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ORIGINAL ARTICLE

전이성 대장암 환자의 원발 종양 위치에 따른 고식적 절제술의 장기 생존율: 단일 기관 후향적 연구

김재현, 진솔, 전민지, 정현엽, 변상환, 정경원, 김성은, 문원, 박무인, 박선자
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Survival Benefit of Palliative Primary Tumor Resection Based on Tumor Location in Patients with Metastatic Colorectal Cancer: A Single-center Retrospective Study

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Background/Aims: The molecular underpinnings of colorectal cancer (CRC) vary according to the tumor location. The advantages of a palliative primary tumor resection in patients with metastatic CRC are controversial. This study examined the survival outcomes of a palliative primary tumor resection based on the tumor location in patients with metastatic CRC.
Methods: The medical records of 600 patients diagnosed with metastatic CRC between January 2000 and June 2018 were reviewed retrospectively. Patients undergoing surgery for both the primary tumor and metastatic lesions were excluded. The clinical factors affecting the long-term outcomes were evaluated according to the primary tumor location, and the long-term survival was compared between patients with and without a palliative primary tumor resection. The data were analyzed using the Kaplan-Meier estimator and multivariate Cox regression models.
Results: The median follow-up duration was 18 months (interquartile range, 10-28). Patients with right-sided CRC had a poor overall- and progression-free survival compared to those with left-sided CRC. In multivariate Cox regression analysis, the palliative primary tumor resection was an independent prognostic factor predicting better overall survival in patients with metastatic CRC, regardless of the primary tumor location.
Conclusions: The primary tumor location influences the prognosis, and that a primary tumor resection can improve the overall survival in patients with metastatic CRC, regardless of the primary tumor location. **(Korean J Gastroenterol 2020;76:17-27)**

Key Words: Colorectal neoplasms; Neoplasm metastasis; Tumor location; Surgery; Prognosis

INTRODUCTION

Colorectal cancer (CRC) was the third leading cause of worldwide cancer-related death in 2018, with an age-standardized mortality rate of 8.9 per 100,000.[1] Approximately one-quarter of patients with newly diagnosed CRC have metastatic lesions and half of the patients eventually proceed to metastatic CRC.[2] Despite the development of new CRC treatments, the overall survival (OS) of patients with metastatic CRC is still less than 30 months.[3]

CRC is a heterogeneous and complex disease resulting from the accumulation of genetic and epigenetic alterations.[4,5]

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The molecular heterogeneity of CRC varies according to the tumor location, and recent biological and clinical data indicate that the molecular pathway differs significantly between right-sided and left-sided CRC.[6] In terms of an embryological origin, right-sided and left-sided CRC derives from the embryonic midgut and embryonic hindgut, respectively.[7] Right-sided CRC is characterized more frequently by high microsatellite instability, CpG island methylation, B-type Raf Kinase (BRAF) mutations, and poor differentiation compared to left-sided CRC.[8,9] These differences result in different clinical behaviors, with right-sided CRC showing a poorer prognosis.[10,11]

Patients with a resectable primary tumor and metastatic lesions can be treated with surgery, and the removal of both the primary tumor and metastatic lesions is associated with favorable outcomes. On the other hand, the survival outcomes of a palliative primary tumor resection in patients with unresectable metastatic CRC remain unclear. A population-based analysis of 37,793 metastatic CRC patients showed that patients who underwent a palliative primary tumor resection had a better overall and disease-free survival.[12] On the other hand, an observational cohort study, including 15,154 metastatic CRC patients, showed that a palliative primary tumor resection was not associated with improved survival compared to systemic chemotherapy.[13] The current National Comprehensive Cancer Network (NCCN) guideline recommendations are as follows: consider a colon resection only if there is an imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms.[14]

In this study, it was hypothesized that a palliative primary tumor resection is an important factor affecting the prognosis of patients with metastatic CRC, and it differs according to the primary tumor location. This study investigated the long-term outcomes based on the primary tumor location in patients with metastatic CRC and compared the survival outcomes based on a palliative primary tumor resection.

