PREDICTABILITIES OF THERAPEUTIC EFFECT AT RECURRENCES OF COLORECTAL CARCINOMAS
BY HISTOPATHOLOGICAL EFFECTS OF PREOPERATIVE CHEMOTHERAPY

M. FUJII, M. KOCHI, T. TANIGUCHI, S. IWAI AND T. TANAKA
Third Department of Surgery, Nihon University School of Medicine, Tokyo, Japan

BACKGROUND
Treatments of recurrent cases of colorectal carcinoma are often difficult, but recent studies report that continuous infusion of high doses of 5-fluorouracil (5-FU) and combined 5-FU plus leucovorin achieve the remarkable response. It is important to know the chemosensitivity for 5-FU in each case, but it is difficult to collect the materials from the recurrent cases for testing chemosensitivity, and also the successful rates themselves of chemosensitivity test have not been achieved.

The purpose of this study is to use the results of histopathological effects of preoperative chemotherapy using UFT as a chemosensitivity test for 5-FU at the time of the recurrence of colorectal carcinoma.

MATERIALS AND METHODS

Patients
Patients under seventy years of age with histologically confirmed colorectal carcinoma were eligible for this study.

UFT
UFT, a new fluoroprimidine developed by S. Fujii et al., is combined with uracil: tegafur=4:1, and does not increase the toxicity of tegafur, and achieves high concentrations of 5-FU in tumor tissues.

In our previous study, we reported that UFT was absorbed without gastrointestinal disturbances, and the concentrations of 5-FU in tumor tissues and metastatic lymphnodes were higher than in normal colorectal tissues and non-metastatic lymphnodes.

UFT was employed as an agent in this study of preoperative chemotherapy, because the characteristics of UFT were suitable when the vascularities of colorectal cancer were maintained, less side effects were noted, and UFT was able to be administered at home.

PREOPERATIVE CHEMOTHERAPY
UFT was orally administered preoperatively at a dose of 600mg/day for 7-10 days, and also administered 300mg at three hours just before operation.

EVALUATION OF HISTOPATHOLOGICAL EFFECT
Resected tumors were stained by routine H.E., and histopathological effects at maximum section were evaluated by the gradings of "The General Rules for the Gastric Cancer Study" of "Japanese Research Society for Gastric Cancer". This classification was mainly defined by quantitative change in the section showing degenerative necrotic fusion. (Table 1.)

RESULTS
Fifty-five patients of colorectal carcinoma were given UFT preoperatively, and the total doses were 4.2-17.4g (average 7.94 ± 2.24).

Although yet undocumented, in 14 of 55 cases (25.5%: 2 cases were grade 3 and 12 cases were grade 2), it was discovered that the patients with a grade 2 or higher were sensitive to 5-FU. (Table 2)
Recurrences were seen in 2 of 14 sensitive cases (14.3%) and in 7 of 41 non-sensitive cases (17.1%) in three years after operation.
Vascular metastasis such as hepatic recurrence were seen in 5 of 7 recurrent cases in the non-sensitive group, but there was no vascular metastasis in the sensitive group.

Four of the sensitive 14 cases and also 28 of the non-sensitive 41 cases were given UFT as an adjuvant chemotherapy. In the adjuvant chemotherapy group, recurrences were seen in one of 4 in the sensitive group (25%) and in 4 of 28 in the non-sensitive group (14.3%).

In the course of study, relationships between chemosensitivity and histopathological effects were examined retrospectively, and a new protocol of prospective study has been created. In the new protocol, sensitive cases are divided into two groups with or without adjuvant chemotherapy, and non-sensitive cases are also divided into two groups.

Table 2. Histopathological Effect

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases</th>
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<tbody>
<tr>
<td>Grade 0</td>
<td>13 cases (23.5%)</td>
</tr>
<tr>
<td>Grade 1a</td>
<td>17 cases (30.9%)</td>
</tr>
<tr>
<td>Grade 1b</td>
<td>11 cases (20.0%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>12 cases (21.8%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2 cases (3.6%)</td>
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</tbody>
</table>

DISCUSSION

5-FU is the only effective drug to treat colorectal carcinomas. It is necessary to know the chemosensitivity for 5-FU in each case, to predict the therapeutic effect. In this study, histopathological effects were evaluated by preoperative chemotherapy using UFT at a dose of 600mg/day for 7-10 days in 55 patients with colorectal carcinomas. As a result, 14 of 55 cases showed a grade 2 or higher. This result in patients was well correlated with the results of the chemosensitivity tests in vivo and in vitro experimental tests for 5-FU. Arterial infusion achieved remarkable responses in metastatic liver tumors of which vascularities were distinct, also the preoperative chemotherapy obtained high 5-FU concentrations in tumor tissues, equal to the concentrations in contacted in vitro chemosensitivity tests, because the drugs were administered before the vascularities were destroyed by surgery.

We considered that the preoperative chemotherapy using UFT was simple, safe, and was able to be administered at home, and was also a reliable chemosensitivity test for 5-FU in patients. Although the sensitivity is different at the time of surgery and at the time of recurrence, it is necessary to predict the therapeutic effects of 5-FU from the histopathological effects in resected specimens, because it is difficult to collect the materials from the recurrent cases for testing chemosensitivity.

Key Words: Colorectal cancer, UFT