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Pattern of Recurrence after Extended Radical Esophagectomy with Three-Field Lymph Node Dissection for Squamous Cell Carcinoma in the Thoracic Esophagus

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Abstract. Factors responsible for recurrence of esophageal cancer were investigated in 90 patients who underwent extended radical esophagectomy with three-field dissection for a squamous cell carcinoma in the thoracic esophagus. The initial tumor recurrence was grouped as either locoregional (site of the primary tumor, anastomotic site, or lymph nodes) or as distant (distant organs, pleura, or peritoneum). Nineteen patients (21%) developed a locoregional recurrence, and 19 (21%) developed a distant recurrence. One (1%) developed both recurrences simultaneously and was classified as a distant recurrence. The locoregional recurrence was correlated with the stage factors, particularly the number of metastasis-positive nodes. For the distant recurrence, vascular invasion was found to have been the most important prognostic factor. Our findings suggested that locoregional recurrence was due to tumor progress related to the extent of lymph node metastasis, whereas distant recurrence was due to the oncologic behavior of the tumor. Locoregional recurrence in patients with limited disease may be reduced by extended radical esophagectomy with three-field dissection. Distant recurrence cannot be controlled by surgery. Adopted postoperative adjuvant therapies showed no effect on recurrence.

The current treatment for a squamous cell carcinoma in the thoracic esophagus remains unsatisfactory because discovery is usually delayed until the onset of dysphagia, by which time the tumor is often at the late stage of its natural history. Curative (R0) resection [1] is the preferred modality for treating an esophageal cancer for most surgeons. However, controversy exists over which type of operation offers the optimal prognosis. The presence of tumor cells at a distance from the primary lesion remains one of the main justifications for extended radical esophagectomy with cervicothoracoabdominal three-field lymph node dissection [2]. Others argue that the presence of distant lymph node involvement is such a poor prognostic factor that survival remains unchanged despite removal of these lymph nodes [3].

Most recurrences have been found in the cervical and upper mediastinum—the cervicothoracic region—following transthoracic esophagectomy with thoracoabdominal two-field dissection [4]. This fact has prompted many esophageal surgeons to adopt extended lymphadenectomy for the neck and upper mediastinum.

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Recent reports have discussed the survival benefit of extended radical esophagectomy with three-field dissection and factors influencing the survival [5, 6]. No report has discussed the pattern of recurrence after this procedure. The purpose of this study was to determine the pattern of recurrence following extended radical esophagectomy with three-field dissection and to identify the prognostic factors responsible for recurrence. The findings from this study suggest the extent of lymphadenectomy necessary and whether adjuvant therapy should be combined.

Materials and Methods

Patient Population

Ninety patients underwent extended radical esophagectomy with three-field dissection between 1985 and 1992 at Kurume University Hospital. The mean age of these patients was 58 years (range 45–70 years). There were 81 men and 9 women. The average length of the tumor was 9 cm (range 1–15 cm). The tumor location according to the TNM classification (UICC 1992) [1] was in the upper thoracic esophagus in 11 (12%), the middle in 49 (54%), and the lower thoracic esophagus in 30 patients (33%). According to the pTNM pathologic classification of the primary tumor, 15 were pT1 (17%), 15 pT2 (17%), and were 60 pT3 (67%). At operation, 26 (29%) patients were node-negative (pN0), and 64 (71%) were node-positive (pN1). Cervical lymph node metastasis (pM1-lymph) was seen in 19 (21%) patients, and celiac node metastasis was seen in 2 (2%) patients: pN0M1 for 3 and pN1M1 for 18 patients. The distribution of lymph node metastasis is shown in Table 1. The postoperative pathologic stage was stage I in 7 (8%) patients, stage IIA in 20 (22%), stage IIB in 14 (16%), stage III in 28 (31%), and stage IV in 21 (23%) patients. The average number of the metastasis-positive lymph nodes was 3 for pN1M0 and 12 for pN1M1. The histopathologic examination revealed lymphatic invasion in 71 (79%) patients and venous invasion in 62 (69%).

