Diseases of the Colon & Rectum

The Clinical and Endoscopic Characteristics, Treatment, and Long-Term Prognosis of Early Colorectal Cancer in Taiwan

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PURPOSE: This study was designed to realize the incidence, clinical and endoscopic characteristics, treatment, and prognosis of early colorectal cancer in Taiwan. METHODS: A retrospective study was conducted to review the data from January 1, 1991 to December 31, 2005 at the National Taiwan University Hospital. Patients' clinical information, demographic data, endoscopic pictures, treatment regimens, pathologic, and outcome details for these cases were reviewed, recorded, and analyzed. Mann-Whitney *U* test and log-rank test were used for the statistical analysis. RESULTS: A total of 61 patients from this 15-year period were included (39 males; mean age of disease onset, 63.5 years). The follow-up period ranged from 0.05 to 15 (mean, 6.8) years. Five-year survival rate in our early colorectal cancer patients was 98.4 percent. The size of the early colorectal cancer ranged from 0.3 to 5 cm with the mean of 1.4 cm. The most common site of early colorectal cancer was the sigmoid colon (56.1 percent). Protruded (Type I) lesions accounted for the majority (73.6 percent) of the cases. Endoscopic polypectomy/mucosectomy was the most common type of treatment (72.3 percent). There was no statistical difference in the survival status between the endoscopic treatment group and the operation group (log-rank test, $P = 0.368$). CONCLUSIONS: Most of the early colorectal cancer lesions could be removed successfully by endoscopic method without mortality and major morbidity. However, regular follow-up after treatment is recommended even after five years to reduce early colorectal cancer mortality and morbidity. [Key words: Clinical; Endoscopic characteristics; Treatment; Prognosis, early; Colorectal cancer

Although colorectal cancer (CRC) is currently not the leading cause of cancer mortality in Taiwan, it is noteworthy that the incidence of CRC has increased recently.[1,2] CRC will become one of the most important diseases worthy of concern within the years to come in Taiwan. Most previous publications on CRC focus on all stages of CRC patients in Taiwan, whereas the early stage of CRC has rarely been discussed.[3,4] Early CRC is customarily defined according to the depth of carcinoma invasion limited to the submucosal layer as proposed for gastric cancer. Severely dysplastic epithelium confined to the mucosa is called severe dysplasia or intramucosal carcinoma, although there is controversy as to this particular lesion. Japanese pathologists tend to use the term "intramucosal or mucosal carcinoma," whereas western pathologists tend to avoid using this term to prevent unnecessary major surgery and mostly use dysplasia only.[5]

Because the management and prognosis are different between the early stage and advanced stage of CRC, better understanding of the clinical characteristics of early stage CRC is desirable. We reviewed

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Table 1.
Initial Presentations of Early Colorectal Cancer

Presentation	Percentile
Colon cancer s/p operation, for follow-up	10.5
Colon polyp, for follow-up	35.1
Healthy checkup	14
Anemia/positive stool occult blood	24.6
Bowel habit change	8.8
Positive lower GI series/PET/digital examination	7
	100

s/p = status post; GI = gastrointestinal; PET = positron emission tomography.

retrospectively the data bank in the National Taiwan University Hospital to examine the incidence, clinical characteristics, treatment, and prognosis of early CRC in Taiwan.

PATIENTS AND METHODS

A retrospective study was conducted to review the data obtained from patients who had been diagnosed as early CRC. The definition of early CRC in this study was colon adenoma with dysplasia/carcinoma or colorectal cancer with invasion limited to the submucosal layer. To obtain a more complete review of such cases, we searched two separate databases for relevant cases during the same 15-year period (from January 1, 1991 to December 31, 2005 inclusively) at the National Taiwan University Hospital. The first database was derived from endoscopic case studies. All cases that had been diagnosed as early CRC lesions during endoscopic examination in the study period were included in our sample. The second database searched was a pathology database containing cases that had been diagnosed, by histopathology, as being colon adenoma with severe dysplasia/carcinoma or colorectal cancer with invasion limited to the submucosal layer. We then pooled the data obtained from these two selected databases.