SUBJECTS AND METHODS

1. Patients and data collection

The medical records of patients diagnosed with metastatic CRC at Kosin University Gospel Hospital (Busan, Korea) between January 2000 and June 2018 were reviewed retrospectively; patients with histologically confirmed colonic or rectal adenocarcinoma were included. Patients whose medical records did not include the clinicopathological and follow-up data, and patients undergoing surgery for both the primary tumor and metastatic lesions were excluded. This study was approved by the Institutional Review Board of Kosin University Gospel Hospital (KUGH 2020-03-036).

The following detailed clinical data were collected: patient age, sex, BMI, blood type, history of smoking or alcohol, family cancer history, performance status, co-morbidities, primary tumor location and metastatic sites, histopathology, biomarkers including microsatellite instability (MSI), KRAS and NRAS, tumor stage, laboratory findings, and treatment outcomes, including chemotherapy, radiotherapy, and surgery.

2. Classification of primary tumor location

The clinicopathological factors were evaluated according to the primary tumor location. Primary tumors originating in the appendix, cecum, ascending colon, hepatic flexure, and transverse colon were classified as right-sided CRC. Primary tumors originating in the splenic flexure, descending colon, sigmoid colon, and rectum were classified as left-sided CRC. Patients with tumors originating on both sides were classified as indeterminate-sided and were excluded.

3. Definition of tumor resection

A palliative primary tumor resection was defined as the removal of the primary tumor without removing the metastatic lesions. The palliative primary tumor resection included a left anterior resection, anterior resection, Miles operation, Hartmann's operation, left hemicolectomy, segmentectomy, right hemicolectomy, and ileocecectomy with a lymph node dissection. No tumor resection was defined when the primary tumor was not removed.

4. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 24.0 (IBM Co., Armonk, NY, USA). A student's t-test and chi-square test were performed for the continuous and categorical variables, where appropriate. The OS was measured from the date of the CRC diagnosis to the date of death or final follow-up. The progression-free survival (PFS) was measured from the date of the CRC diagnosis to the date of recurrence or final follow-up. CRC recurrence was diagnosed based on the radiological and endoscopic histopathological data. Kaplan-Meier curves were used to con-

Table 1. Baseline Characteristics according to the Tumor Location

Characteristic	Right-sided (n=143)	Left-sided (n=457)	p-value
Age (years)	63 (32-83)	60 (31-91)	0.004
Sex			0.001
Male	68 (47.6)	289 (63.2)	
Female	75 (52.4)	168 (36.8)	
Body mass index (kg/m^2)			0.003
<20	25 (17.5)	90 (19.7)	
≥20 and <23	35 (24.5)	178 (38.9)	
≥23	77 (53.8)	182 (39.8)	
Missing	6 (4.2)	8 (1.5)	
Blood type			0.646
A	53 (37.1)	158 (34.9)	
B	38 (26.6)	107 (23.6)	
AB	16 (11.2)	48 (10.6)	
O	31 (21.7)	129 (28.5)	
Missing	5 (3.5)	11 (2.4)	
Smoking			0.788
None	107 (74.8)	342 (75.0)	
Current	11 (7.7)	42 (9.2)	
Ex-smoker	25 (17.5)	72 (15.8)	
Alcohol			0.822
None	110 (76.9)	339 (74.3)	
Current	33 (23.1)	117 (25.7)	
Family history (cancer related)			0.930
No	127 (89.4)	409 (89.7)	
Yes	15 (10.6)	47 (10.3)	
ECOG performance status			0.893
0	95 (66.4)	311 (68.1)	
1	37 (25.9)	113 (24.7)	
2	8 (5.6)	20 (4.4)	
3	1 (0.7)	6 (1.3)	
4	0 (0.0)	1 (0.2)	
Missing	2 (1.4)	6 (1.3)	
Co-morbidities			0.705
Hypertension	51 (35.7)	154 (33.7)	
DM	35 (24.5)	88 (19.3)	
CLD	7 (4.9)	18 (3.9)	
IHD	4 (2.8)	6 (1.3)	
CKD	3 (2.1)	5 (1.1)	
COPD	2 (1.4)	3 (0.7)	
Histology			<0.001
Well differentiated	15 (10.5)	76 (16.6)	
Moderate differentiated	89 (62.2)	324 (70.9)	
Poorly differentiated	23 (16.1)	36 (7.9)	
SRC & mucinous type	16 (11.2)	21 (4.6)	