Table 1. Lymph node metastasis and recurrence in 90 patients with a carcinoma in the thoracic esophagus who underwent extended radical esophagectomy with three-field dissection.

Node	Extent of lymphadenectomy (%)	Metastasis at operation (%)	First site of recurrence (%)
Cervical nodes			
Submandibular			
Right	0	0	1 (1)
Left	0	0	0
Internal jugular			
Right	6 (7)	1 (1)	3 (3)
Left	10 (11)	0	3 (3)
Supraclavicular			
Right	90 (100)	10 (11)	3 (3)
Left	90 (100)	6 (7)	3 (3)
Cervical paraesophageal			
Right[a]	87 (97)	3 (3)	1 (1)
Left	86 (96)	6 (7)	6 (7)
Thoracic nodes			
Right recurrent nerve	90 (100)	29 (32)	0
Left paratracheal	86 (96)	13 (14)	2 (2)
Right paratracheal	45 (50)	3 (3)	1 (1)
Infra-aortic arch	53 (59)	3 (3)	1 (1)
Periesophageal	90 (100)	18 (20)	0
Infracarinal	90 (100)	10 (11)	0
Lower posterior mediastinal	90 (100)	8 (9)	0
Abdominal nodes			
Paracardiac			
Right	90 (100)	23 (26)	0
Left	90 (100)	10 (11)	0
Lesser curvature	90 (100)	14 (16)	0
Left gastric	90 (100)	12 (13)	0
Celiac[b]	44 (49)	2 (2)	2 (2)
Abdominal para-aortic	0	0	2 (2)
Other nodes			
Axillary			
Right	0	0	0
Left	0	0	1 (1)

[a]Includes the cervical paraesophageal and paratracheal nodes.
[b]Includes the common hepatic, splenic, and celiac nodes.

Surgical Procedure and Its Indication

Our criteria for selecting extended radical esophagectomy with three-field dissection were age less than 70 years, no associated severe disease, and achievable locally curative (R0) resection. Our procedure consisted of subtotal esophagectomy with mediastinal lymphadenectomy through a right thoracotomy, upper abdominal lymphadenectomy, construction of a gastric pedicle, cervical lymphadenectomy, and esophagogastrostomy. During this operation the following lymph nodes were resected: supraclavicular, cervical paraesophageal, and paratracheal nodes in the neck; the right recurrent nerve; the left paratracheal, periesophageal, infracarinal, and lower posterior mediastinal nodes in the thorax; and the paracardiac, lesser curvature, and left gastric nodes in the abdomen [7]. The right paratracheal, infraaortic arch, and celiac nodes were resected in half the patients. The internal jugular nodes were resected in only 10% of patients (Table 1).

Adjuvant Therapies

Fifty-five (57%) patients received postoperative adjuvant therapies according to the Japanese Esophageal Oncology Group (JEOG) protocol [8]. Postoperative chemotherapy was given to 45 patients: (1) 18 patients in two courses of cisplatin (70 mg/m^2) and vindesine (3 mg/m^2) and (2) 27 patients in two courses of cisplatin (70 mg/m^2) and 5-fluorouracil (700 mg/m^2) for 5 days. Postoperative radiotherapy was given to six patients each in a total dosage of 50 Gy to the neck and upper mediastinum (T-shape). No adjuvant therapy was given to the other 39 patients.