Finally, only those cases that had been checked with endoscopy and had the diagnosis confirmed with pathology as being examples of early CRC were included in this study. Clinical information, demographic data, endoscopic pictures, treatment regimens, pathologic details, and outcome details for these patients with early CRC were reviewed, recorded, and analyzed. For clearer classification of early CRC lesions endoscopically, their macroscopic morphologies were categorized according to the *General Rules for Clinical and Pathologic Studies on Cancer of the Colon, Rectum and Anus* established by the Japanese Society for Cancer of the Colon and Rectum.[6] The tumor size was defined according to the pathologic findings. The follow-up period was defined from the first follow-up after treatment of early CRC until the last follow-up date that could be traced.

Mann-Whitney *U* test was used for comparing the age of onset, location of lesions, and tumor size between the Type I (protruded) and Type II (flat, superficial/depressed) lesions. Log-rank test was used for analyzing the survival status between the endoscopic treatment group and the operation group.

RESULTS

In this 15-year period, a total of 61 patients (39 males) who met the criteria and had complete data were included for analysis. The age of disease onset ranged from 34 to 82 (mean, 63.5) years. The follow-up period ranged from 0.05 to 15 (mean, 6.8) years. Two patients died of colorectal cancer (3.3 percent) during the follow-up period, both were recurrence of disease with the presentations of multiple liver metastasis. Five-year survival rate in our patients with early CRC was 98.4 percent. The initial presentations of these patients are summarized in Table 1. The most common initial presentations for early CRC in these patients were with the histories of colon polyp/colorectal cancer (45.6 percent).

Among these patients, there were one synchronous cancer and six metachronous cancers. The patient with synchronous cancers had a 0.6 cm Ip (pedunculated) and another 0.6 cm Ip lesion at sigmoid and descending colon respectively. Both were removed successfully by endoscopic mucosectomy/polypectomy. All patients with metachronous cancer were postoperation or postpolypectomy patients with early CRC receiving regular follow-up, and all of the early CRC found in this study period could be removed by polypectomy. The morphologies of them were three Isp (subpedunculated), one Ip (pedunculated), one IIc (depressed), and one IIa + IIc (flat elevated with depression). They had been followed from 3.6 to 10.8 years; five survived and one patient died of hemorrhagic stoke.

The size of the early CRC in this study ranged from 0.3 to 5 (mean, 1.4) cm. The distribution of the lesions revealed that the most common site of early CRC was the sigmoid colon (56.1 percent), followed by the rectum as the second common site involved

Table 2.
Distribution of Early Colorectal Cancer

Location	Percentile
Sigmoid colon	56.1
Rectum	18.2
Descending colon	10.7
Transverse colon	7.5
Ascending colon	7.5

(18.2 percent; Table 2). Table 3 shows a summary of the results of the macroscopic morphology of these early CRC cases according to the endoscopic pictures. Type Ip was the most common subtype of lesion (36.8 percent), and protruded (Type I) lesions accounted for the majority (73.6 percent). When comparing the age of onset, location of lesions, and tumor size between Type II (flat, superficial/depressed) and Type I (protruded) lesions by using the independent paired *t*-test, only the age of onset was statistically different between these two groups. Older age of onset tended to be in Type II (69.2 ± 10.7 years) rather than in Type I (62.3 ± 10 years; $P = 0.042$). There is no difference in right-side and left-side distribution between Type I and Type II lesions. There also is no difference in tumor size between Type I (1.64 ± 1.03 cm) and Type II (1.14 ± 0.61 cm) lesions ($P = 0.106$), although the mean size of Type II lesions was smaller. When subgrouping the tumors as 1) polyps with dysplasia, 2) polyps with carcinoma, and 3) Stage I colorectal adenocarcinoma of UICC-TNM system, polyps with carcinoma accounted for the majority cases (48.4 percent; Table 4).

Endoscopic polypectomy/mucosectomy for these early CRC cases was the most common type of treatment (72.3 percent), followed by laparotomy (13.8 percent). Two patients received laparoscopic colectomy (3.1 percent). Seven patients received endoscopic treatment first and laparotomy later because of uncertain tumor-free margin (10.8 percent).

Table 3.
Endoscopic Morphology of Early Colorectal Cancer

Type	Percentile
Ip	36.8
Isp	19.3
Is	17.5
IIa	1.8
IIb	0
IIc	12.3
IIa + IIc	12.3

Ip = pedunculated; Isp = subpedunculated; Is = sessile; IIa = flat elevated; IIb = flat; IIc = depressed; IIa + IIc = flat elevated with depression.

