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Prognostic factors predicting survival in incurable stage IV colorectal cancer patients who underwent palliative primary tumor resection. Retrospective cohort study

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ABSTRACT

Background: The aim of this study is to estimate prognostic factors predicting survival in patients with incurable stage IV colorectal cancer (CRC), who underwent palliative primary tumor resection (PTR) with chemotherapy.
Materials and methods: We retrospectively performed an analysis using clinicopathological parameters of 103 patients with incurable stage IV CRC, who underwent palliative PTR with chemotherapy between 2006 and 2010. Prognostic factors associated with overall survival (OS) were evaluated by univariate and multivariate analyses.
Results: The median follow-up time was 17.5 months (range 2.4–60.5) for the total cohort (n = 103). There were five independent factors related to OS in univariate analysis (body mass index, tumor differentiation, pT, pN stage and local clearance of the primary tumor). A multivariate analysis revealed that pT, pN and local clearance of the primary tumor were prognostic factors related to OS. Median survival months (95% CI) were pT1, 2, 3: 21.5 (16.23–26.77) months vs. pT4: 13.73 (9.94–17.53) months, pN-: 29.7 (22.55–35.99) months vs. pN+: 17.1 (15.0–19.41) months and R0: 18.57 (16.65–20.48) months vs. R1, 2: 12.43 (9.95–14.91) months.
Conclusion: Locally advanced primary tumor (high pT stage, positive regional lymph node, and local residual primary tumor) was associated with poorer OS in incurable stage IV CRC patients, who underwent palliative PTR with chemotherapy. The PTR appears to result in better OS in patients with a primary tumor that is not locally advanced.

1. Introduction

Colorectal cancer (CRC) is one of the most common malignant neoplasms worldwide. Each year about 20% of CRC diagnosed patients have stage IV CRC. An estimated 75–90% of these patients has incurable synchronous metastases and requires palliative management [1]. Recent guidelines from the National Comprehensive Cancer Network suggest that palliative primary tumor resection (PTR) should only be considered if the patient has an unequivocal risk of obstruction or significant bleeding [2]. In asymptomatic patients, considering PTR as the preferred management is still controversial. Nevertheless, up to 75% of elderly CRC patients presenting with incurable synchronous metastases still underwent palliative PTR in the US population [3]. Recently, a population-based study reported that a statistically significant survival benefit was found in patients who underwent PTR over 12 years in a large cohort of CRC patients with incurable synchronous metastases [4].

When 5-fluorouracil was the only active agent, chemotherapy was considered generally ineffective in treating incurable stage IV CRC. However, in the past decade with the development of modern chemotherapy such as oxaliplatin, irinotecan, cetuximab and bevacizumab, the overall survival (OS) with chemotherapy alone has improved to almost 17–23 months for CRC patients with incurable synchronous metastases in phase 3 trials [5–7].

Therefore, the role of palliative PTR may need to be re-evaluated in the new era of chemotherapy. Although some studies [8–13] recently have reported increased survival benefits with palliative PTR in the new era of chemotherapy, no firm conclusions can be drawn with regard to the role of PTR in patients with incurable synchronous metastases due to a lack of data available from randomized studies. In this situation, it

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can be difficult to decide whether to resect the primary tumor. Palliative PTR may not be the optimal treatment for all patients. Therefore, before selecting PTR as treatment for CRC patients with incurable synchronous metastases, it is important to select the groups of patients who had survival benefits with this procedure. Clearly, only patients who can benefit from palliative PTR should be considered for this procedure.

The aim of this study is to estimate prognostic factors predicting survival in patients with incurable stage IV CRC, who underwent palliative PTR with chemotherapy.

2. Methods

Patients were retrospectively selected from the database at Severance Hospital. A review of the cancer center and colorectal service databases was performed between January 2006 and December 2010. Incurable stage IV CRC was defined as a stage impossible to undergo a complete resection of metastatic lesions. 485 patients were identified accordingly. From 485 patients, 382 patients were excluded sequentially by the following criteria. Exclusion criteria included: 135 patients who did not undergo chemotherapy (preoperative or postoperative) due to poor performance status [Eastern Cooperative Oncology Group (ECOG) performance status $>$ 2] or patients' refusal; 221 patients who did not receive palliative PTR; 6 patients who received a nonresective procedure (stoma or bypass); 20 patients who eventually received curative resection or intervention for metastatic disease. The remaining eligible 103 patients with incurable stage IV CRC, who received both palliative PTR and chemotherapy were retrospectively analyzed.