The criteria of the JEOG randomized control trials were (1) histologic evidence of squamous cell carcinoma; (2) performance status 0–3; (3) absence of a double primary cancer; (4) less than 75 years old; (5) start of adjuvant therapy within 2 months after esophagectomy; (6) good organ function, indicated by leukocytes (WBCs) $\geq$ 4000/mm^3, platelets $\geq$ 10,000/mm^3, hemoglobin (Hb) $\geq$ 10 g/dl, glutamate transaminase (GOT) and pyruvate (GPT) within double normal range, total bilirubin (TB) within normal range, creatinine $\leq$ 1.2 mg/dl, blood urea nitrogen (BUN) $<$ 25 mg/dl, and creatinine clearance (C_{CR}) $\geq$ 60 ml/min; and (7) informed consent. Among the 90 patients, only 34 (38%) were eligible for entering a JEOG trial. The remaining 56 (62%) were not eligible and chose surgery alone or surgery plus postoperative chemotherapy by themselves based on informed consent.

Follow-up Examinations

Patients were closely examined every month during the first 2 years after surgery. During the third year they were examined every 2 months; and during the fourth and fifth years every 3 months. Thereafter, they were examined every 6 months. The minimum follow-up period was 3 months, and the maximum was 106 months in patients without recurrence, with an average follow-up of 47 months. During each follow-up visit, the patient underwent a clinical evaluation, blood biochemistry examination including tumor markers, and chest radiography. Endoscopy, ultrasonography (US) of the neck and abdomen, and computed tomography (CT) of the neck, thorax, and abdomen were performed every year. Detection of a suspected recurrence at any one site precipitated a thorough detailed investigation to confirm or refute the occurrence and to examine every other site.

All lymph node recurrences were clinically diagnosed using US, CT, and magnetic resonance imaging (MRI). Our criteria of lymph nodes with metastasis were as follows: larger than 1 cm in diameter, round shape, marginal enhancement on the contrast-enhanced CT, high intensity on the short inversion time inversion recovery sequence (STIR) of MRI, and enlargement during the follow-up period. Five patients underwent cervical or abdominal lymph node dissection, and histologic evidence of recurrence was obtained. The others with lymph node recurrence underwent radiotherapy or chemoradiotherapy and were examined with US, CT, and MRI before and after treatment to evaluate the efficacy of the treatment for a recurrence.

Definition of Locoregional and Distant Recurrence

The first recurrence was noted, and any additional recurrence found within 1 month was considered to have occurred simultaneously. These lesions were classified as locoregional (at the local site of the primary tumor, the anastamotic site, or the lymph nodes) or distant (in the distant organs, pleura, or peritoneum). Simultaneous locoregional and distant recurrences were classified as a distant recurrence.

Statistical Methods

The significance was calculated by univariate analysis using chi-square and by multivariate analysis using Cox's proportional hazard model [9]. The survival rates were calculated using the Kaplan-Meier method.

Results

Operative Results

The hospital mortality rate after extended radical esophagectomy with three-field dissection was 2% (2/90) with no mortality within 30 days. Both of these patients had developed a recurrence. The postoperative complications are shown in Table 2. Recurrent laryngeal nerve paralysis was most frequent (74%), being temporary in 40% and permanent in the other 34%. Half the patients with permanent paralysis could recover a normal voice without treatment through compensation by the contralateral vocal cord. As a result, the remaining half of the patients were treated with vocal cord fixation by silicone injection.

Table 2. Postoperative complications after extended radical esophagectomy with three-field dissection.

	Incidence	
Complication	No.	(%)
Recurrent laryngeal nerve paralysis	67	74
Permanent	31	34
Temporary	36	40
Leak at the esophageal anastomosis	29	32
Aspiration pneumonia	23	26
Hepatitis	13	14
Sepsis	12	13
Anastomotic stricture	9	10
Tracheal ulcer	9	10
Pneumonia	6	7
Pyothorax	5	6
Leak at the abdominal anastomosis	4	4
Left subphrenic abscess	3	3
Purulent osteomyelitis	3	3
Hepatic failure	2	2
Respiratory failure	2	2
Bleeding (reoperation)	2	2
Ileus	2	2
Disseminated intravascular coagulation	2	2
Cholecystitis, bleeding gastric ulcer, pulmonary alveolar fistula, pancreatitis, Horner syndrome, severe arrhythmia, thoracic duct fistula (in the neck), chylothorax, peritonitis, renal failure	1 each	1

