The Efficacy of Postoperative Chemotherapy with Cisplatinum and Pepleomycine for Esophageal Cancer

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From May 1984 to August 1991, 58 patients without preoperative adjuvant therapy underwent resection of the esophagus for esophageal cancer. Three weeks after esophagectomy, one cycle of postoperative chemotherapy, consisting of intravenously infused cisplatinum at a dose of 70mg/m² on day 1 and intramuscular pepleomycine at a dose of 5mg/body from day 1 to day 5, was administered in the 24 patients. In all patients receiving chemotherapy, mild fatigue or poor appetite occurred after drug administration, but severe drug toxicity, such as bone marrow depression, gastrointestinal bleeding or pulmonary fibrosis, did not occur. Eighteen patients (75%) died from cancer. The 3-year survival rate was 22.9% and the 5-year survival rate was 17.1%. In the patients who underwent curative operations, the 3-year and 5-year survival rates were 46.2% and 27.7%. However, there was no significant difference in the survival rates between the patients with postoperative chemotherapy and patients with esophagectomy alone. We conclude that one cycle of postoperative chemotherapy with cisplatinum and pepleomycin does not affect the survival of patients undergoing esophagectomy for esophageal cancer.

Introduction

Esophageal carcinoma is a serious malignant disease with a poor prognosis, although a curative resection is more successful in patients receiving preoperative radiation or chemotherapy than in patients receiving only surgery. In patients with potentially resectable esophageal cancer, combined modality treatment is often performed after surgical resection. In this study, we retrospectively evaluated the efficacy of postoperative chemotherapy for resectable esophageal cancer.

Materials and Methods

Patients Selection and Evaluation

From May 1984 to August 1991, 58 patients underwent esophagectomy without preoperative combined-modality treatment for potentially resectable and histologically proven squamous cell carcinoma of the esophagus. The patients were retrospectively classified into two groups. Twenty-four patients who had no complications, such as anastomotic leakage or prolonged ventilation support due to respiratory failure and who could start to consume food orally within 2 weeks after surgery, underwent postoperative chemotherapy (Group 1). Their performance status was above grade 3. Thirty-four patients did not undergo any postoperative combined-modality treatment, because these patients did not start eating within 2 weeks after surgery due to postoperative complications (Group 2). Their performance status was below grade 4. The characteristics of the patients in the two groups are shown in Table 1.

Table 1. Characteristics of 58 Patients Undergoing Esophagectomy without Preoperative Combined-Modality Treatment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Postoperative chemotherapy (n = 24)</th>
<th>No postoperative chemotherapy (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64.0 ± 8.3</td>
<td>66.3 ± 8.8</td>
</tr>
<tr>
<td>Female/Male</td>
<td>5:19</td>
<td>2:32</td>
</tr>
<tr>
<td>Location of tumor</td>
<td>5 (20.8)</td>
<td>0 ( 0 )</td>
</tr>
<tr>
<td>Cervical esoph.</td>
<td>2 ( 8.3 )</td>
<td>1 ( 2.9 )</td>
</tr>
<tr>
<td>Upper intrathoracic esoph.</td>
<td>7 (29.2)</td>
<td>24 (70.6)</td>
</tr>
<tr>
<td>Middle intrathoracic esoph.</td>
<td>8 (33.3)</td>
<td>7 (20.6)</td>
</tr>
<tr>
<td>Lower intrathoracic esoph.</td>
<td>2 ( 8.3 )</td>
<td>2 ( 5.9 )</td>
</tr>
<tr>
<td>Abdominal esoph.</td>
<td>6 (25.0)</td>
<td>15 (44.1)</td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td>18 (75.0)</td>
<td>19 (55.9)</td>
</tr>
<tr>
<td>Stage</td>
<td>14 (58.3)</td>
<td>22 (64.7)</td>
</tr>
<tr>
<td>Curative resection</td>
<td>10 (41.7)</td>
<td>12 (35.3)</td>
</tr>
</tbody>
</table>

Surgery

In fifty-eight patients, thoracoabdominal esophagectomy
and reconstruction were performed with the gastric tube pulled up to the neck through the retrosternal route. In these patients, the cervical, posterior mediastinal and perigastric lymph nodes were dissected.

