



A Study of Patients Having Survived Curative Operation for Esophageal Cancer for Five Years or More

Hamabe, Yutaka ; Ikuta, Hajime ; Narita, Kouichi ; Nakamura, Yoshiki ; Yamamoto, Masahiro ; Saitoh, Yoichi

(Citation)

The Kobe journal of the medical sciences, 42(5):333-346

(Issue Date)

1996-10

(Resource Type)

departmental bulletin paper

(Version)

Version of Record

(URL)

<https://hdl.handle.net/20.500.14094/E0000970>



A STUDY OF PATIENTS HAVING SURVIVED CURATIVE OPERATION FOR ESOPHAGEAL CANCER FOR FIVE YEARS OR MORE

Yutaka HAMABE, Hajime IKUTA, Kouichi NARITA,
Yoshiki NAKAMURA, Masahiro YAMAMOTO, and Yoichi SAITOH

First Division, Department of Surgery,
Kobe University School of Medicine

INDEXING WORDS

resected esophageal cancer; curative resection; prognostic
factors; long-term survival

SYNOPSIS

In order to analyze the prognostic factors for curatively resected esophageal cancer, 42 patients who had survived their operation more than 5 years (long-term survivors) were compared for clinicopathologic items with 30 recurrent patients who had died within 5 years postoperatively (recurrent cases). Moreover, to estimate the prognosis for the current survivors, we investigated the cause of death of long-term survivors who had died.

Received for publication : October 17, 1996

Authors' names in Japanese : 濱辺 豊, 生田 肇, 成田 晃一
中村 吉貴, 山本 正博, 齋藤 洋一

This comparison showed that the rate of lymphatic invasion was 36.4% and of blood vessel invasion 19.4% for the survivors, much lower than those of the recurrent cases which were respectively 62.1% and 31.0%. It was found that the significantly unfavorable prognosis-determinant factors was lymphatic invasion ($p < 0.05$). Ten out of 12 n(+) survivors (83.3%) had a single metastasing region, one in the neck, three in the mediastinum and six in the abdomen. This was not significantly different from the recurrent cases, of whom, ten out of 14 n(+) cases had a single metastasing region, six in the mediastinum and four in the abdomen. As for the number of metastatic lymph nodes, nine out of 12 n(+) survivors (75%) had only one metastatic lymph node, and none of them had more than three. On the other hand, two of the recurrent cases had more than three. Of the 42 long-term survivors, 21 patients are still alive (current survivors' average age: 70.1 ± 7.9) and 21 have died. The cause of death was recurrence in six cases, metachronous primary malignant tumor in three, other disease in six and unknown in six. The average age of death was 62.1 ± 10.3 in cases of recurrence or double cancer, and 71.8 ± 9.5 in others. The former were thus significantly younger than the latter ($p < 0.05$).

INTRODUCTION

The prognosis for esophageal cancer has been poor, in spite of some recent therapeutic improvement for various

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

malignant neoplasms. Even curatively resected esophageal cancers are known to sometimes recur. According to a report on treatment results for esophageal carcinoma,⁷⁾ the 5-year survival rate for cII(relative curative resection⁸⁾) was 23.74% and for cIII(absolute curative resection) 45.62%. The aim of this study was to evaluate the prognostic factors for cases curatively resected for esophageal cancer. Furthermore, we analyzed the long-term prognosis for the patients having survived more than 5 years postoperatively.

MATERIALS AND METHODS

At our department, 297 esophageal cancer patients were resected between March 1970 and August 1996. Of these, 145 patients had curative operation which consists of esophageal resection and regional lymphnode dissection without residual tumors. Forty two patients resected curatively have survived their operation for esophageal cancer more than 5 years (survivors). In order to analyze their prognostic factors, these 42 patients were compared for clinicopathologic items with 30 recurrent patients who had died within 5 years after curative operation(recurrent cases) (Table I). The types of recurrence were organ recurrence(18 cases), lymph node recurrence(16 cases), local recurrence(3 cases) and recurrence of anastomotic site (3 cases) (ten cases showed more than one type). The sites of organ recurrence were lung (11), bone (6)

and liver (5) (Table II). Moreover, to help us evaluate the prognosis for the current survivors, we investigated the cause of death of long-term survivors who had died.

In principle, intra-thoracic esophagectomy was performed by means of right thoracotomy for intra-thoracic esophageal cancer and pull-through esophagectomy for cervical esophageal cancer. Left thoracotomy combined with RII ⁸⁾ lymphadenectomy was used for lower esophagectomy in cases of abdominal esophageal cancer. About adjuvant therapy, chemotherapy or radiotherapy was done to 35 patients preoperatively and 28 patients postoperatively.