Of the 90 patients, 39 (43%) patients died of recurrence. Fourteen (16%) patients died of other causes after a mean follow-up of 28 months (range 3–86 months): six due to a second primary cancer, three to aspiration pneumonia, two to lung tuberculosis, one to malnutrition, one to occlusion of the superior mesenteric artery, and one to bleeding from a tracheal ulcer caused by radiotherapy. All of these patients had shown no evidence of recurrence prior to their death. Thirty-seven (41%) patients are alive with a mean survival period of 47 months to date. The survival curves of these patients are shown in Figure 1.

Pattern of Recurrence

With respect to the initial tumor recurrence, among the 39 patients with a recurrence, there were 19 with a locoregional recurrence (17 in the lymph nodes, 1 in the lymph nodes and local region, and 1 at the anastamotic site), 19 with a distant recurrence (9 in the lung, 4 in bone, 3 in the liver, 2 in the skin, and 1 in the brain), and one with a mixed recurrence (in the lymph nodes and liver). The latter patient was classified as having a distant recurrence. The distribution of the first site(s) of lymph node recurrence is shown in Table 1. Lymph node recurrences were found in the neck in five patients, in the cervicothoracic region in five, in the left upper mediastinum in three, in the abdomen in four, and in the left axillary nodes in one. All abdominal lymph node recurrences were seen in the celiac or paraaortic regions.

Of the 19 patients with a distant recurrence, 8 subsequently developed a locoregional recurrence. Of 19 patients with a locoregional recurrence, 7 subsequently developed a distant organ recurrence. During the terminal period, among the 39 patients with a recurrence were 12 (31%) patients with only a locoregional recurrence, 11 (28%) with only a distant recurrence, and 16 (41%)

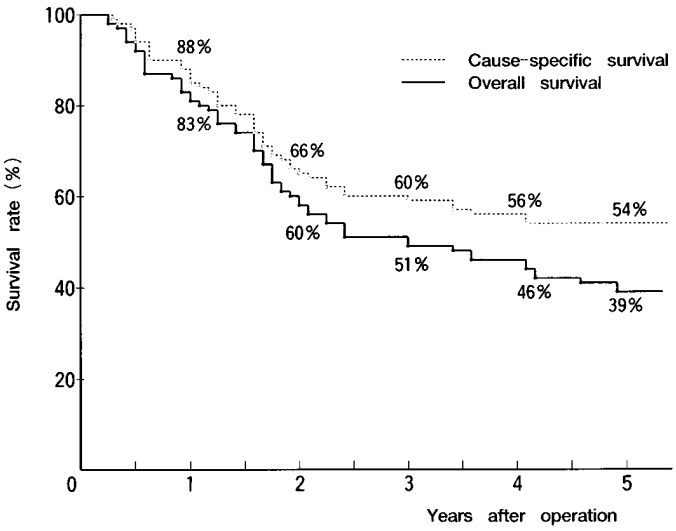

Fig. 1. Survival curves of 90 patients who underwent extended radical esophagectomy with three-field dissection for esophageal cancer.

with a mixed recurrence (Table 3). Overall, 28 (72%) patients developed a locoregional recurrence, and 27 (69%) developed a distant recurrence.

Disease-free Interval and Survival after Recurrence

Recurrence was found after a mean period of 11 months (range 1–59 months) after surgery. The mean postrecurrence survival was 8 months. The disease-free interval (DFI) until a locoregional recurrence was 11 months, and the survival period after the locoregional recurrence was 7 months. In contrast, the DFI in those with a distant recurrence was 11 months, and the survival period after a distant recurrence was 9 months. There was no difference in the DFI or in the survival between locoregional recurrence and distant recurrence (Table 4).