Table 1. Continued

Characteristic	Right-sided (n=143)	Left-sided (n=457)	p-value
Biomarker analysis			
Microsatellite			0.302
MSS	18 (12.6)	64 (14.0)	
MSI-low	1 (0.7)	2 (0.4)	
MSI-high	2 (1.4)	2 (0.4)	
Missing	122 (85.3)	389 (85.2)	
KRAS/NRAS			0.036/0.479
Wild	14 (9.8)/17 (11.9)	81 (17.7)/72 (15.8)	
Mutation	20 (14.0)/1 (0.7)	45 (9.8)/4 (0.9)	
Missing	109 (85.3)/125 (87.4)	331 (72.4)/381 (83.4)	
Metastatic site			
Liver	90 (62.9)	323 (70.7)	0.098
Lung	33 (23.1)	123 (26.9)	0.384
Distant lymph nodes	32 (22.4)	99 (21.7)	0.908
Peritoneum	51 (35.7)	80 (17.5)	<0.001
Bone	10 (7.0)	32 (7.0)	1.0
Ovary	7 (4.9)	17 (3.7)	0.624
Spleen	6 (3.5)	7 (1.5)	0.098
Adrenal gland	2 (1.4)	3 (0.7)	0.501
Pancreas	1 (0.7)	4 (0.9)	1.0
Abdominal wall	1 (0.7)	3 (0.7)	1.0

Values are presented as mean (range) or number (%).
ECOG, Eastern Cooperative Oncology Group; DM, diabetes mellitus; CLD, chronic liver disease; IHD, ischemic heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; SRC, signet ring cell; MSS, microsatellite stable; MSI, microsatellite instability.

struct survival curves based on cumulative incidences and compared using a log-rank test. The Cox proportional hazards regression model was used to assess the factors affecting the OS and PFS. p values <0.05 were considered significant.

RESULTS

1. Baseline characteristics and laboratory findings according to the tumor location.

Six hundred and six patients were diagnosed with metastatic CRC between January 2000 and June 2018. One hundred and forty-three patients (23.8%) had right-sided CRC, and 457 patients (76.2%) had left-sided CRC. Six subjects had tumors located on both the right and left sides, whose origin could not be determined and were excluded. The mean age was 61 years, and 357 subjects (59.5%) were male. The median follow-up duration was 18 months (interquartile range, 10-28). Several differences in the baseline characteristics, including age, sex, BMI, histology, and metastatic sites were observed between patients with right-sided and left-sided CRC. Table 1 lists the baseline characteristics. The blood tests showed similar findings between patients with right- and left-sided CRC, except that patients with right-sided CRC had low hemoglobin, high platelet count, and high CA 19-9 levels. These were assessed at the time of diagnosis and are summarized in Table 2.

2. Treatment outcomes according to tumor location

Of the 600 patients included, 570 (95.0%) were treated with chemotherapy, and 99 patients (16.5%) were treated with radiotherapy (Table 3). One hundred fifty-three patients (25.5%) were treated with more than three lines of chemotherapy, which was more common in patients with left-sided CRC compared to right-sided CRC (27.8% vs. 18.2%). The first-line regimen (irinotecan, oxaliplatin, capecitabine, or fluorouracil) was similar in patients with right and left-sided CRC, biological treatment (cetuximab or bevacizumab) was not performed. A palliative primary tumor resection was per-

