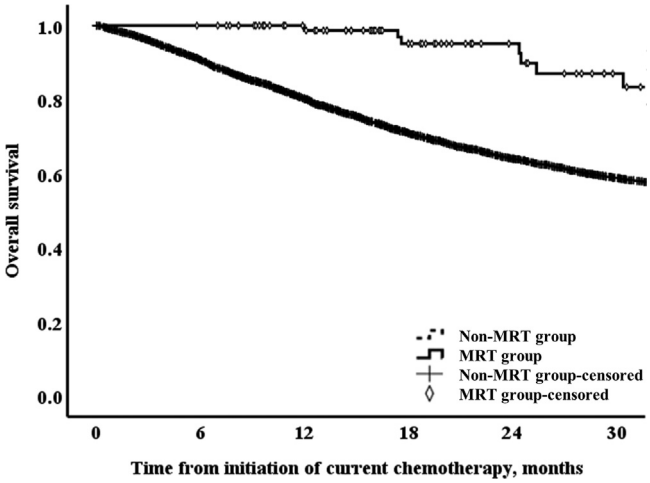
Figure 4 Overall survival in patients treated with systemic chemotherapy and metastasis-directed radiotherapy (MRT group) and those with metastatic or recurrent colorectal cancer treated with systemic chemotherapy without MRT (non-MRT group) *

*No statistical comparison was attempted.



inhibitor therapy effectively delayed the next line of systemic therapy by a significant amount of time (median time to change in systemic therapy, 12.6 months).[17]

Despite several successful randomized phase II trials of MRT (mostly using SBRT) in primary oligometastatic disease,[14,18,19] there is a significant unmet need for histology-specific studies that could potentially change routine oncology practice. Furthermore, there still exists a paucity of data on oligoprogressive or oligopersistent metastases, particularly from mCRC. Thompson et al. reported the outcomes of SBRT in 165 patients with mCRC in 2020.[20] Among them, 16 (10%) patients received MRT for oligoprogression. The median time to change the systemic therapy was 4.9 months, and 25% of patients maintained the same drug at 3 years. Pembroke et al. reported the outcomes of SBRT in 163 patients with multiple histology (mCRC: 17 cases [30%]), and median progression-free survival was 6.4 months in the oligoprogression group.[12] In our study, the median time to change systemic therapy was 9.5 months, which was consistent with, or slightly higher than, those reported previously. The discrepancy can be partly explained by the timing of MRT, patient selection, or metastatic sites. Of particular note is our finding that the time to change systemic therapy was not affected by the presentation type (oligoprogressive, 9.5 vs. oligopersistent, 8.9 months), although further studies are needed to draw more solid conclusions. Considering that the patients with mCRC should generally change the systemic therapy owing to disease progression within approximately 6 months, prolongation of this duration to 9.5 months would be clinically meaningful.

Our study sample comprised patients with oligoprogressive (60.4%) and oligopersistent (39.6%) diseases, and these are considered subcategories of the spectrum of the oligometastatic state. Patients with oligoprogression had a few metastases that progressed with a context of controlled metastatic disease after responding to systemic therapy, which presented in approximately 50% of metastatic diseases.[5,6,11] In this situation, physicians should administer subsequent treatments for controlling progressive cell clones with features of drug resistance. In contrast, oligopersistence is a slightly distinct entity that is controlled by systemic therapy.[5,11] In patients, the timing of local therapy is the main issue, as the goal is to treat the remaining lesions before any kind of progression for local consolidation. Most studies suggest that progression occurs in almost all original disease sites by analyzing the pattern of progression related to drug resistance.[21] Indeed, oligoprogression and oligopersistence are the direct consequence of the repopulation of residual disease-containing chemotherapy-resistant clones. Therefore, the incorporation of local treatment into systemic therapy is supported to avoid or to delay progression occurring at any of the preoccupied disease sites with an intention to salvage for oligoprogression[15,19,22–24] and to consolidate for oligopersistence.[18,25]

In our study involving patients with mCRC, infield tumor control following MRT remained modest. Dell'Acqua et al. and Jethwa et al. also reported infield tumor control of 70% following MRT for consecutive oligometastasis in mCRC.[26,27] Since radiation dose and histology are important factors influencing infield tumor control, further studies should be conducted to determine the impact of these factors in establishing an appropriate MRT scheme for oligometastatic disease. Furthermore, the molecular properties of oligometastatic solid tumors should be considered when performing MRT.[28] For instance, in the case of CRC, which was the focus of the current study, tumor genomic mutations, such as KRAS mutations or BRAF mutations, are associated with mortality, local recurrence, and radiation resistance.[27] These findings encourage

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biomarker development for this oligometastatic state that could potentially benefit from MRT by targeting the oligometastasis of each solid tumor.[29,30]

This study had some limitations inherent to its retrospective single-center study design with a small cohort. In addition, patient and tumor characteristics were relatively heterogeneous considering that the cohorts were previously administered multiple line chemotherapy and other prior treatments. Further, there is a strong selection bias regarding whether to administer MRT to oligometastatic lesions, which was decided via a multidisciplinary approach meeting. As emerging evidence has been accumulated regarding SBRT for oligometastatic diseases, more patients in the later period received MRT. Because we did not count the number of metastasis in all 4157 patients with mCRC, the incidence of oligoprogressive or oligopersistent disease in our study could be inaccurate and underestimated (2.2%). Furthermore, because patients with genuine de novo oligometastatic disease generally underwent metastasectomy with or without SBRT at our institution, patients in this study represented those with unresectable/inoperable disease or with a history of polymetastatic disease. MRT was delivered with different fractionation schedules, based on the number of lesions, and at various sites. We also recognize that our study has restrictions related to toxicity assessment through the review of medical records. Nevertheless, to the best of our knowledge, there are few reports of MRT to oligoprogressive or oligopersistent disease from mCRC. In addition, the increased administration period of ongoing systemic chemotherapy is hypothesis-generating, considering that MRT can reduce costs by postponing the change of next-line systemic therapy in oligometastatic mCRC.[26]

Conclusions

MRT prolonged the time to change systemic therapy and had a favorable infield tumor control in the oligoprogressive or oligopersistent setting of mCRC. Maintenance of ongoing systemic chemotherapy while introducing MRT may defer the change to next-line systemic therapy. However, due to the limitations and heterogeneity of the previous and present data, we are awaiting the results of ongoing, well-designed prospective trials. Considerable research is being focused on using MRT in the oligoprogression setting: (1) a randomized trial of SBRT to all oligoprogressions in breast or lung cancer (NCT03808662), (2) the UK-funded HALT trial (NCT03256981), a phase II/III trial on SBRT in patients with lung cancer carrying an oncogenic driver mutation, (3) the STOP trial (NCT02756793) on lung cancer, the first completed randomized controlled trial looking at SBRT for oligoprogression, (4) the TRAP trial (NCT03644303) on castrate-resistant prostate cancer, and (5) the AVATAR registry-based study (ACTRN12620001212943) on oligoprogressive estrogen receptor-positive breast cancer.

Clinical Practice Points

- The treatment strategy for oligometastatic tumor is increasingly being recognized as important.
- In our study on metastatic colorectal cancer (mCRC), metastasis-directed radiotherapy (MRT) for oligoprogressive or oligopersistent disease showed durable tumor regression and improved overall survival in addition to the current systemic therapy by controlling increasing local lesions.
- Additionally, nearly one-third of patients did not require the next-line systemic therapy for 1 year.
- Our findings demonstrate the promise that MRT has for disease suppression of oligoprogressive or oligopersistent mCRC.

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Disclosure

The authors declare no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clcc.2021.10.009.

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