Factors Influencing Recurrence

Table 5 shows the recurrences in relation to various clinicopathologic factors. Recurrence was more frequent in those with a primary upper thoracic esophageal cancer than in those with a middle thoracic esophageal cancer ($p < 0.05$). No recurrence occurred from a pT1 tumor ($p < 0.001$). Recurrence was less frequent in the node-negative patients than in the pM1-lymph patients ($p < 0.05$) and was increasing in frequency in proportion to the number of lymph nodes with positive metastasis ($p < 0.01$). Postoperative adjuvant therapy and the histologic grade showed no correlation with recurrence. Lymphatic invasion and vascular invasion were significant factors for recurrence ($p < 0.05$ and $p < 0.001$, respectively).

A locoregional recurrence was often seen in patients with metastatic involvement of the cervical or celiac lymph nodes (M1-lymph) at surgery, whereas locoregional recurrence was rarely seen in those without nodal involvement ($p < 0.01$). Locoregional recurrence increased in proportion to the number of nodes with positive metastasis ($p < 0.001$). The depth of invasion

Table 3. Pattern of recurrence during the initial and terminal periods after extended radical esophagectomy with three-field dissection.

Pattern of recurrence	Initial period	Terminal period
Locoregional alone	19 (49%)	12 (31%)
Distant organ alone	19 (49%)	11 (28%)
Mixed	1 (2%)	16 (41%)
Total	39 (100%)	39 (100%)

(pT), lymphatic invasion, and vascular invasion were each a significant factor for locoregional recurrence ($p < 0.05$, $p < 0.05$, $p < 0.001$, respectively). The site of the tumor, adjuvant therapy, and histologic grade each showed no correlation with the observed pattern of recurrence.

Distant organ recurrence was correlated with the depth of invasion (pT) and with vascular invasion ($p < 0.05$, $p < 0.001$, respectively). The other factors were not prognostic.

Multivariate Analysis

Table 6 shows the results of the multivariate analysis of similar factors using Cox's proportional hazard model for locoregional and distant recurrence. The number of lymph nodes with positive metastasis at surgery was shown to be a significant factor for locoregional recurrence ($p = 0.002$), whereas lymphatic invasion and venous invasion were each significant factors for distant recurrence ($p = 0.020$, $p = 0.013$, respectively).

Discussion

Clinicopathologic Factors Influencing Recurrence after Extended Radical Esophagectomy with Three-field Dissection

In the present series, the prognostic factors for recurrence were the site of tumor, pT, pN, pM-lym, number of metastasis-positive nodes, lymphatic invasion, and vascular invasion. These were completely similar to the prognostic factors for a locoregional recurrence. In contrast, the prognostic factors for distant recurrence were only pT and vascular invasion. The multivariate analysis also revealed that locoregional recurrence was correlated with the number of nodes with positive metastasis, whereas distant recurrence was correlated with both lymphatic invasion and vascular invasion. It can be considered that locoregional recurrence is mainly influenced by the tumor stage, particularly the extent of lymph node metastasis, whereas distant recurrence is not influenced by the tumor stage but is influenced by the oncologic behavior of the tumor. Accordingly, locoregional recurrence can be easily predicted by the number of the metastasis-positive nodes and pM-lym (i.e., cervical or celiac lymph node metastasis), whereas distant recurrence can seldom be predicted by clinicopathologic factors. Kitagawa et al. [10] reported that the proto-oncogenes *int-2/hst-1* co-amplification was significantly correlated with a high incidence of eventual metastasis in distant organs. Further oncological research is needed to predict distant recurrence.

Table 4. Disease-free interval and survival for locoregional and distant recurrences after extended radical esophagectomy with three-field dissection.

Outcome	No recurrence	Locoregional	Distant	p*
DFI (months)	47.1 ± 24.6	10.5 ± 7.4	11.4 ± 12.5	0.787
Survival (months)	47.1 ± 24.6	17.6 ± 10.3	20.0 ± 20.6	0.651

DFI: disease-free interval.
*Locoregional recurrence versus distant organ recurrence.