Table 2. Laboratory Findings (at Diagnosis) according to the Tumor Location

	Right-sided (n=143)	Left-sided (n=457)	p-value
Hemoglobin (g/dL)	10.9±2.3	11.9±2.1	<0.001
WBC count (×10^3/μL)	8.5±2.9	8.1±2.9	0.199
Platelet (×10^3/μL)	334.4±125.7	299.8±166.3	0.022
Albumin (g/dL)	3.8±0.5	4.0±1.9	0.128
AST (U/L)	31.3±24.6	34.9±29.3	0.177
ALT (U/L)	22.5±9.4	26.6±27.4	0.101
Alkaline phosphatase (U/L)	147.2±164.8	148.1±174.2	0.959
Total bilirubin (mg/dL)	0.7±0.3	0.9±3.7	0.433
Total cholesterol (mg/dL)	169.9±49.1	182.1±56.5	0.035
Triglyceride (mg/dL)	103.0±77.3	105.2±54.1	0.728
LDL cholesterol (mg/dL)	112.9±83.5	116.5±54.0	0.631
HDL cholesterol (mg/dL)	41.8±17.0	41.5±14.5	0.814
LDH (IU/L)	604.9±515.4	614.9±505.2	0.839
Glucose (mg/dL)	108.8±29.7	108.5±35.3	0.954
HbA1c (%)	7.1±1.6	7.4±1.8	0.484
CEA (ng/mL)	326.6±1,196.4	459.3±1,389.7	0.308
CA19-9 (U/mL)	869.4±2,017.3	407.6±1,219.4	0.011
HS-CRP (mg/dL)	3.6±5.0	2.8±4.9	0.238

Values are presented as mean±standard deviation.
WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; LDH, lactate dehydrogenase; HbA1c, hemoglobin A1c; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; HS-CRP, high sensitivity C-reactive protein.

Table 3. Treatment Outcomes according to the Tumor Location

	Right-sided (n=143)	Left-sided (n=457)	p-value
Chemotherapy			
Total number	14 (1-60)	16 (1-142)	0.055
≥Third line[a]	26 (18.2)	127 (27.8)	0.028
Regimen (first line)			0.604
Irinotecan-based	46 (32.2)	135 (29.5)	
Oxaliplatin-based	77 (53.8)	254 (55.6)	
Capecitabine-based	5 (3.4)	15 (3.3)	
Fluorouracil-based	7 (4.6)	28 (6.1)	
No chemotherapy	8 (5.4)	22 (4.8)	
Biologics			0.576
Cetuximab	11 (7.7)	44 (9.6)	
Bevacizumab	35 (24.5)	108 (23.6)	
Radiotherapy	19 (13.3)	80 (17.5)	0.539
Primary tumor	2 (1.4)	29 (6.3)	
Metastatic site	17 (11.9)	51 (11.2)	
Surgery			0.027
Palliative primary tumor resection	87 (60.8)	228 (49.9)	
No tumor resection	56 (39.2)	229 (50.1)	

Values are presented as mean (range) or number (%).
[a]Number of patients with more than three lines of chemotherapy.