The data was analyzed with the Student's t test and the chi-square test. Survival curves and rates were estimated with the Kaplan-Meier method, and difference in survival curves was determined with Cox-Mantel test. P values less than 0.05 were considered significant.

RESULTS

The survival rates of curatively operated cases and non-curatively operated cases were significantly different ($p < 0.01$) (Fig. 1): the 5-year survival rates of the former was 36.1% and of the latter 9.5%. A comparison of the two groups by clinicopathologic variables shows that there were six cases of cervical esophagus and five of abdominal esophagus among the long-term survivors but there was one case of cervical

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

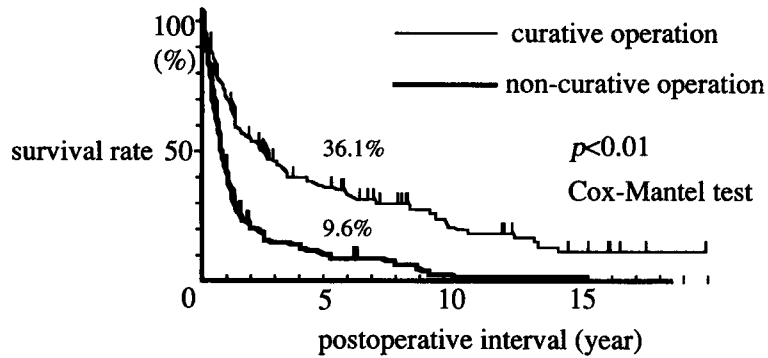


Fig. 1. Survival rate according to curability.

Table I. Patients with esophageal cancer according to curability.

curability	No. of patients with resected esophageal cancer
curative resection	145
survivors more than 5 years	42
recurrent cases within 5 years	30
survivors within 5 years and dead cases caused by other disease	73
non-curative resection	152
total	297

Table II. Type of recurrence.

Type of recurrence	No. of patients (n=30)
organ	18
lung	11
bone	6
liver	5
lymph node	16
local recurrence	3
anastomotic site	3

(ten cases showed more than one type)

Table III. Location of esophageal cancers between survivors and recurrent cases.

location	No. of survivors (n=42)	No. of recurrent cases (n=30)
cervical esophagus	6	1
intra-thoracic esophagus	31	29
abdominal esophagus	5	0

Table V. Region and number of metastatic lymph node between survivors and recurrent cases with metastasis.

	No. of survivors with metastasis (n=12)	No. of recurrent cases with metastasis (n=14)
1) region		
one region	10	10
neck	1	0
mediastinum	3	6
abdomen	6	4
two region		
mediastinum and abdomen	2	4
2) number		
one	9	7
two	1	3
three	2	2
more than three	0	2

Table VI. Cause and average age of death in 42 survivors.

cause of death	No. of patients	average age
alive cases	21	70.1 ± 7.9 (6y ~ 18years)
dead cases	21	67.7 ± 10.8 (5y ~ 14years)
recurrent	6	62.1 ± 10.3 71.8 ± 9.5 $p < 0.05$
metachronous malignant tumor	3	
other disease	6	
unknown	6	

(): postoperative duration

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

Table IV. Clinicopathologic characteristics between survivors and recurrent cases.

clinicopathologic variables	survivors (n=42)	recurrent cases (n=30)	p valve
Age	57.6	61.3	NS
Sex(M/F)	28/14	23/7	NS
Size(cm)	4.74	5.35	NS
Histologic type			
well	16	7	NS
moderately	7	9	
poorly	12	13	
others	7	1	
Depth of invasion			
mm-sm	13	6	NS
mp	6	6	
a1	10	4	
a2	7	13	
Grade3	6	1	
Node metastasis			
n0	30	16	NS
n1	2	1	
n2	10	13	
Lymphatic invasion			
(+)	12 (36.4%)	18 (62.1%)	$p<0.05$
(-)	21	11	
others	9	1	
Venous invasion			
(+)	6 (19.4%)	9 (31.0%)	NS
(-)	25	20	
others	11	1	
Stage			
0	10	6	NS
I	5	4	
II	10	1	
III	14	19	
others	3		
Preoperative therapy			
(+)	20	15	NS
(-)	22	15	
Postoperative therapy			
(+)	14	14	NS
(-)	28	16	
Postoperative complication			
(+)	21	14	NS
(-)	18	16	
unknown	3		