Table 5. Prognostic factors for recurrence after extended radical esophagectomy with three-field dissection

	Recurrence		Site of recurrence	
Prognostic factor	No (n = 51)	Yes (n = 39)	Locoregional (n = 19)	Distant (n = 20)
Site				
Upper (n = 11)	4 (36)	7 (64)*	4 (36)	3 (27)
Middle (n = 49)	34 (69)	15 (31)	7 (14)	8 (16)
Lower (n = 30)	13 (43)	17 (57)	8 (27)	9 (30)
Primary tumor[a]				
pT1 (n = 15)	15 (100)	0***	0*	0*
pT2 (n = 15)	8 (54)	7 (47)	3 (20)	4 (27)
pT3 (n = 60)	28 (47)	32 (53)	16 (27)	16 (27)
Nodal involvement[a]				
pN0, pM0 (n = 26)	20 (77)	6 (23)*	1 (4)**	5 (19)
pN1, pM0 (n = 43)	23 (53)	20 (47)	8 (19)	12 (28)
pN0/N1, pM1 (n = 21)[b]	8 (38)	13 (62)	10 (48)	3 (14)
No. of nodes with positive metastasis				
0 (n = 26)	20 (77)	6 (23)**	1 (4)***	5 (19)
1 (n = 21)	14 (67)	7 (33)	3 (14)	4 (19)
2–4 (n = 21)	11 (52)	10 (48)	5 (24)	5 (24)
≥ 5 (n = 22)	6 (27)	16 (73)	10 (41)	6 (32)
Adjuvant therapy[c]				
Yes (n = 51)	28 (55)	23 (45)	13 (25)	10 (20)
No (n = 39)	23 (59)	16 (41)	6 (15)	10 (26)
Histopathologic grading[a]				
G1 (n = 34)	16 (47)	18 (53)	8 (24)	10 (29)
G2 (n = 41)	27 (66)	14 (34)	8 (20)	6 (15)
G3 (n = 15)	8 (53)	7 (47)	3 (20)	4 (27)
Lymphatic invasion[a]				
L1 (n = 71)	35 (49)	36 (51)*	19 (27)*	17 (24)
L0 (n = 19)	16 (84)	3 (16)	0	3 (16)
Venous invasion[a]				
V1 (n = 62)	24 (39)	38 (61)***	18 (29)***	20 (32)***
V0 (n = 28)	27 (96)	1 (4)	1 (4)	0

Numbers in parentheses are percents.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$, when compared with no recurrence.
[a]TNM classification (UICC 1992).
[b]Cervical or celiac lymph node metastasis at surgery (or both) (pM1-Lym).
[c]Postoperative chemotherapy or radiotherapy.

Lymphadenectomy: Reduction in the Incidence of Locoregional Recurrence?

There have been no comparative studies on recurrence between extended radical lymphadenectomy and less radical lymphadenectomy. It has been reported by various authors that the proportion of locoregional recurrence versus distant organ recurrence after transhiatal esophagectomy was similar to that after transthoracic esophagectomy with two-field dissection [4, 11, 12]. As shown in the present study, this proportion was equal also after extended radical esophagectomy with three-field dissection. However, the long-term survival after three-field dissection was better than that after transhiatal esophagectomy and better than that after two-field dissection, when comparing survival rates in the literature [4, 11]. The incidence of all recurrences may be reduced by extended radical lymphadenectomy. A comparative study is needed be-

Table 6. Results of multivariate analysis for locoregional and distant recurrences after extended radical esophagectomy with three-field dissection.