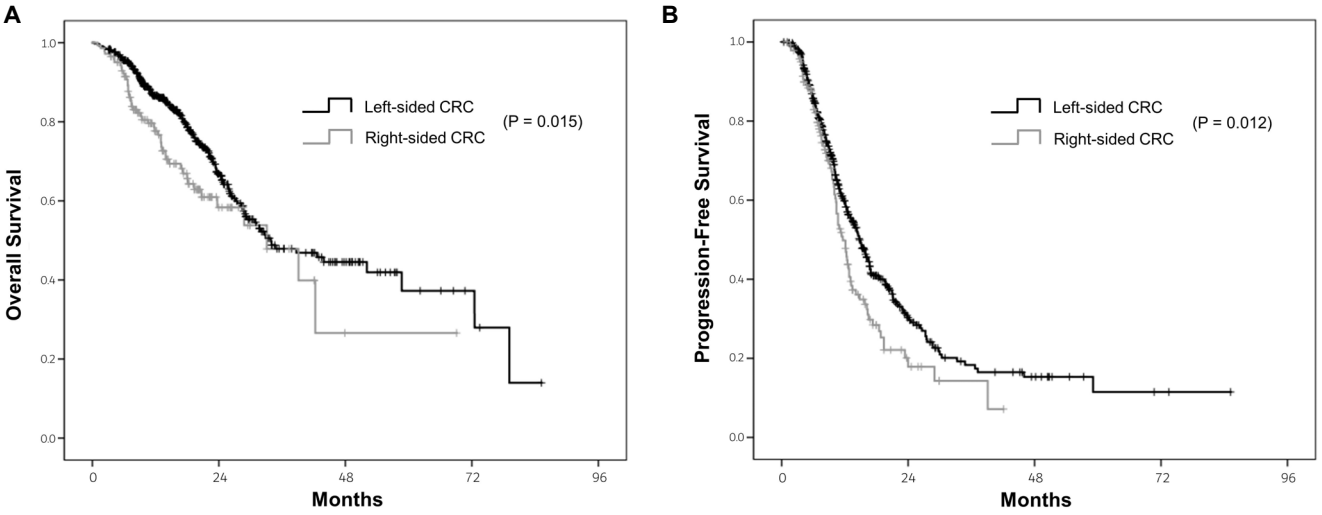

Fig. 1. Kaplan-Meier analysis showing the overall survival (A) and progression-free survival (B) for patients with metastatic colorectal cancer based on primary tumor location. CRC, colorectal cancer.

Table 4. Comparison of the Survival Outcomes according to Tumor Location between Patients with and without Palliative Primary Tumor Resection

	Right-sided (n=143)	p-value	Left-sided (n=457)	p-value
1-year OS		<0.001		<0.001
Palliative primary tumor resection (%)	70.1		78.5	
No tumor resection (%)	33.9		54.6	
3-year OS		0.043		<0.001
Palliative primary tumor resection (%)	8.0		16.2	
No tumor resection (%)	0.0		5.7	
1-year PFS		<0.001		<0.001
Palliative primary tumor resection (%)	47.1		53.1	
No tumor resection (%)	16.1		31.0	
3-year PFS		0.520		0.179
Palliative primary tumor resection (%)	2.3		5.7	
No tumor resection (%)	0.0		3.1	

OS, overall survival; PFS, progression-free survival.

formed more in patients with right-sided CRC.

3. OS and disease-free survival according to tumor location

Fig. 1 shows the Kaplan-Meier curves for OS and PFS according to the tumor location. Patients with right-sided CRC had a poorer OS and PFS than those with left-sided CRC. The long-term outcomes for patients with or without a palliative primary tumor resection were evaluated. Table 4 lists the 1-year and 3-year OS/PFS rates for patients with or without a palliative primary tumor resection. Patients who underwent a palliative primary tumor resection had a significantly better 1-year OS and PFS than those without a tumor resection, regardless of the primary tumor location. These results were similar compared to the 3-year OS between a palliative primary tumor resection and no tumor resection, regardless of the primary tumor location. Figs. 2, 3 show the Kaplan-Meier curves for the OS and PFS for patients with right-sided and left-sided CRC according to the palliative primary tumor resection. Patients who underwent a palliative primary tumor resection had a better OS and PFS than those without a tumor resection, regardless of the primary tumor location.