esophagus and none of abdominal esophagus among the recurrent cases (Table III). With regard to other clinicopathologic variables, there were no significant differences in age, sex, tumor size, histologic type, depth of invasion, node metastasis, adjuvant therapy, histologic stage or postoperative complications. However the rate of lymphatic invasion was 36.4% and of blood vessel invasion 19.4% for the survivors, much lower than those of the recurrent cases, which were respectively, 62.1% and 31.0%. It was found that the significantly unfavorable prognosis-determinant factor was lymphatic invasion ($p < 0.05$) (Table IV). Lymph node metastasis was noted in 12 survivors and 14 recurrent cases. Ten out of 12 n(+) survivors (83.3%) had a single metastasing region, one in the neck, three in the mediastinum and six in the abdomen. There was not significantly different from the recurrent cases, of whom 10 out of 14 n(+) (71.4%) had a single metastasing region, six in the mediastinum and four in the abdomen. As for the number of metastatic lymph nodes, nine out of 12 n(+) survivors (75%) had only one metastatic lymph node metastasis, one case had two, and two cases had three, but none of them had more than three. On the other hand, seven out of the 14 n(+) recurrent cases (50.0%) had one metastatic lymph node, three cases had two and two cases had three, while two of the recurrent cases had more than three metastatic lymph nodes (Table V).

Of the 42 survivors, 21 patients are still alive and their average age is 70.1 ± 7.9 (mean $\pm$ SD) (postoperative interval: 6 ~ 18 years), and 21 have died. The cause of death

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

was recurrence of the esophageal cancer in 6 cases, metachronous primary malignant tumor in 3, other disease in 6 and unknown in 6 (postoperative interval: 5 ~ 14 years). Metachronous primary malignant tumors consisted of gastric cancer, spinal tumor and cystoadenocarcinoma of the liver. The average age of death among long-term survivors was 62.1 ± 10.3 years in the nine cases of recurrence or double cancer, and 71.8 ± 9.5 years in the other 12 cases. The former were thus significantly younger than the latter ($p < 0.05$) (Table VI). In addition to the metachronous primary malignant tumors identified in three of the dead, two of these tumors were seen in the survivors (rectal cancer and tongue tumor). The rate of complicated metachronous primary malignant tumor for the 42 long-term survivors was 11.9%.

DISCUSSION

Even with improvements in operative methods, radiotherapy and chemotherapy, the prognosis for esophageal cancer remains unsatisfactory. The 5-year survival rate after resection has been reported as 18.5%⁷⁾ and 24.4%⁹⁾. Even after complete resection, 5-year survival rate was only 28.2%.⁹⁾ According to the report on treatment results for esophageal carcinoma in Japan,⁷⁾ the 5-year survival rate for relative curative resection is 23.74% and for absolute curative resection 45.62%. At our department, the 5-year survival rate for curative operations was 36.1% and has been a similarly poor

(Fig. 1). The prognostic factors for resected esophageal cancer in items of clinicopathologic variables has been reported in some literatures.^{3,5,6,9,11)} Depth of invasion, volume of invasion, lymph node metastasis and distant metastasis are obviously unfavorable prognosis-determinant factors. In this study, we aimed to investigate the prognostic factors for curatively resected esophageal cancer. For comparison with the 5-year survivors, we selected the patients with curatively resected esophageal cancer who had died owing to recurrence within 5 years postoperatively. Because of the need for accurate prognostic factors, we excluded the cases whose cause of death was other diseases or unknown.

There were few differences in clinicopathologic items between the survivors and the recurrent cases because both groups were operated on in a so-called curative manner. However, some significant features could be identified. First, concerning the location of the tumor, cervical and abdominal esophageal cancer had a more favorable prognosis than intrathoracic esophageal cancer surrounded by thoracic aorta, trachea and main bronchus and which could not undergo en bloc lymphadenectomy of the regional lymph nodes satisfactorily. Second, lymphatic and blood venous invasion were unfavorable prognosis-determinant factors, either with existing or without lymph node metastasis at the time of operation (lymphatic invasion; $p < 0.05$).

The frequency of lymph node metastasis was similar for both groups, but not in metastatic region and number. Among

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

the long-term survivors, metastasis to only the abdominal region and solitary lymph node metastasis were featured. Among the recurrent cases, on the other hand, the rate of occurrence of two regional lymph node metastases or non-solitary lymph node metastasis was higher. According to some reports, the number of metastatic positive lymph nodes is apparently one of the most reliable prognostic factors with regard to breast cancer.¹⁾ Concerning esophageal cancer, we previously reported³⁾ that the number of metastatic lymph nodes was a reflection of the prognosis for resected esophageal cancer, and that the 1-year survival rate of cases featuring more than three metastatic lymph nodes was 9.5%, while none of them survived for 5 years. Omori reported¹¹⁾ that almost all patients with distant lymph node metastases, with more than three positive nodes, or with positive nodes both in the thorax and abdomen died due to recurrence within 3 years postoperatively. In a report preceding this study of curatively resected cases, we noted that in cases of non-curative resection, the region or the number of metastatic lymph nodes was a usefully prognosis-determinant factor. We therefore think that solitary abdominal lymph node metastasis represents a favorable condition in case of esophageal cancers accompanied by lymph node metastasis.