	Locoregional		Distant (organ)	
Prognostic factor	Chi-square	*p*	Chi-square	*p*
Site	1.14	0.286	0.29	0.587
Length	0.49	0.483	0.08	0.774
pT	3.38	0.066	0.26	0.609
pM lymph[a]	1.26	0.262	2.38	0.123
No. of positive nodes	9.69	0.002*	0.95	0.329
Adjuvant therapy	0.90	0.343	0.29	0.592
Grading	1.19	0.276	3.36	0.067
Lymphatic invasion	2.89	0.089	5.44	0.020*
Venous invasion	3.21	0.073	6.20	0.013*

[a]Cervical or celiac lymph node metastasis (or both).
*Significant.

tween recurrence after extended radical lymphadenectomy and recurrence after less radical lymphadenectomy.

Isono et al. [4] reported that the incidence of lymph node recurrence after transthoracic esophagectomy with two-field dissection was most frequent (61%) in the cervicothoracic and mediastinal regions. This incidence was 42% after extended radical esophagectomy with three-field dissection in the present series, indicating that three-field dissection may have reduced recurrence in the cervicothoracic or mediastinal regions as compared to two-field dissection.

Adjuvant Therapies: Effect on Recurrence

Postoperative adjuvant therapies such as radiotherapy and chemotherapy had no influence on the incidence of any recurrence in this series. Teniere et al. [13] reported, based on a randomized control trial, that postoperative radiation therapy did not improve survival in any group (patients with or without lymph node metastasis). The JEOG revealed, based on a randomized control study [14], that postoperative chemotherapy using two courses of cisplatin with vindesine did not improve survival in any group (patients with or without lymph node metastasis). These results suggest that postoperative adjuvant therapies, including radiotherapy and chemotherapy, do not influence the pattern of recurrence and do not improve survival after extended radical esophagectomy with three-field dissection. More clinical trials are needed involving extended radical esophagectomy with three-field dissection combined with preoperative chemotherapy and adjuvant chemotherapy based on a chemosensitivity test [15].

Conclusions

Esophageal cancer remains a complex therapeutic challenge. At present we consider that surgery offers the best chance for potential cure. Extended radical esophagectomy with three-field dissection is, however, merely an extensive local therapy and should be combined with proper adjuvant therapy in patients at high risk for recurrence. The incidence and pattern of recurrence are possibly influenced not only by therapeutic factors including surgical procedures and adjuvant therapies but also by various histologic and biologic factors. We consider that the risk for locoregional recurrence in a patient with limited disease can be reduced by extended radical esophagectomy with three-field dissection. However, distant recurrence cannot be controlled by surgery because it is affected mainly by the oncologic behavior of the tumor. Further studies on a large sample size are needed to establish the role of extended radical esophagectomy and adjuvant therapy more definitively and to improve the survival of patients with an esophageal cancer.

Résumé

Nous avons analysé les facteurs associés à une récidive chez 90 patients opérés d'une oesophagectomie radicale étendue (trois voies d'abord) pour un carcinome épidermoïde de l'oesophage. La récidive tumorale initiale a été soit loco-régionale (au niveau de la tumeur primitive, l'anastomose et/ou les ganglions lymphatiques) soit distante (organes à distance, plévre et/ou le péritoine). Dix-neuf patients (21%) ont eu une récidive locorégionale et 19 (21%) ont eu une récidive à distance. Un patient (1%) avait les deux et a été classé avec les récidives à distance. La récidive loco-régionale était corrélée avec le stade et, en particulier, avec le nombre de ganglions lymphatiques envahis. Nos données suggèrent que la récidive loco-régionale est en rapport avec l'évolution tumorale et l'étendue des métastases ganglionnaires alors que les métastases à distance étaient plutôt le fait du potentiel malin de la tumeur. L'éventualité d'une récidive loco-régionale peut être évitée, chez le patient ayant une maladie limitée, par une oesophagectomie radicale étendue par triple voie d'abord. Les métastases à distance, cependant, ne peuvent être contrôlées par la chirurgie. La fréquence des récidives n'est pas influencée par la chimiothérapie postopératoire adjuvante.