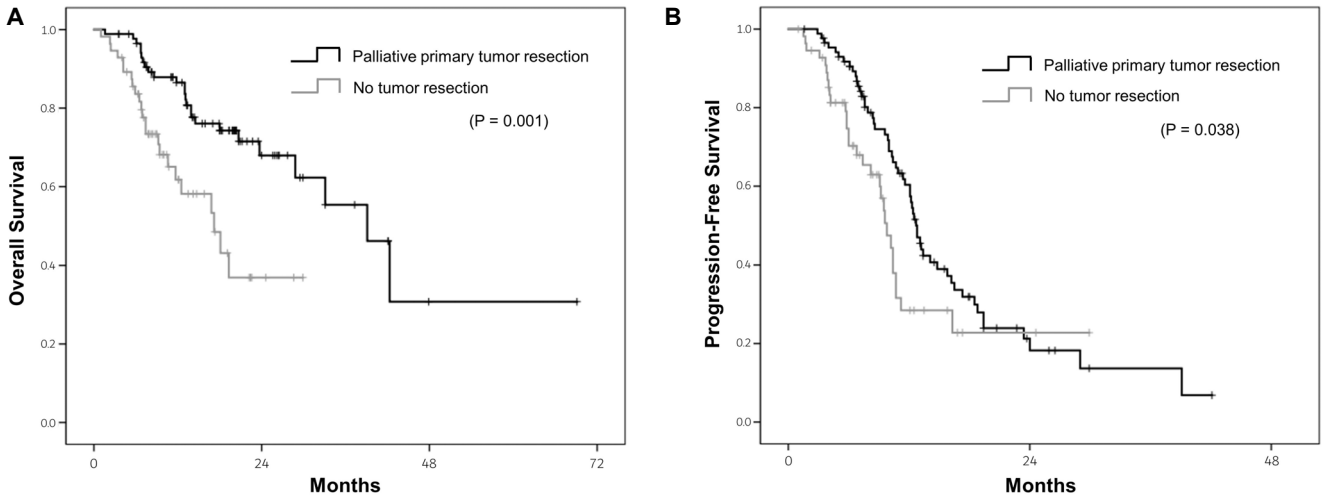

Fig. 2. Kaplan-Meier analysis showing the overall survival (A) and progression-free survival (B) for patients with right-sided colorectal cancer based on palliative primary tumor resection.

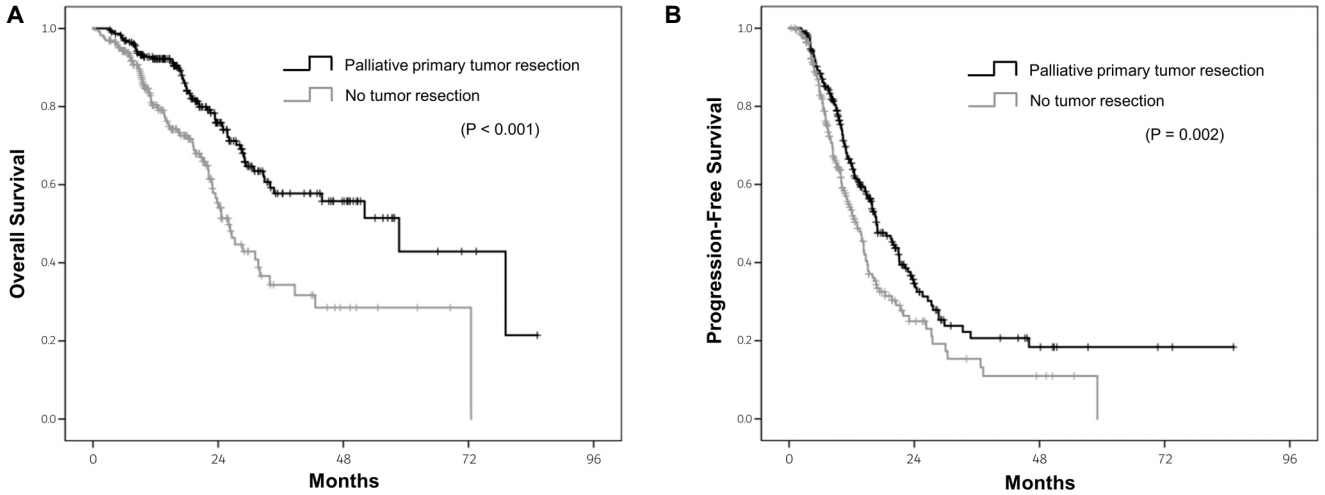

Fig. 3. Kaplan-Meier analysis showing the overall survival (A) and progression-free survival (B) for patients with left-sided colorectal cancer based on palliative primary tumor resection.

