Intraoperative Radiation Therapy for Pancreatic Carcinoma

The Choice of Treatment Modality

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Summary

Ninety patients with carcinoma of the pancreas treated between 1976 and 1990 were reviewed retrospectively. Intraoperative radiation therapy (IORT) in combination with external beam radiation therapy (EBRT) for localized but unresectable tumors (n = 29) prolonged survival significantly more than IORT alone (n = 16) (p < 0.01); it seems EBRT enhanced or contributed to the better results obtained with IORT plus EBRT. Moreover, IORT, alone or in combination, relieved pain. Adjuvant IORT for residual tumors (n = 20) might not effectively prolong survival, because the difference in survival rate between noncurative resection plus IORT and nonresection plus IORT in combination with EBRT was not significant. Curative tumor resection of stage III disease in combination with IORT (n = 9) resulted in significantly longer survival as compared with curative tumor resection alone (n = 8) (p < 0.05). It may be advisable to administer IORT in combination with EBRT to patients with advanced pancreatic carcinoma, avoiding aggressive tumor resection, when curative tumor resection cannot be performed.

Key Words: Pancreatic cancer; intraoperative radiation therapy; external beam radiation therapy.

Introduction

Despite recent progress in diagnostics and therapeutics, the prognosis of pancreatic carcinoma remains dismal. This can be attributed mainly to two reasons. One is that distant metastases, to the liver for example, develop in a high percentage of patients after resection of the primary tumor. The other reason is that tumor cells have already spread insidiously to the retroperitoneal tissues, and they often cannot be cleared away completely, even when extensive dissection is performed.

Recently, intraoperative radiation therapy (IORT) (1) has been utilized for unresectable pancreatic carcinoma in many institutes (2–6). However, IORT for resected carcinoma, as an adjuvant has not been prevalent, and the efficacy of adjuvant IORT remains uncertain.

We introduced IORT for unresectable pancreatic carcinoma in 1976, and it has also been used for resectable carcinoma in an attempt to decrease local recurrence. The purpose of this study is to retrospectively analyze patients treated by IORT, and to evaluate IORT as an adjuvant therapy for resected carcinoma. Additionally, on the basis of autopsy find-
Table 1
Treatment Modalities, TNM Staging, and Median Followup

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment modality</th>
<th>No. of patients</th>
<th>Stage I (T1, T2 N0M0)</th>
<th>Stage II (T3 N0M0)</th>
<th>Stage III (Any T, N1M0)</th>
<th>Median followup, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nonresection + IORT (^a)</td>
<td>16</td>
<td>0</td>
<td>10</td>
<td>6</td>
<td>5.5</td>
</tr>
<tr>
<td>2</td>
<td>Nonresection + IORT + EBRT (^b)</td>
<td>29</td>
<td>0</td>
<td>21</td>
<td>8</td>
<td>11.9</td>
</tr>
<tr>
<td>3</td>
<td>Curative resection + IORT ± EBRT</td>
<td>11 (10)</td>
<td>2</td>
<td>0</td>
<td>9</td>
<td>44.4</td>
</tr>
<tr>
<td>4</td>
<td>Noncurative resection + IORT ± EBRT</td>
<td>20 (17)</td>
<td>0</td>
<td>2</td>
<td>18</td>
<td>12.0</td>
</tr>
<tr>
<td>5</td>
<td>Curative resection alone</td>
<td>14</td>
<td>5</td>
<td>1</td>
<td>8</td>
<td>42.0</td>
</tr>
</tbody>
</table>

\(^a\)IORT: Intraoperative radiation therapy.
\(^b\)EBRT: External beam radiation therapy.
\(^c\)(): Number of patients treated with EBRT.

ings, the choice of treatment modality according to the stage of tumors is discussed.

Patients and Methods

Between October 1976 and February 1990, 90 patients (53 men and 37 women, mean age 61.5 yr) with histologically confirmed adenocarcinoma of the pancreas were treated at the Department of Surgery, Tokyo Metropolitan Komagome Hospital. Patients with cystadenocarcinoma, islet cell carcinoma, and periampullary carcinoma of the duodenum were excluded from this study. IORT for unresectable tumors was introduced in 1976, and it has also been administered to 31 consecutive patients with resectable tumors since 1983.

According to the treatment modality, the study population was classified into five groups: group 1, consisting of 16 patients with localized unresectable tumors who had been treated with IORT alone; group 2, 29 patients with localized unresectable tumors treated with IORT and then with external beam radiation therapy (EBRT); group 3, 11 patients with curatively resected tumors treated with IORT, 10 of which were also treated with EBRT; group 4, 20 patients with noncuratively resected tumors treated with IORT, 17 of which were also treated with EBRT; and group 5, 14 patients, who had undergone tumor resection alone. Curative resection was defined as the absence of tumor cells at surgical margins on the basis of microscopic findings. Treatment modalities, staging of the tumors classified according to the TNM system (7), and median followup, are summarized in Table 1. It should be mentioned that stage II unresectable tumors could not be distinguished from those in stage III, because peripancreatic lymph node involvement was not thoroughly assessed in patients with stage II unresectable tumors.

Surgical Procedures

In case of unresectable tumors of the pancreatic head, frozen sections of needle biopsy specimens of the tumors, and peripancreatic lymph nodes were histopathologically examined before IORT. Distal gastrectomy was performed to obtain good tumor exposure and avoid concomitant irradiation of the duodenum, which also probably reduced the risk of radiation ulcer of the duodenum owing to inevitable adverse scattered radiation. Hepaticojejunostomy was performed when necessary to overcome preexisting obstructive jaundice.

As for resectable tumors, these were resected as far as anatomically resectable, despite possible local lymph node metastases or tumor invasion to the retroperitoneal region or major vessels. Dissection of the lymph nodes was practiced along the common hepatic artery, celiac axis, superior mesenteric artery (SMA), hepatoduodenal ligament, and the peri-pancreatic region. Dissection of retroperitoneal connective tissues, including the nerve plexuses, was