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Comparison of clinicopathological characteristics and prognosis between early and late recurrence after curative surgery for colorectal cancer

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Abstract

BACKGROUND: Despite curative surgery for colorectal cancer, some patients experience tumor recurrence. Whether early recurrence is associated with a shorter postrecurrence survival period compared with late recurrence remains unknown.

METHODS: A total of 395 patients with tumor recurrence after curative surgery for colorectal cancer were enrolled and divided into early (<3 years) and late (≥3 years) recurrence groups. Clinicopathologic characteristics, recurrence patterns, and postrecurrence survival were compared.

RESULTS: For stage I and II colorectal cancer, patients with T4 lesions tended to experience early recurrence. For stage III colorectal cancer, early recurrence was more common in patients with N2 disease. Patients with older age, mucinous-type tumors, poorly differentiated histology, the presence of lymphovascular invasion, or multiple site recurrence tended to die <2 years after recurrence. Median postrecurrence survival was similar for the 2 groups. Patients undergoing resection of liver or lung metastases demonstrated longer postrecurrence survival compared with those who did not undergo resection.

CONCLUSIONS: Compared with late recurrence, early recurrence does not indicate a worse outcome in colorectal cancer.

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Despite aggressive surgical resection and adjuvant therapy, approximately one-third of all patients undergoing curative surgery for colorectal cancer will experience recurrence.[1–3] Postoperative surveillance is scheduled for these patients after curative resection, with the principal aim of identifying and treating asymptomatic recurrence at an early stage and improving survival.[2,4] However, the optimal intensity of follow-up and the optimal surveillance tools remain controversial. Most guidelines suggest a more intense follow-up program in the first 3 years after surgery, and routine surveillance is not recommended beyond 5 years.[5–8] However, recurrence continues to occur beyond 5 years after surgery.[9] The clinical and pathologic features of early and late recurrence after curative surgery for colorectal cancer have seldom been reported.[9,10] No studies have compared the difference for each stage regarding early or late recurrence or its impact on postrecurrence survival. It is therefore unclear whether the early recurrence of colorectal cancer after curative surgery is associated with shorter postrecurrence survival than is late recurrence.

In this study, we compared the clinical and pathologic features of early (<3 years) and late (≥ 3 years) recurrence in colorectal cancer patients after curative resection for each stage. The characteristics of patients who survived >2 years after recurrence were also analyzed.

Methods

Data were retrieved from a prospectively collected colorectal cancer database in a tertiary hospital. The database includes the following 4 components: (1) demographic data, including age, gender, pretreatment tumor markers, and any neoadjuvant treatment; (2) surgical data, including the tumor location and the surgical method used; (3) pathologic data for the tumor, including histologic type, gross appearance, size, grade of differentiation, presence or absence of lymphovascular emboli, tumor invasion depth, number of positive lymph nodes, and total number of retrieved lymph nodes; and (4) follow-up data, including adjuvant treatment with chemotherapy and/or radiotherapy, date of recurrence, site of recurrence with subsequent treatment, and condition at last follow-up.

In total, 2,012 patients underwent curative resection for colorectal cancer at Taipei Veterans General Hospital between January 2000 and December 2005. Fifty-four patients were excluded because of surgical mortality, and 403 (20.6%) experienced recurrence during follow-up. Eight additional patients were excluded because their recurrence originated from metachronous colorectal cancers. Because most current practice guidelines suggest a more intense follow-up program during the first 3 years after surgery, we used 3 years as the cutoff to define early and late recurrence. Three hundred twelve patients experienced tumor recurrence <3 years after curative resection and were defined as the early-recurrence group; patients with tumor recurrence after 3 years were defined as the late-recurrence group (n = 83). Before surgery, a routine survey including chest radiography and abdominal computed tomography was performed for tumor staging. Radical resection with lymph node dissection was performed. The pathology slides were reviewed by a specialized pathologist and tumor staging was based on the tumor-node-metastasis staging criteria.[11] Among patients with recurrence, 175 patients had rectal cancer and 43 received neoadjuvant chemoradiation. Adjuvant chemotherapy was administered to most patients with stage III disease and some with high-risk stage II disease. The adjuvant treatment consisted of 5-fluorouracil-based chemotherapy for 6 months.

A surveillance program was provided for all patients. It included follow-up appointments every 3 months for the first 2 years, every 6 months for the next 3 years, and yearly thereafter. The follow-up included a physical examination, measurement of the carcinoembryonic antigen level, chest x-ray, abdominal sonography, and/or abdominal computed tomography. If tumor recurrence was suspected, further studies, such as chest computed tomography, whole-body bone scans, or whole-body positron emission tomography, were performed to determine the site of recurrence. Recurrence was defined as a recurrent lesion that was confirmed by pathology or by progressively increasing size in imaging studies. Locoregional recurrence was defined as tumor recurrence on the previous anastomosis line or in the soft tissue or lymph nodes near the previous surgical site. Distant lymphadenopathy was defined as enlarged or conglomerated para-aortic, pulmonary hilar, supraclavical, or inguinal lymph nodes. Postrecurrence survival was defined as the duration between the date of tumor recurrence and the date of the last follow-up. Six patients who had follow-up periods <2 years after recurrence were excluded from the analysis of postrecurrence survival. The last follow-up date was October 2011 for the surviving patients. The median follow-up time in survivors was 69.2 months.

Statistical analyses were conducted using SPSS version 16.0 (SPSS, Inc, Chicago, IL). Categorical data were compared using chi-square or Fisher's exact tests as indicated. Postrecurrence survival was analyzed using the Kaplan-Meier method, and the difference was tested using the log-rank test. P values $<.05$ were considered statistically significant.

Results

Recurrence occurred more frequently in patients with original stage III disease (64.3% of all recurrence). Among the 220 patients with colon cancer and recurrence, 2 received neoadjuvant chemotherapy. Among the 175 patients with rectal cancer and recurrence, 43 received neoadjuvant chemoradiation, and 33 of these 43 patients experienced recurrence within 3 years. The timing of recurrence did not differ between patients who did or did not received neoadjuvant chemotherapy ($P = .696$; Table 1).