Table 4.
Subgroup of Early Colorectal Cancer

Subgroup	Percentile
Polyps with dysplasia	21.9
Polyps with carcinoma	48.4
Carcinoma, UICC-TNM Stage I	29.7

UICC = The International Union Against Cancer.

Pathologic study after operation showed the absence of cancer tissue in four of seven operation specimens. Among those patients who had received endoscopic polypectomy/mucosectomy, only one patient had minor bleeding after the procedure with hemostasis achieved by hemoclip. No perforation was noted. Two patients received operation at other hospitals; no lymph node data could be traced. In the other patients who had received operation, none of them had lymph node involvement (lymph nodes examined from 2–10 (mean, 4) according to the pathologic report. There was no statistical difference in the survival status between the endoscopic treatment group and the operation group (log-rank test, $P = 0.368$).

DISCUSSION

In the 15-year study period, at least 61 patients of early CRC were diagnosed and managed in our hospital. To obtain the ratio of early to total CRC cases in our hospital, we also checked the total number of CRC cases in the same period. Between 1991 and 2005, a total of 15,035 patients had received colonoscopy at our hospital; and 1,453 patients were diagnosed as CRC. Therefore, the ratio of early to total CRC cases was 4.2 percent, which was similar to that (4.3 percent) reported by Tung and Wu[3] but lower than that (18–22 percent) observed in Japan[7,8] and (20–30 percent) Western countries.[9–11] Although the study population was different, higher rate of detection can be attributed mainly to screening. It is desirable to increase the early CRC ratio as much as possible because early CRC has much better prognosis than advanced CRC. We hope the description about the morphology and distribution of early CRC from the results of this study can increase the further detection rate of early CRC and improve the overall survival status of CRC.

Flat (superficial) and depressed colorectal malignancies were first recognized in the 1980s,[12–16] and between 12 and 40 percent of their colonic neoplasms are reported to be flat rather than polypoid.[17] Our study results showed that protruded (Type I) lesions accounted for 73.6 percent of the cases, with

the rest being flat/superficial/depressed (Type II) lesions. The ratio of Type II to Type I lesions (26.4–73.6 percent) was in the range reported by the Japanese. Okamoto has reported that Type II lesions tend to have the following clinical characteristics: 1)higher frequency in older patients; 2) higher frequency in the right colon; 3) smaller size; and 4) lower frequency of containing adenomatous component.[18] Our results also revealed that Type II lesions occurred more frequently in older patients and tended to be smaller than Type I lesions. However, we observed no difference in distribution between the left side and right side. The findings of this study and that of Tung and Wu[3] show that the most common site of early CRC occurrence was at the sigmoid colon, followed by the rectum in our study and the descending colon in that of Tung and Wu.[3]

Most (72.3 percent) of our patients were treated endoscopically without major complications. The survival status was similar between the surgically treated and endoscopically treated patients. No mortality or perforation was noted in our series, except a minor bleeding, which also was treated endoscopically. Endoscopic treatment for early CRC is a safe, effective, and relatively minimal invasive choice of treatment consistently observed in our study and others'.[19,20] Although several reports indicated that early CRC limited in the mucosal layer tended not to metastasize and treatment by endoscopic removal is generally deemed sufficient,[3,19–22] 1 percent of the cases in the literature had a residual, recurrent, or even metastasis outcome.[19,23] From our experience, early CRC still has the possibility of metastasis without local recurrence after a longer follow-up period. Compared with that of previous reports,[20,23] our follow-up period was the longest one (mean, 6.8 years). Two patients died of colorectal cancer with disease recurrence of multiple liver metastasis during our follow-up period. Both were elder patients (81-year-old males), who received mucosectomy and polypectomy, respectively. These two patients died 4.9 years and 5.7 years after endoscopic treatment. Therefore, we recommended that regular follow-up is still necessary for posttreatment of patients with early CRC even after five years, and liver metastases should always be monitored carefully.

CONCLUSIONS

Early CRC accounted for 4.2 percent of all patients with CRC. The most common sites of these lesions were at the sigmoid colon with the mean size of 1.4 cm. Protruded (Type I) lesion was the most common endoscopic morphology. Most of the early CRC lesions could be removed successfully by endoscopic method without mortality and major morbidity. However, careful follow-up, especially of the liver status, was strongly recommended even five years after treatment.

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