Investigating the long-term prognosis for the survivors, we noted that these patients were quite old. In fact, the average age of the current 21 survivors is 70 years old. Even for patients who have survived more than 5 years postoperatively, prognosis-determinant factors were also

malignant tumor, recurrence of esophageal cancer or metachronous primary malignant neoplasmas. The average age of patients who died due to malignant tumors was lower ($p < 0.05$) than that for other diseases or unknown causes. Mori et al. reported¹⁰⁾ that among 10-year survivors after operation, the cause of death was recurrence in 10.9% and double cancer in 20.3%. Moreover, Habu et al. reported²⁾ an investigation of prognostic factors of early gastric cancer showing that primary cancer in other organs was found in 4.3%, which was more frequently than the rate expected for the general population. In addition, we reported⁴⁾ recently that in 21 cases surviving for at least 10 years after operation for esophageal cancer, metachronous primary malignant tumors had developed in five cases (23.8%). On the basis of these findings, we should seriously consider the possibility of occurrence of metachronous or other primary cancer at the time of follow-up for treated malignant tumors.

As a result of this clinicopathologic study of curatively operated esophageal cancer, we conclude that a favorable prognosis can be expected for cervical and abdominal esophageal cancer. The unfavorable prognosis-determinant factors are lymphatic invasion and occurrence more than three metastatic lymph nodes. Investigating the cause and age of death among patients who had survived for 5 years, the presence of a malignant tumor (recurrence or double cancer) was reflected in their average age of death.

CURATIVE OPERATION FOR ESOPHAGEAL CANCER

REFERENCES

1. Cascinelli, N., Singletary, E., Greco, M., Ames, F., Testori, A., Baldini, M., Morabito, A., Bufalino, R., Shallenberger, R., Guinee, V., Leo, E., and Balch, C.: Tumori. 1989. 75.123/131. Long-term survival and prognostic factors for 2170 breast cancer treated at two cancer centers(Milan and Houston).
2. Habu, H., Takeshita, K., Sunagawa, M., and Endo, M.: Jpn. J. Surg. 1987. 17. 248/255. Prognostic factors of early gastric cancer-results of long-term follow-up and analysis of recurrent cases.
3. Hamabe, Y., Sato, Y., and Saitoh, Y.: Nippon Geka Gakkai Zasshi(J. Jpn. Surg. Society). 1988. 89. 805/814. (English Abst.) A clinicopathological study of prognostic factors on esophageal cancer.
4. Ikuta, H., Hamabe, Y., Narita, K., Shiraishi, T., Matsuura, T., Nishida, M., Oosawa, M., Yamamoto, M., and Saitoh, Y.: Jpn. J. Cancer. Clin. 1996. 42. 509/514. (English Abst.) Studies of resected esophageal cancer associated with other primary malignant tumors.
5. Ikuta, H., Hamabe, Y., Osawa, M., Kuroda, D., Kato, M., and Saitoh, Y.: Nippon Rinsho Geka Igakukai Zasshi(J. Jpn. Society for Clin. Surg.). 1993. 54. 11/15. (English Abst.) Study of long survivors for ten years or more after operation for an esophageal cancer.
6. Ikuta, H., Hamabe, Y., Shiraishi, T., Nishida, M., Matsuura, T., Oosawa, M., Yamamoto, M., and Saitoh, Y.: Nippon Rinsho Geka Igakukai Zasshi(J. Jpn. Society for Clin. Surg.). 1994. 55. 3023/3028. (English Abst.) Study on the cases of non-curative resection for thoracic esophageal cancer.

7. Japanese Research Society for Esophageal Diseases (National Cancer Center, Tokyo, Japan). 1990. The report of treatment results of esophageal carcinoma in Japan. No.10.
8. Japanese Society for Esophageal Diseases (Kanehara&Co.LTD, Tokyo, Japan). 1992. Guide lines for the clinical and pathologic studies on carcinoma of the esophagus. 8th edition.
9. Kan, Y., Min, Y., and Zhi, Y.: Ann. Thorac. Surg. 1987. 43. 176/181. Cancer of esophagus and esophagogastric junction: analysis of results of 1,025 resections after 5 to 20 years.
10. Mori, S. and Ishida, M.: Jpn. J. Gastroenterol. Surg. 1985. 18. 2429/2435. (In Japanese) Esophageal carcinoma cases surviving for more than ten years in Japan.
11. Omori, N.: Nippon Geka Gakkai Zasshi (J. Jpn. Surg. Society). 1987. 88. 413/421. (English Abst.) Prognosis of the patients with carcinoma of the thoracic esophagus, with special reference to the number of metastatic lymph nodes and their metastatic portions.