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Primary Tumor Resection is a Powerful Predictor of Long-term Outcome of Left-side Obstructive Colorectal Cancer

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ABSTRACT

Background: Stent placement and per anus ileus catheterization have important roles as a bridge to surgery for patients with left-side obstructive colorectal cancer (OCC). However, a predictor of the long-term outcome of left-side OCC has not been elucidated.
Methods: Between 2001 and 2017, 40 patients with left-side OCC, 80 years of age or younger, who underwent emergency surgery at Kashiwa Hospital, Jikei University, were enrolled into this retrospective study. We compared 24 patients undergoing primary tumor resection with temporary colostomy with 16 patients undergoing only the creation of the decompression colostomy without primary tumor resection as the first operation.
Results: Three of 16 patients (19%) who underwent only the creation of colostomy as the first operation could undergo the primary tumor resection as the secondary operation a month after the first operation. The other 13 patients who could not undergo the primary tumor resection received intensive chemotherapy consecutively. The 5-year survival rate of the patients with primary tumor resection as the first operation was 56.5%, whereas that of patients with only the creation of colostomy as the first operation was 18.8% ($p<0.001$). The fact that the primary tumor resection could not be performed was an independent risk factor by multivariate analyses ($p=0.002$).
Conclusion: Primary tumor resection is a powerful predictor of long-term outcome of left-side OCC.
Key words: obstructive colorectal cancer, primary tumor resection, predictor, stoma

Abbreviations:
OCC - obstructive colorectal cancer,
FOLFOX - folinic acid plus oxaliplatin,
CapeOX - capecitabine plus oxaliplatin,
CEA - carcinoembryonic antigen,
CT - computed tomography,
PET - positron emission tomography.

INTRODUCTION

Intestinal obstruction often occurs in patients with advanced colorectal cancer. Patients with acute left-side colonic obstruction have traditionally undergone emergency surgery that often requires the creation of a stoma, and approximately 40% of them will never have their stoma reversed (1-3). Those with a permanent colostomy have a lower health-related quality of life. Stent placement can not only relieve the tumor obstruction but also buy sufficient time for intestinal preparation (4-7). Per anus ileus catheterization can also temporarily relieve part of the intestinal obstruction and buy time for pre-operative preparation (8,9). Those procedures have important roles as a bridge

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to surgery. However, a predictor of the long-term outcome of left-side obstructive colorectal cancer (OCC) has not been elucidated.

MATERIALS AND METHODS

Between 2001 and 2017, 40 patients with left-side OCC, 80 years of age or younger, who underwent emergency operation at Kashiwa Hospital, Jikei University, were enrolled into this retrospective study. They consisted of 24 patients undergoing primary tumor resection with temporary colostomy, so called Hartmann's operation, and 16 patients undergoing only the creation of the decompression colostomy without primary tumor resection as the first operation. The medical records of all patients were reviewed and classified according to the Japanese Classification of Colorectal Carcinoma (10).

Treatment after the first surgery

The primary tumor resection group (n=24) received oxaliplatin combination intensive chemotherapy, such as infusional 5-fluorouracil and folinic acid plus oxaliplatin (FOLFOX), S-1 (Taiho Pharmaceuticals Co. Ltd, Tokyo, Japan) plus oxaliplatin (SOX), capecitabine plus oxaliplatin (CapeOX), for 6 months. After the chemotherapy, the patients without recurrence underwent intestinal reconstruction with closure of the colostomy. The other patients with recurrence received intensive chemotherapy consecutively according to the Japanese Society for Cancer of the Colon and Rectum guidelines (11) without closure of the colostomy.

Conversely, 16 patients with only the creation of the decompression colostomy as the first operation were scheduled to undergo the secondary operation, primary tumor resection, a month after the first operation. The patients who could not undergo the secondary operation received intensive chemotherapy consecutively according to the guidelines (11). The patients who could undergo the secondary operation also received intensive chemotherapy consecutively according to the guidelines (11) after the secondary operation.

