Acta Med. Nagasaki 38:193 – 195

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

Katsunobu Kawahara, Shinji Akamine, Noriaki Itoyanagi, Tsutomu Tagawa, Akihiro Nakamura, Masashi Muraoka, Hiroharu Tsuji, Shinsuke Hara, Yutaka Tagawa, Hiroyoshi Ayabe and Masao Tomita

First Department of Surgery, Nagasaki University School of Medicine, Nagasaki, Japan

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 surival 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 esophaqus. 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

Variables	Postoperative chemotherapy (n = 24)	No postoperative chemotherapy (n = 34)
Age	64.0 ± 8.3	66.3 ± 8.8
Female/Male	5:19	2:32
	Number of patients (%)	
Location of tumor		
Cervical esoph.	5 (20.8)	0 (0)
Upper intrathoracic esoph.	2 (8.3)	1 (2.9)
Middle intrathoracic esoph.	7 (29.2)	24 (70.6)
Lower intrathoracic esoph.	8 (33.3)	7 (20.6)
Abdominal esoph.	2 (8.3)	2 (5.9)
Lymph node metastasis		
Negative	6 (25.0)	15 (44.1)
Positive	18 (75.0)	19 (55.9)
Stage		
Stage 0	0 (0)	0 (0)
Stage I	0 (0)	7 (20.6)
Stage IIA	6 (25.0)	8 (23.5)
Stage IIB	4 (16.7)	2 (5.9)
Stage III	14 (58.3)	17 (50.0)
Curability		
Curative resection	14 (58.3)	22 (64.7)
Palliative resection	10 (41.7)	12 (35.3)

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/m^2 on day 1 and intramuscular pepleomycine (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	Number of patients (%)	
	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)

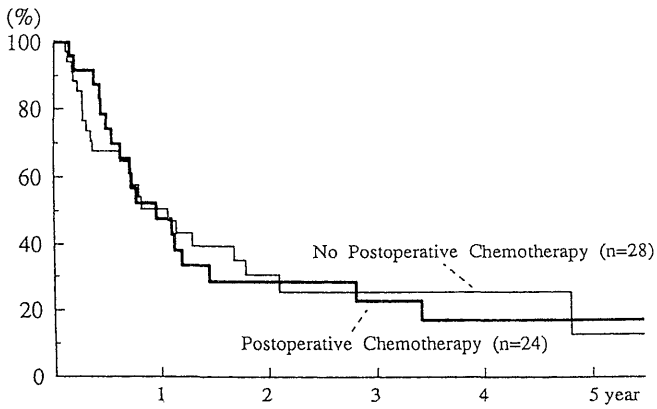

Fig. 1. Overall cumulative survival curves.

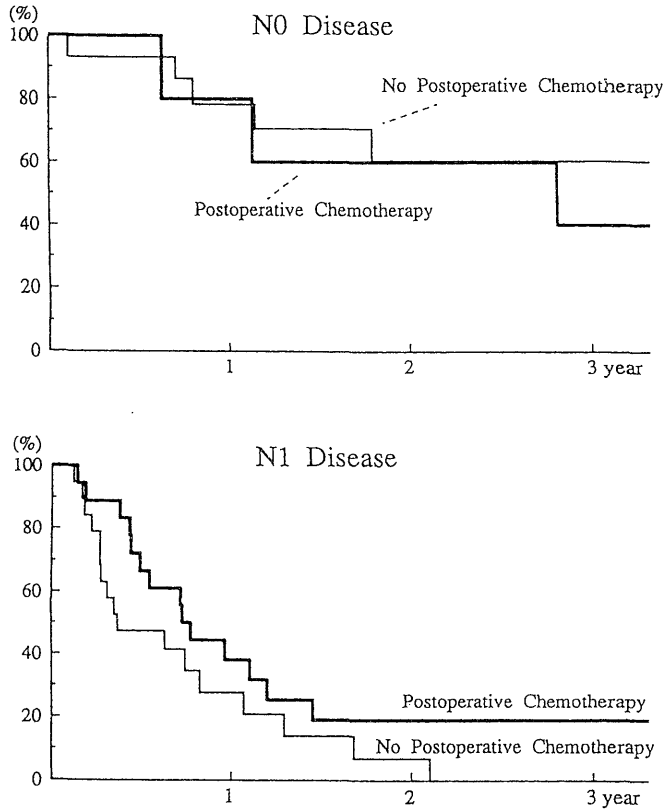

Fig. 2. Cumulative survival curves by nodal involvement.