**Postoperative Chemotherapy**

Three weeks after surgery, one cycle of postoperative chemotherapy was administered, consisting of intravenously infused cisplatinum (CDDP) at a dose of 70mg/m² on day 1 and intramuscular pepleomycin (PEP) at a dose of 5mg/body from day 1 to day 5.

**Data Analysis**

The survival rate was determined by the Kaplan-Meier method, and the Cox-Mantel method was used for statistical evaluation of differences in survival rates, with a p value of 0.05 considered significant.

**Results**

There were no significant differences in characteristics (Table 1) or in survival outcome (Table 2, Fig. 1-3) between patients with postoperative chemotherapy consisting of CDDP/PEP and those without combined modality treatment. Eighteen patients (75%) died from cancer in Group 1 and 18 (52.9%) in Group 2. The one-year cumulative survival rate was 47.6% in Group 1 and 50.6% in Group 2; the 3-year survival rates were 22.9% and 25.5%, respec-

| Table 2. Outcome in 58 patients followed from 1 to 8 years |
|---------------------------------|-----------------|-----------------|
| Outcome                        | Postoperative chemotherapy | No postoperative chemotherapy |
| Alive (disease free)           | 6 (25.0)         | 10 (29.4)       |
| Cancer death                   | 18 (75.0)        | 18 (52.9)       |
| Death from other disease       | 0 (0)            | 6 (17.6)        |

**Fig. 1. Overall cumulative survival curves.**

**Fig. 2. Cumulative survival curves by nodal involvement.**

**Fig. 3. Cumulative survival curves by curability.**
tively, and the 5-year survival rates were 17.1% and 12.8%.

In the patients who underwent curative operations, the
3-year and 5-year survival rates were 46.2% and 27.7%,
respectively in group 1 and 42.9% and 21.5% in group 2.
Hematogenic metastasis occurred in 8 patients (33.8%) in
Group 1 and 7 (20.6%) in Group 2, lymphogenic metastasis
in 1 (4.2%) and 2 (5.9%), respectively, and local recur-
rence in 4 (16.7%) and 4 (11.8%) in the two groups,
respectively. In all patients receiving chemotherapy, mild
fatigue or poor appetite occurred after drug administration,
but severe drug toxicity, such as bone marrow depression,
gastrointestinal bleeding or pulmonary fibrosis, did not
occur.

Discussion

In our institution, from 1970 to 1985 preoperative radiation
had been administered in doses of from 35 to 50 Gy for
resectable esophageal cancer, but prognosis of the patients
had not improved comparing with patients of historical
control. Some of nonrandomised studies (1, 2, 3, 4) sug-
gested no advantage for resectable esophageal cancer, and
the optimal preoperative radiation is not clear. Therefore,
principally postoperative chemotherapy was chosen for
resectable esophageal cancer. Combination therapy of pe-
pleomycin and cisplatinum was adopted, because in the
majority of our patients, histologic type of the esophageal
cancer was squamous cell carcinoma.

Essentially, it should be analyzed to compare the sur-
vival by postoperative chemotherapy in the patients who
are selected randomly. Although this study is not a random-
ized trial, it demonstrates that postoperative chemotherapy
consisted of cisplatinum and pepleomycin may not be
effective for resectable esophageal cancer. On the contrary,
it may be bad for the survival in patients after esopha-
gectomy.

Recently, prospective randomized trials consisting of
preoperative cisplatinum-based chemotherapy with con-
comitant radiation therapy were performed in some insti-
tutions (5, 6, 7, 8). These combined-modality therapy re-
sulted in pathologic complete responses in 20% to 40%.
These results support the use of all three modalities as the
optimal approach for the potential cure of esophageal
cancer. However, because the number of patients was small
and these study included both squamous cell carcinoma and
adenocarcinoma, the results need to be confirmed and
compared with esophagectomy alone. Furthermore, we
should try a prospective randomized study, consisting of
preoperative chemo-radiotherapy.

We conclude that one cycle of postoperative chemo-
therapy with cisplatinum and pepleomycin does not affect
the survival of patients undergoing esophagectomy for
esophageal cancer.

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