The American Journal of Surgery (2011) 201, 726–733

The American Journal of Surgery®

Clinical Science

Prognostic factors for survival after salvage surgery for locoregional recurrence of colon cancer

Takashi Akiyoshi, M.D., Ph.D.[a,*], Yoshiya Fujimoto, M.D.[a], Tsuyoshi Konishi, M.D., Ph.D.[a], Hiroya Kuroyanagi, M.D., Ph.D.[a], Masashi Ueno, M.D., Ph.D.[a], Masatoshi Oya, M.D., Ph.D.[a], Satoshi Miyata, Ph.D.[b], Toshiharu Yamaguchi, M.D., Ph.D.[a]

[a]Gastroenterological Center, Department of Gastroenterological Surgery, Cancer Institute Hospital; [b]Genome Center, Bioinformatics Group, Cancer Institute Hospital, Tokyo, Japan

KEYWORDS:
Colon cancer;
Locoregional recurrence;
Salvage surgery;
Prognostic factor

Abstract

BACKGROUND: Although locoregional recurrence after rectal cancer resection has been extensively investigated, studies of salvage surgery for locoregionally recurrent colon cancer are scarce. This study aimed to determine the predictors of postsalvage survival for locoregionally recurrent colon cancer.

METHODS: We studied 45 consecutive patients who underwent macroscopically complete resection of locoregionally recurrent colon cancer between April 1988 and December 2007. The primary end point was cancer-specific survival, and 20 clinical variables were analyzed for their prognostic significance.

RESULTS: Cancer-specific 5-year survival for the entire cohort of 45 patients was 46%. Multivariate survival analysis showed that margin status ($P = .0311$), number of locoregional recurrent tumors ($P = .0002$), pathological grade ($P = .0416$), largest tumor diameter ($P = .0247$), and distant metastasis ($P = .0006$) were independently associated with cancer-specific survival.

CONCLUSIONS: Salvage surgery for locoregional recurrence of colon cancer can provide a chance for long-term survival in selected patients.

Locoregional recurrence is a key determinant of outcome in patients operated on for colorectal cancer. Locoregional recurrence after rectal cancer resection has an important influence on both survival and quality of life, and has therefore been extensively investigated.[1,2] However, the problem of locoregional recurrence after curative resection of colon cancer has been less well studied. The recently reported locoregional recurrence rate following curative surgery for colon cancer varies from 3% to 15%.[3–8] Considerable efforts have been made to improve survival in patients with recurrence in the liver after colon cancer resection through the use of aggressive liver surgery and chemotherapy,[9] but there have been few reports on salvage surgery and the outcome of patients with locoregional recurrence after curative resection of colon cancer. The present study aimed to analyze our institutional experience of salvage surgery for locoregional recurrence of colon cancer and to determine the predictors of postsalvage survival.

The authors have no conflicts of interest or financial ties to disclose.

* Corresponding author. Tel.: +81 03 3520 0111; fax: +81 03 3520 0141.

E-mail address: takashi.akiyoshi@jfcr.or.jp

Manuscript received November 23, 2009; revised manuscript February 25, 2010

0002-9610/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjsurg.2010.03.003

Patients and Methods

Study population

We evaluated 45 consecutive patients at our institution who underwent initial resection for locoregional recurrence following macroscopically curative resection of primary colon cancer between April 1988 and December 2007. Demographic information and clinicopathological data regarding the primary and recurrent tumors and their management, salvage operations, and operative complications were retrospectively collected from the database, chart review, operative reports, and pathology reports. Primary tumors were staged according to the American Joint Committee on Cancer tumor-node-metastasis (TNM) staging system. Twenty variables were selected for prognostic factor analysis (Table 1) by consideration of their potential relationship to survival. One patient was lost to follow-up because of a behavioral problem, and the median follow-up for the remaining survivors was 51 months (range 18–132 months). For comparison, survival of 10 consecutive patients who underwent palliative resection with macroscopic residual tumor (R2 resection) for locoregional recurrence of colon cancer during the same period was evaluated. Of these, 7 patients underwent initial surgery for colon cancer at our institution and 3 patients at other hospitals.

Definitions

The sites of locoregional recurrence were divided into 4 groups on the basis of established criteria.[10,11] Sites were defined as disease occurring at the anastomosis (peri-anastomotic), in the mesentery or nodal basin (mesentery/nodal), in the retroperitoneum, or in the peritoneum. Tumor recurrence at nonregional sites such as the liver or lungs was recorded as distant metastasis. Para-aortic lymph node metastasis due to recurrent tumor was recorded as a distinct entity from distant metastasis. The types of resection for locoregional recurrent disease were defined as R0 resection (negative microscopic margins) or R1 resection (positive microscopic margins without gross residual disease). Local disease-free interval was calculated from the time of initial resection to the diagnosis of recurrence. Operative mortality was defined as death within 30 days of operation or during the initial hospitalization.

Statistical analysis

The primary measured end point was cancer-specific survival, which was estimated using the Kaplan–Meier method. Cancer-specific survival was defined as the period from salvage surgery to cancer-related death. Univariate analyses of the effect of covariates on the end point were analyzed using the log rank test. Multivariate analysis was performed using the Cox proportional hazards model with a stepwise (forward selection/ backward elimination) method (significance level to enter = .20, significance level to stay = .05). The results of Cox model analysis are reported with hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical analysis was performed using SPSS software (SPSS-Japan, Inc, Tokyo, Japan) and $P \leq .05$ was considered statistically significant.

Results

Primary and recurrent tumor characteristics

The patient and tumor backgrounds of the 45 patients included in this study are summarized in Table 1. The median age at salvage surgery was 63 years (range 32–83 years), and 25 patients (56%) were male. All patients underwent macroscopically complete resection of the primary tumor, but pathological examination revealed microscopically positive margins in 5 patients (11%).

Sixteen patients (36%) complained of symptoms at diagnosis of recurrence. Symptoms were pain in 6 patients (abdominal pain in 3, back pain in 2, anal pain in 1), rectal bleeding in 3, ileus in 2, altered bowel habits in 2, hematuria in 1, and other symptoms in 2 patients. Twenty-nine patients (64%) were asymptomatic. Of these, recurrence was suspected following surveillance computed tomography (CT) in 9 patients, surveillance colonoscopy in 7 patients, elevation of carcinoembryonic antigen (CEA) in 6, positron emission tomography (PET) in 2, elevation of carbohydrate antigen 19-9 (CA19-9) in 1, and for other reasons in 4 patients. The median local disease-free interval was 22 months (range 3–71 months).

The most common sites for locoregional recurrence were peri-anastomotic (19 patients, 42%), followed by mesentery/nodal (10 patients, 22%), peritoneum (10 patients, 22%), and retroperitoneum (6 patients, 13%). Locoregional tumors in the peritoneum, mesentery/nodal, and retroperitoneum were multiple in 6 (60%), 2 (20%), and 1 (17%) patient, respectively, whereas locoregional recurrences at peri-anastomotic sites were solitary in all patients.

Salvage surgery

Tumor resection with and without colectomy was performed in 41 (91%) and 4 (9%) patients, respectively. Thirty patients (67%) required an extended resection with en bloc removal of adjacent organs or structures, as summarized in Table 2. Pancreato-duodenectomy (PD) and total pelvic exenteration (TPE) were performed in 4 and 2 patients, respectively. The median operating time was 395 minutes (range 135–920 min), and the median estimated blood loss was 800 mL (range 20–13,000 mL). A negative resection margin (R0) of locoregional recurrent tumor was obtained in 40 patients (89%), and 5 patients (11%) had R1 resections.