4. Factors affecting long-term outcomes

The factors affecting the long-term outcomes were assessed according to the tumor location by multivariate analysis using the Cox proportional hazards regression. As shown in Table 5, a palliative tumor resection was a significant prognostic factor affecting the better OS (hazard ratio [HR], 0.41; 95% CI, 0.22-0.76; p=0.004), but not PFS (HR, 0.63; 95% CI, 0.39-1.01; p=0.053) in patients with right-sided CRC. Poorly differentiated histology and CA 19-9 also influence the survival outcomes. A palliative tumor resection was found to be a significant prognostic factor for a better OS (HR, 0.53; 95% CI, 0.37-0.75; p<0.001) and PFS (HR, 0.76; 95% CI, 0.58-0.99; p=0.041) in patients with left-sided CRC (Table 6). Poorly differentiated histology, CEA, CA19-9, and LDH also affect the survival outcomes.

DISCUSSION

These findings show the prognostic roles of primary tumor location and primary tumor resection in patients with metastatic CRC. The data suggest that a primary tumor resection can improve the OS in patients with metastatic CRC, regardless of the primary tumor location.

In the present study, patients with right-sided CRC had sev-

Table 5. Prognostic Factors in Patients with Metastatic Colorectal Cancer and a Right-sided Primary Tumor

Predictor	OS			PFS		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)						
<70	1			1		
≥70	0.51	0.24-1.08	0.077	1.08	0.65-1.78	0.771
Sex						
Female	1			1		
Male	1.71	0.92-3.19	0.089	1.26	0.79-2.01	0.328
Histology						
Well differentiated	1			1		
Moderate differentiated	1.11	0.40-3.09	0.840	2.30	0.95-5.55	0.064
Poorly differentiated	4.90	1.70-16.49	0.006	3.93	1.46-10.61	0.007
SRC & mucinous type	2.36	0.64-8.73	0.195	1.90	0.67-5.37	0.228
CEA (ng/mL)						
<20.0	1			1		
≥20.0	1.30	0.66-2.54	0.447	0.83	0.50-1.36	0.453
CA 19-9 (U/mL)						
<30.0	1			1		
≥30.0	1.63	0.79-3.35	0.185	2.14	1.26-3.66	0.005
LDH (IU/L)						
<400	1			1		
≥400	1.55	0.84-2.85	0.162	1.06	0.68-1.66	0.792
Surgery						
No tumor resection	1			1		
Palliative primary tumor resection	0.41	0.22-0.76	0.004	0.63	0.39-1.01	0.053
Biologic treatment						
Without biologics	1			1		
With biologics	0.60	0.32-1.11	0.103	1.40	0.89-2.18	0.145

OS, overall survival; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; LDH, lactate dehydrogenase.

eral characteristics that differed from those with left-sided CRC, which included older age, more female patients, BMI 23 kg/m^2 or higher, poorly differentiated/signet ring cell/mucinous histology, and peritoneal metastasis. These findings are consistent with other recent data,[6,8,9] which likely result from different molecular carcinogenesis pathways between right- and left-sided CRC. The primary tumor location is associated with the prognosis in CRC patients, and generally, right-sided CRC has a poorer outcome.[15-17] The data shows that patients with right-sided CRC have poorer survival outcomes than those with left-sided CRC. In propensity score analysis, right-sided CRC was diagnosed at a more advanced state within stage IV disease and showed significantly poorer prognosis than left-sided CRC.[18] In this study, the characteristics of patients with right-sided CRC, including older age, more female patients, and more poorly differentiated/signet ring cell/mucinous histology, are considered as contributors to poorer survival benefits. A primary tumor location influences the selection of the chemotherapy regimen in patients diagnosed with metastatic CRC. A retrospective analysis of the CRYSTAL and FIRE-3 trials analyzed RAS wild-type populations. They showed that first-line FOLFIRI (irinotecan, fluorouracil, and leucovorin) plus cetuximab benefitted patients with left-sided CRC more than those with right-sided CRC.[7] A meta-analysis of first-line clinical trials, including PRIME, CRYSTAL, FIRE-3, and the CALGB/SWOG 80405 study, indicated that patients with RAS wild-type left-sided CRC had a significant survival benefit from the addition of an anti-epidermal growth factor receptor (EGFR) antibody to conventional chemotherapy.[19] Based on these results, the current NCCN