Resumen

Los factores responsables de recurrencia fueron investigados en 90 pacientes sometidos a esofagectomía ampliada con 3 campos de disección linfática, por carcinoma escamocelular del esófago torácico. La recurrencia inicial del tumor fue clasificada según fuera local-regional (en el lugar del tumor primario, el lugar de la anastomosis y/o los ganglios linfáticos) o distante (órganos distantes, pleura y/o peritoneo). Diecinueve pacientes (21%) desarrollaron recurrencia local-regional y 19 (21%) recurrencia distal. Uno (1%) desarrolló ambos tipos de recurrencia en forma simultánea y fue clasificado como recurrencia distante. La recurrencia local-regional apareció correlacionada con factores de estadificación, en particular con el número de ganglios positivos. En cuanto a la recurrencia distante, la invasión vascular probó ser el factor pronóstico de mayor importancia. Nuestros hallazgos sugieren que la recurrencia local-regional se debe al progreso del

tumor en relación con el grado de extensión de las metástasis ganglionares, en tanto que la recurrencia distante se debe al comportamiento oncológico del tumor. La recurrencia local-regional en pacientes con enfermedad limitada puede ser reducida mediante esofagectomía con disección ganglionar de 3 campos. Sin embargo, la recurrencia distante no puede ser controlada con la cirugía. Las terapias coadyuvantes postoperatorias adoptadas no demostraron tener efecto en cuanto a la recurrencia.

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Invited Commentary

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It is tempting, and probably accurate, to say that the group from Karume University School of Medicine has "gone about as far as you can go" in the surgical treatment of squamous cell carcinoma of the esophagus. They have carried out extended subtotal esophagectomy and three-field lymphadenoectomy in a group of patients selected for relatively low risk (age less than 70, no associated severe disease) and disease potentially curable by surgical resection. Then they have studied in great detail and with statistical percision the patterns of tumor recurrence in these patients along with the usual criteria of success or failure of treatment.

A number of the findings in this study are predictable but important nonetheless. An example is the fact that node-positive patients have recurrent tumor more frequently than do node-negative patients. Other findings bring a hopeful ray of light, such as the fact that there were no tumor recurrences in pT1 patients, which means that at some early stage squamous cell carcinoma of the esophagus is curable by surgical resection alone. This suggests that surveillance programs leading to early detection might be useful to patients. Whether such programs would stand up to the scrutiny of cost/benefit analysis is another question. In areas of relatively high incidence, they probably would. In the United States they would be a tough sell, at best.

Like most good clinical studies, and this is a particularly well crafted and carefully conducted one, more questions are raised then answered. The authors logically conclude that local recurrence of tumor depends mostly on the stage of the tumor, and distant recurrence depends more on the "oncologic behavior" of the tumor. Should we then recommend early operation alone for early stage disease and neoadjuvant chemoirradiation for others? Which patients should receive adjuvant therapy postoperatively and what therapy? Are patients who present greater risks or who have more advanced local disease likely to benefit or even be able to tolerate radical surgery with or without neoadjuvant or postoperative adjuvant chemotherapy, irradiation, or both? The answers to these and other questions await additional investigation.

The authors are to be commended for their careful planning and meticulous study when carrying out this clinical investigation. Operative mortality of 2% following such radical surgery is remarkably good; and 39% five-year survival for the entire group with 15% of the deaths due to causes other than tumor is outstanding. The relatively high prevalence of recurrent nerve palsy, anastomotic leaks, and aspiration pneumonia document the fact that this extensive surgery and should not be carried out just anywhere. Such patients need and deserve the kind of expert surgery and careful perioperative care that these patients received. Until carcinoma of the esophagus can be prevented we will continue to need careful evaluation of the treatment outcomes such as that presented here by Drs. Bahnsali, Fujita, and their colleagues.