Clinicopathological Features of Perforated Colorectal Cancer

MASAICHI OGAWA, MICHIKAI WATANABE, KEN ETO, TAKAHIRO OMACHI, MAKOTO KOSUGE, KEN HANYU, LOHTA NOAKI, TETSUJI FUJITA and KATSUHIKO YANAGA

Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan

Abstract. The aim of this retrospective study was to determine clinicopathological factors pertinent to the prognosis of perforated colorectal cancer (PCRC). Patients and Methods: A retrospective review of clinical records of 17 cases of emergency primary resection for PCRC (stage IIIa in 2, stage IIIb in 6 and stage IV in 9) was performed. Result: The 5-year survival rate was 31% (31% for stage III and 12% for stage IV). When compared with non-PCRC (533 cases) in stage III (78.8%) or stage IV (14.8%), the 5-year survival rate of stage III perforated colorectal cancer was clearly worse (p<0.01) than the non-perforated counterpart. For stage IV, however, the two groups had a similar prognosis. MST of the PCRC was 31 months for stage III and 12 months for stage IV. Approximately half of the recurrence pattern of stage III (75%), or stage IV (44%) PCRC was peritoneal carcinomatosis. As for the type of operations performed, Hartmann’s procedure was the preferred technique (71%), for which mortality and morbidity rate were both low. Conclusion: Because of the high incidence of peritoneal carcinomatosis and low 5-year survival rate, stage III PCRC should be regarded as a stage IV disease, for which postoperative chemotherapy seems essential.

The treatment for perforated colorectal cancer (PCRC) is not an easy task because most cases are already stage IV at the onset of the disease and not eligible for curative surgery (1-10). For colorectal cancer, the reported incidence of perforation ranges from 3% to 10% (1-3). It has been accepted that the emergency surgery for perforated colorectal cancer has a worse progress than those treated by elective surgery (4-6). As to the survival rate of PCRC, Badia et al. observed 1-year survival rate of 52% and 2-year survival rate of 40% (1). The 5-year survival rate varies from 32% to 52.8% (2, 3, 7). In 1986, Steinberg et al. found that neoplastic perforation was only a significant indicator for disease-free survival (8). This retrospective study sought to determine clinicopathological factors pertinent to the prognosis of PCRC.

Patients and Methods
A total of 535 patients underwent resection of colorectal cancer at Jikei University Hospital between January 1998 and December 2000. Of these, 17 patients were PCRC, consisting of 13 men and 4 women, with an age between 25 and 87 [71±8.4 (mean±SD)] years. The definition of PCRC is perforation at the site of the cancer and proximally to the tumor in case of obstruction. The follow-up data of the patients were updated in January 2006. In this series, the cancer was located in the right colon in 2 (12%), cecum in 1 (6%), ascending colon in 1 (6%), left colon in 15 (88%), descending colon in 2 (12%), sigmoid colon in 6 (35%), and rectum in 7 cases (41%). In terms of TNM classification, stage IIIa in 2 (12%), stage IIIb in 6 (35%), and stage IV in 9 cases (53%). All patients received fluorouracil- and leucovorin-based chemotherapy and same mode of follow-up.

Patients information collected from the medical records included the age, gender, location, size and histological grade of the primary tumor. The histological depth of invasion, lymphatic or venous invasion, TNM classification (11), and prognosis were also recorded. Patients who underwent emergency surgery of PCRC were compared with non-PCRC patients who underwent elective surgery.

Statistical analysis. Survival time was calculated from the date of resection, to the date of death or date of the latest follow-up. Survival curves were plotted according to the Kaplan-Meier method; statistical differences were analyzed by the log-rank test. The statistical analyses were performed with Stat View software version 5.0 (Abacus Concepts, Berkeley, CA, USA) and SPSS software version 11.0 (SPSS Inc, Chicago, IL, USA). A p-value less than 0.05 was regarded as statistically significant.

Results
Histopathological factors. Macroscopic findings resulted in a broad range of types; type 2 in 8 (47%), type 3 in 6 (35%), and type 4 in 3 cases (18%). The maximal diameter of the tumor was 61±13 mm. Tumor histology was poorly differentiated adenocarcinoma in 1 (6%), moderate differentiated adenocarcinoma in 9 (53%), and well differentiated adenocarcinoma...
in 7 cases (41%). All cases were lymphatic invasion, and venous invasion showed in 12 cases (72%).