Treatment schedule

All patients were followed for 5 years; during this period, physical examinations, routine blood analyses, and serum carcinoembryonic antigen (CEA) measurements were conducted every two months after surgery. Computed tomography (CT) was performed every 2 months or when a patient's serum CEA value was higher than the normal level of 5.0 ng/ml. Colonoscopy was performed every year or when a stool sample was positive for blood. Positron emission tomography (PET) or PET/CT was occasionally employed to detect occult metastasis for patients who had equivocal conventional imaging studies.

Statistical analysis

Continuous variables are expressed as the mean and range. The Wilcoxon rank-sum test was used for the comparison of continuous variables, and a chi-squared test was used for the comparison of categorical data. Survival rate after surgery was examined by the Kaplan-Meier method and by log-rank analysis. Variables affecting postoperative survival were analyzed using the Cox proportional hazards regression. A p-value of less than 0.05 indicated significance. All data were analyzed with IBM SPSS Statistics, version 24.0 (IBM Japan, Ltd, Tokyo, Japan).

RESULTS

Comparison of characteristics between the primary tumor resection group and only the creation of the decompression colostomy group in the first operation (table 1)

Significant differences were identified in mean surgical time, mean blood loss, mean postoperative hospital stay, stage, and metastatic site, while significant differences were not found in mean age, gender, and primary tumor location. All 24 patients undergoing primary tumor resection with temporary colostomy could undergo intestinal reconstruction with closure of the colostomy after the intensive chemotherapy. Three of 16 patients (19%) who underwent only the creation of the decompression colostomy as the first operation could undergo the primary tumor resection as the secondary operation a month after the first operation. The other 13 patients who could not undergo the primary tumor resection received intensive chemotherapy consecutively according to the guidelines (11).

Comparison of the 5-year survival rate between the primary tumor resection group and only the creation of the decompression colostomy group in the first operation

The 5-year survival rate of the 24 patients who underwent the primary tumor resection as the first operation was 56.5%, whereas that of the 16 patients

Table 1 - Comparison of characteristics primary tumor resection group and only the creation of colostomy group in the first operation

Characteristic	Primary tumor resection (n=24)	Only creation of colostomy (n=16)	p value
Mean age (range), years	69.3 (53-80)	68.1 (45-80)	0.765
Gender, n (%)			0.101
Male	13 (54)	13 (81)	
Female	11 (46)	3 (19)	
Tumor location			0.199
Colon	8 (33)	9 (56)	
Rectum	16 (67)	7 (44)	
Mean tumor diameter (rang), mm	80.8 (70-140)	–	
Pathology, n (%)			
Well differentiated adenocarcinoma	2 (8)	–	
Moderately differentiated adenocarcinoma	22 (92)	–	
Mean surgical time (min)	232.7 (80-562)	80 (45-130)	< 0.001
Mean blood loss (ml)	390.2 (0-860)	10.0 (0-70)	< 0.001
Mean postoperative hospital stay (days)	15.5 (10-30)	10.8 (8-18)	< 0.001
Stage, n (%)			
II	8 (33)	0 (0)	
III a	5 (21)	3 (19)	
III b	1 (4)	0 (0)	
IV	10 (42)	13 (81)	
Metastatic sites, n (%)			0.001
Peritoneum	0 (0)	13 (81)	
Liver	10 (42)	6 (38)	
Lung	3 (13)	2 (13)	

who underwent only the creation of the decompression colostomy was 18.8%, and the difference was significant (p<0.001) (*figure 1*).

Cox proportional hazards regression for postoperative survival

To determine the variables affecting postoperative survival, 5 variables (age, gender, stage, primary tumor location, and primary tumor resection) were analyzed using the Cox proportional hazards regression. Stage (p=0.001) and primary tumor resection (p=0.002) were identified as independent contributing factors to postoperative recurrence (*table 2*).