Table 6. Prognostic Factors in Patients with Metastatic Colorectal Cancer and a Left-sided Primary Tumor

Predictor	OS			PFS		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)						
<70	1			1		
≥70	0.89	0.57-1.38	0.605	0.78	0.57-1.08	0.139
Sex						
Female	1			1		
Male	1.12	0.78-1.62	0.546	1.20	0.91-1.58	0.191
Histology						
Well differentiated	1			1		
Moderate differentiated	1.51	0.85-2.67	0.158	0.98	0.60-1.60	0.924
Poorly differentiated	4.28	2.05-8.92	<0.001	0.78	0.35-1.75	0.541
SRC & mucinous type	2.66	1.01-7.02	0.048	0.82	0.30-2.25	0.703
CEA (ng/mL)						
<20.0	1			1		
≥20.0	1.23	0.80-1.90	0.340	1.45	1.09-1.92	0.010
CA 19-9 (U/mL)						
<30.0	1			1		
≥30.0	1.53	1.07-2.18	0.020	1.22	0.91-1.65	0.182
LDH (IU/L)						
<400	1			1		
≥400	1.17	0.80-1.71	0.416	1.44	1.08-1.91	0.012
Surgery						
No tumor resection	1			1		
Palliative primary tumor resection	0.53	0.37-0.75	<0.001	0.76	0.58-0.99	0.041
Biologic treatment						
Without biologics	1			1		
With biologics	0.95	0.67-1.34	0.762	0.96	0.74-1.25	0.780

OS, overall survival; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; LDH, lactate dehydrogenase.

guidelines recommend the addition of anti-EGFR antibody to conventional chemotherapy for metastatic CRC patients with KRAS/NRAS/BRAF wild type genes and left-sided tumors.[14]

The data revealed a survival benefit of palliative primary tumor resection. In this study, a palliative primary tumor resection was performed more in patients with right-sided CRC than those with left-sided CRC (60.8% vs. 49.9%, Table 3). Multivariate analysis revealed a palliative primary tumor resection to be an independent prognostic factor for a better OS, regardless of the primary tumor location. Surgical resection of the primary tumor is a curative treatment for CRC patients without metastasis. On the other hand, the role of primary tumor resection for CRC patients with metastases is unclear. A reduction of the tumor burden may lead to a better response to systemic therapy in patients with metastatic CRC.[20] A reduction of the tumor burden has a survival benefit for primary renal or ovarian tumors with metastatic lesions.[21,22] A recent study suggested that a primary tumor resection can prevent micro-metastases to the liver parenchyma by increasing the angiogenic markers, including vascular endothelial growth factor (VEGF) A, VEGF receptor 1, VEGF receptor 2, and placental growth factor.[23] On the other hand, some studies reported worsening liver or lung metastases after a primary tumor resection, which was attributed to the depletion of anti-angiogenic proteins, such as angiostatin and endostatin produced by the primary tumor.[24,25] Further studies will be needed to clarify the role of the primary tumor resection for patients with metastatic CRC.

This study had several limitations. First, this study had a retrospective, single-center design, which means the selection

bias could not be avoided, even though an attempt was made to minimize bias by repeatedly reviewing the medical records. Second, the efficacy of an anti-EGFR antibody plus conventional chemotherapy depending on the location of the primary tumor could not be confirmed, because the number of tests for KRAS/NRAS and the proportion of patients treated with biologics were not high enough to assess the efficacy. Third, tumors originating from the transverse colon were classified as right-sided CRC for the convenience of analysis, but classifying transverse colon cancer as right-sided vs. left-sided is controversial. To overcome this limitation, further well-designed studies for the characterization of transverse colon cancer will be needed.

In conclusion, this study showed that the primary tumor location has a prognostic effect on patients with metastatic CRC. Moreover, a palliative primary tumor resection is a significant prognostic factor affecting better OS, regardless of the primary tumor location. Based on these results, a palliative primary tumor resection is a suitable option for patients with metastatic CRC to improve the long-term outcomes, regardless of the primary tumor location.

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