**Cumulative survival rate.** The overall 5-year survival rate of PCRC was 31%, consisting of 31% in stage III and 12% in stage IV (Figure 1). The 5-year survival rate of 533 patients who underwent surgery for non-perforated colorectal cancer (non-PCRC) was 78.8% for stage III and 14.8% for stage IV. In stage III, PCRC had a significantly worse prognosis ($p<0.01$) as compared with the non-PCRC. For stage IV, however, the 5-year survival rate was not significantly different between those two groups. For PCRC, the mean survival time (MST) of stage III was 31 months as compared to 12 months for stage IV. In this study, perforation of the colorectal cancer in stage III was an independent factor for short survival (13% for PCRC and 78.8% for non-PCRC; $p<0.01$).

**Clinical feature.** For stage III PCRC, 75% of the recurrence pattern was peritoneal carcinomatosis, as compared to 44% for stage IV PCRC (Figure 2). In these 17 cases, the following operations were performed: right hemicolectomy and primary ileo-transverse anastomosis in 2 (12%), a Hartmann’s procedure in 14 (82%) and sigmoid-colectomy in 1 case (4%). All cases underwent peritoneal lavage and drainage. As for the type of operations performed, Hartmann’s procedure was the preferred technique (71%), for which mortality and morbidity rate were both low (Table 1). In 2 cases, there was respiratory infection.

**Discussion**

In the literature, neoplastic perforation has been reported to be the only significant indicator for survival because the spillage of tumor cells into the peritoneal cavity would lead to wide-spread interperitoneal tumor dissemination (8, 9), while one report describes the absence of negative impact of perforation on survival (10, 11). Concerning the effect of spillage of tumor cells, Lehnert et al. have reported that viability-free cancer cells were not demonstrated in the peritoneal cavity of patients with perforated GI cancer, and the metastatic efficacy of cancer cells that are possibly shed during perforation is uncertain in the presence of peritonitis (12). Chen and Sheen-Chen found that the 5-year survival rate of patients with perforation at the site of the cancer was similar to that of uncomplicated cancer, and that spillage of tumor cells into the peritoneal cavity through a perforation at the site of the tumor was not an indicator of a poor prognosis (9). However in the present study, for stage III PCRC, 75% of the recurrence pattern was peritoneal carcinomatosis, as opposed to 44% for stage IV PCRC. Therefore, with respect to the long-term prognosis, perforation of the colorectal cancer in stage III is an independent factor (13% for PCRC and 78.8% for non-PCRC; $p<0.01$).

The operative mortality of elective surgery for colorectal cancer is 3%, whereas that for perforated (including obstructive) colorectal cancer is increased 2 to 4 folds (13). It is well-established that primary resection of the diseased segment is chosen in most colorectal emergency operations (14-16). In the present study, primary resection was performed in 94% (16/17) of patients. Left-sided resection with immediate anastomosis in the presence of peritoneal sepsis is still debated in the literature (15-17). Biondo et al. had reported that immediate anastomosis can be performed safely after the use of intraoperative antegrade colonic irrigation, and perforated primary anastomosis in 61 (48%) of 127 patients with peritonitis. In their report, 2 patients (8.7%) with diffuse peritonitis died, and anastomotic leakage developed in only 1 patient. For generalized peritonitis due to large bowel perforation, especially for left-side one, appropriate treatment remains controversial, but Hartman’s operation has become popular during the last decades (14, 18). Bielecki et al. reviewed the Mannheim peritonitis index (MPI) of large bowel perforation. In their conclusion, no patient with MPI less than 25, even with primary anastomosis died, while 38.5% of the patients with MPI between 26 and 36 died (19). Minopoulos et al. described for the treatment of emergency surgery to CRC that the choice of operative procedures depends on the conditions of the patient, the experience of surgeon, and the means that the hospital provides (20). The presented results suggest that Hartman’s procedure was the preferred technique for the left-sided PCRC, and such a surgical strategy seems to account for the low morbidity.

In conclusion, the prognosis of stage III perforated colorectal cancer is poor, and the recurrence pattern of PCRC is mainly by peritoneal seeding, for which intensive adjuvant chemotherapy should be conducted.

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**Table I. Operation techniques and mortality and morbidity.**

<table>
<thead>
<tr>
<th>Operation methods</th>
<th>Stage III (n=8)</th>
<th>Stage IV (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hartman’s procedure</td>
<td>8</td>
<td>6</td>
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<tr>
<td>colostomy</td>
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<td>1</td>
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<tr>
<td>colectomy+primary anastomosis</td>
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<td>2</td>
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<tr>
<td>Morbidity</td>
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<td>2*</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>0</td>
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*Respiratory infection.
Figure 1. The five-year survival rate of PCRC. The overall five-year survival rate of PCRC was 31%, consisting of 31% in stage III and 12% in stage IV.

Figure 2. Recurrence pattern of PCRC. For stage III, 75% of the recurrence pattern was peritonitis carcinomatosa, as opposed to 44% for stage IV.
References