Patients and tumor characteristics included 22 clinicopathological parameters [age, sex, body mass index (BMI), performed procedure, carcinoembryonic antigen (CEA) at diagnosis, American Society of Anesthetists (ASA) score, comorbidity, mode of surgery, primary tumor location (colon, rectum), site of metastases (liver, lung, peritoneum, bone and other organs), number of distant metastatic organs, preoperative chemotherapy, tumor differentiation, pathologic T stage (pT), pathologic N stage (pN, regional lymph node), lymphovascular invasion, number of total retrieved lymph nodes and local clearance of primary tumor (R0, R1, R2)]. The seventh edition of the American Joint Committee on Cancer (AJCC) TNM classification was used for staging of primary tumor. Two patients survived 30 days or less postoperatively. These two patients received emergency PTR due to primary tumor perforation during the period of preoperative chemotherapy and were included in the statistical analysis. This study was approved by the institutional review board of the Yonsei University College of Medicine. This study has been reported in line with the STROCCS criteria [14].

3. Statistical analysis

Continuous parameters were presented as means ($\pm$ SD). Categorical parameters were presented as the total number (percentage) in patient and tumor characteristics. OS was defined as the time from initiation of treatment, either palliative chemotherapy or PTR, to the time of death from any cause. All parameters were analyzed for OS using the Kaplan-Meier method and the log-rank test. Cox regression analyses were used to discriminate independent prognostic factors for OS. The difference was statistically significant for $p < 0.05$. The statistical software package SPSS version 18 (SPSS, Chicago, IL) was used for all analysis.

4. Results

4.1. Patient and tumor characteristics

Table 1 shows 22 clinicopathological parameters of 103 patients. The main organ of metastases was the liver (n = 70, 68%) followed by peritoneum (n = 48, 46.6%) and lung (n = 28, 27.2%). There was

Table 1
Patient and tumor characteristics.

Parameter	No. of patients (%)
	n = 103
Age	
Mean (range)	59.6 (25–85)
Sex	
Male	58 (56.3%)
Female	45 (43.7%)
BMI	
Mean ($\pm$ SD)	22.4 ($\pm$ 3.4)
CEA[a] levels at diagnosis(ng/ml)[b]	
Median (range)	11.2 (0.83–7418)
ASA[c]	
1	51 (49.5%)
2	49 (47.6%)
3	2 (1.9%)
4	1 (1%)
Comorbidity[d]	
No	61 (59.2%)
Yes	42 (40.8%)
Primary tumor location	
Colon	72 (69.9%)
Rectum	28 (27.2%)
Colon & Rectum[e]	3 (2.9%)
Liver metastasis	
No	33 (32%)
Yes	70 (68%)
Lung metastasis	
No	75 (72.8%)
Yes	28 (27.2%)
Peritoneum metastasis	
No	55 (53.4%)
Yes	48 (46.6%)
Bone metastasis	
No	94 (91.3%)
Yes	9 (8.7%)
Other organ metastasis[f]	
No	76 (73.8%)
Yes	27 (26.2%)
No. of distant metastatic organs	
1	50 (48.5%)
2	33 (32%)
≥ 3	20 (19.5%)
Preoperative Chemotherapy	
No[g]	72 (70%)
Yes	31 (30%)
Mode of surgery	
Elective	65 (63.1%)
Emergency	38 (36.9%)
Performed Procedures	
Colon	72
Right hemicolectomy	25
Left hemicolectomy	9
Transverse colectomy	2
Anterior resection	22
Hartmann's procedure	11
Near total colectomy	3
Rectum	28
Abdomino-perineal resection	5
Low anterior resection	19
Hartmann's procedure	4
Colon & Rectum	3
Total proctocolectomy	2
Low anterior resection & Rt. hemicolectomy	1
Primary tumor differentiation	
Well	10 (9.7%)
Moderate	68 (66.0%)
Poor	12 (11.7%)
Others[h]	13 (12.6%)
T stage	
pT1	1 (1%)
pT2	3 (2.9%)
pT3	50 (48.5%)
pT4	49 (64.6%)
N stage	

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