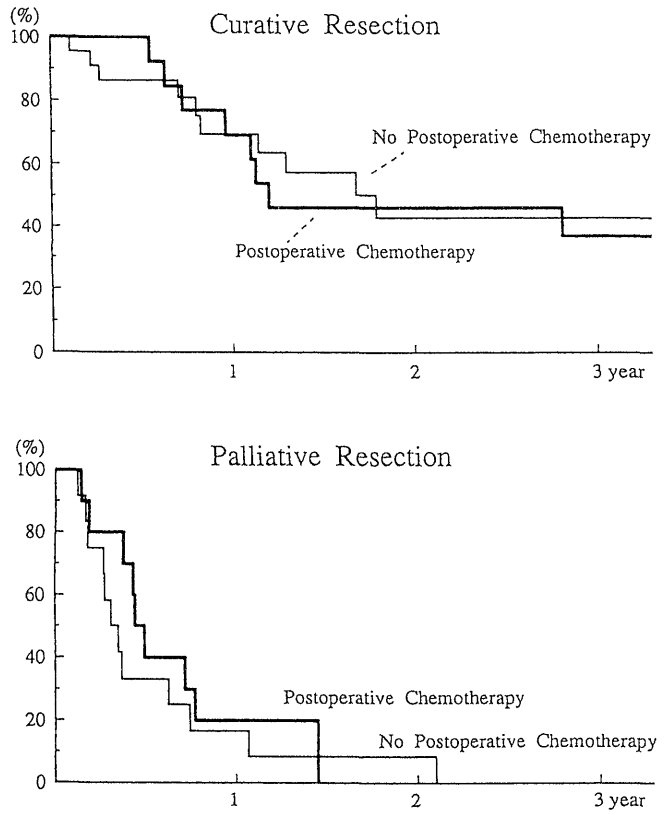

Fig. 3. Cumulative survival curves by curability.

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 recurrence 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 nonrandmised studies (1, 2, 3, 4) suggested 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 pepleomycine 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 survival by postoperative chemotherapy in the patients who are selected randomly. Although this study is not a randomized 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 esophagectomy.

Recently, prospective randomized trials consisting of preoperative cisplatinum-based chemotherapy with concomitant radiation therapy were performed in some institutions (5, 6, 7, 8). These combined-modality therapy resulted 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 chemotherapy with cisplatinum and pepleomycin does not affect the survival of patients undergoing esophagectomy for esophageal cancer.

References

1) Guernsey JM, Dogget RL, Mason GR, et al.: Combined treatment of cancer of the esophagus. Am J Surg 117:157, 1969.
2) Kelsen DP, Ahuja R, Hopfan S, et al.: Combined modality therapy of esophageal carcinoma. Cancer 48:34,1981.
3) Maeta M, Koga S, Adachi H, et al.: Preoperative radiotherapy and intra-abdominal metastasis of the lymph node in the surgical treatment of carcinoma of the thoracic esophagus. Surg Gynecol Obstet 165:235, 1987.
4) Wu YK, Huang KC: Chinese experience in the surgical treatment of carcinoma of the esophagus. Am J Surg 190:361, 1979.
5) Seydel HG, Leichman L, Lattin P, et al.: Preoperative radiation and chemotherapy for localized squamous cell carcinoma of the esophagus: An ATOG study. Int J Radiat Oncol Biol Phys 14:33, 1988.
6) Forastiere AA, Orringer MB, Perez-Tamayo C, et al.: Concurrent chemotherapy and radiation therapy followed by transhiatal esophagectomy for local-regional cancer of the esophagus. J Clin Oncol 8:119, 1990.
7) Wolf WG, Vaughn AL, Seigler HF, et al.: Survival of patients with carcinoma of the esophagus treated with combined-modality therapy. J Thorac Cardiovasc Surg 105:749, 1993.
8) Naunheim KS, Petruska PJ, Roy TS, et al.: Preoperative chemotherapy and radiotherapy for esophageal carcinoma. Thorac Cardiovasc Surg 103:887, 1992.