DISCUSSION

In the best supportive care without any systemic therapy, the median survival time of patients with unresectable colorectal cancer has been reported to be

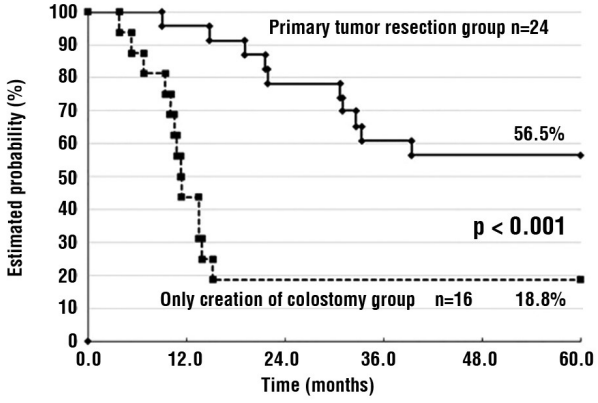

Figure 1 - Comparison of the 5-year survival rate between the primary tumor resection group and only the creation of the decompression colostomy group in the first operation

Table 2 - Multivariate analyses using the Cox proportional hazard model for postoperative recurrence

Variable	Hazard ratio (95% confidence interval)	p value
Age (years)		
≥ 70	0.780 (0.299-2.038)	0.612
< 70	1	
Gender		
Female	1.019 (0.357-2.905)	0.972
Male	1	
Stage		
IV	33.752 (4.097-271.439)	0.001
Other	1	
Primary tumor location		
Rectum	1.191 (0.461-3.076)	0.718
Colon	1	
Primary tumor resection		
Not performed	32.550 (3.593-294.926)	0.002
Performed	1	

approximately 8 months (12). Although recent systemic therapy has extended MST to approximately 30 months (13–15), unresectable colorectal cancer remains difficult to cure. The purpose of systemic therapy is to prolong the survival time and control symptoms by delaying tumor progression. Initially, unresectable colorectal cancer may become resectable after successful systemic therapy. Randomized controlled trials involving PS 0–2 patients have shown that systemic therapy is associated with a significantly longer survival time than BSC without any systemic therapy (12,16).

In this study, 3 of 16 patients (19%) who underwent only the creation of the decompression colostomy as the first operation could undergo primary tumor resection as the secondary operation a month after the first operation. The overall survival times of the patients without the primary tumor resection were within 14 months after the first operation if intensive chemotherapy was performed. The fact that the primary tumor resection could not be performed was an independent risk factor by multivariate analysis (p=0.002).

Recently, much attention has been given to stent placement and per anus ileus catheterization as a bridge to surgery for patients with left-side OCC (4-9). The advantages of those procedures include avoidance of colostomy, relief of obstruction, shorter hospitalization, and better quality of life. However, the long-term outcome of left-side OCC after those procedures has not been elucidated (17). The European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline does not recommend using stenting as a bridge to surgery as the standard treatment for symptomatic left-side OCC because of the possible adverse effects on long-term outcomes (18). Stenting and catheterization are amenable to palliative therapy for patients with left-side OCC.

In patients undergoing curative resection, it has been reported that the prognosis does not differ between obstructive and non-obstructive cancers in stage-specific comparisons (19). When patients with left-side OCC are encountered, we should first evaluate the possibility of primary tumor resection by laparoscopic or open surgery.

CONCLUSION

In conclusion, primary tumor resection is a powerful predictor of long-term outcome of left-side OCC; however, a large-scale prospective study is needed to clarify this issue.

Conflicts of interest and source of funding

The authors declare no conflict of interests.

Ethics approval and consent to participate

The Ethics Committee for Biomedical Research of the Jikei Institutional Review Board approved the protocol of this study [30-221(9242)]. Individual patient consent is not required.

Consent for publication

The written consent to publish images or other personal or clinical details of participants was obtained from the patient.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

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