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# Follow-up and recurrence after a curative esophagectomy for patients with esophageal cancer: the first indicators for recurrence and their prognostic values

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**Abstract**
***Background.*** No standardized methods exist for the follow-up and treatment of recurrence after a curative esophagectomy for patients with thoracic esophageal cancers.
***Methods.*** One hundred seventy-five patients with thoracic esophageal cancer underwent a curative resection and were followed up during a median period of 3.0 years (3 months–18 years). The time to recurrence, the first indicators (FIs) to suspect recurrence, and the factors predictive of prognosis after recurrence were investigated.
***Results.*** Recurrence occurred in 72 (41.1%) of 175 patients. Forty (55.6%) and 22 (30.6%) of 72 cases presented with recurrences in the first and second year after the initial operation, respectively. Clinical visit (anamnesis and physical examination), tumor markers, and imaging were FIs in 39 (54.2%), 33 (45.8%), and 49 (68.1%) of 72 patients with recurrence, respectively. Imaging was the exclusive FI in 19 (26.4%) cases. A multivariate analysis showed the favorable prognostic factors after recurrence to be recurrence later than 1 year after the initial operation and a case in which the FI was only imaging.
***Conclusions.*** Intensive follow-up is required in the first 2 years after surgery, and early detection of recurrence is important. The accumulation of clinical data based on a fixed schedule with consensus is necessary to obtain more definite evidence for the diagnosis and treatment of recurrent esophageal cancer.

**Key words** Esophageal cancer · Esophagectomy · Postoperative follow-up · First indicators for recurrence · Prognostic factors after recurrence

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## Introduction

Despite the recent improvement in the treatment outcome for the patients with esophageal cancer by multimodality therapy, including extensive lymph node dissection [1], postoperative recurrence is observed in a considerable number of patients [2–4]. Curative treatment of patients with recurrence is necessary to further improve the prognosis after an esophagectomy.

The guidelines for diagnosis and treatment of carcinoma of the esophagus as stated by the Japan Esophageal Society [5] separately describe methods of follow-up after the initial treatments and the treatment strategies for recurrences of each initial treatment, i.e., endoscopic resection, curative esophagectomy, and definitive chemoradiation. However, critical evidence to justify these guidelines is very limited for both the follow-up method and treatment of recurrences, and no definite guiding principles have been established in Japan. This limitation is also true in Western countries. A few recommendations for follow-up observation after surgery are noted in the guidelines of the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO) [6,7], although no references showing evidence are cited. Large-scale clinical studies addressing the methods of follow-up observation after treatment seem difficult to design, because the choice of the initial treatment for esophageal cancer varies markedly depending on the stage of the disease and the general condition of the patient at the time of diagnosis. Moreover, it appears to be difficult to directly adapt the data from Western countries to Japanese patients with esophageal cancers because there are large differences in the proportions of the predominant histology, in the surgical methods used, and in survival rates after surgery between Japan and the Western countries [1].

Many reports have shown the rate, timing, and mode of recurrence after a curative esophagectomy and the treatment outcomes of recurrent esophageal cancers, some of which also note the predictive factors of recurrence [2–4,8,9]. However, very few articles describing effective follow-up

methods, first clinical indicators to suspect recurrence, or factors predictive of the prognosis after the treatment of recurrence have so far been published for esophageal cancers. This study investigated the time to recurrence and predictive factors of recurrence after a curative esophagectomy with an extended lymph node dissection for esophageal cancer. Furthermore, in our study we tried to clarify the first clinical indicators to suspect recurrence and their prognostic values, using retrospective data obtained by a fixed schedule of follow-up observation in this institute. The effective postoperative follow-up strategy for patients who undergo a curative esophagectomy with an extended lymph node dissection for esophageal cancers is discussed based on the results of this study.

## Patients and methods

### Patients

One hundred seventy-five patients with thoracic esophageal cancer underwent a transthoracic esophagectomy with a three-field lymph node dissection with no pathological residual tumor (R0) between 1989 and 2006 in the National Kyushu Cancer Center, Japan. All cancers were pathologically diagnosed to be squamous cell carcinoma. The characteristics of the patients with and without recurrence are shown in the Results section. The median follow-up period was 3.0 years (range, 3 months–18 years).

### Surgical procedure

All 175 patients underwent transthoracic esophagectomy through a right-side thoracotomy. The alimentary tract was reconstructed using a gastric tube made of the greater curvature of the stomach, with cervical esophagogastric anastomosis by hand-sewn or instrumental anastomosis [10] through a retrosternal or posterior mediastinal route.

An extended radical lymph node dissection was then performed in three fields. A complete dissection of the middle and lower mediastinal nodes was performed via a right thoracotomy, including the periesophageal, parahiatal, subcarinal, and aortopulmonary window nodes. The dissection of the lymph nodes in the upper mediastinum included the nodes along the bilateral recurrent laryngeal nerves by carefully exposing them, from the level of the aortic arch to the thoracic inlet for the left nerve and near the origin at the base of the right subclavian artery for the right nerve. The remaining nodes along the recurrent laryngeal nerves, which were anatomically inseparable chains extending from the upper mediastinum to the lower neck, were also dissected through a cervical U-shaped incision, together with the lower deep cervical nodes located posterior and lateral to the carotid sheath. The lymph node dissection in the abdomen included the nodes along the celiac, left gastric, and common hepatic arteries, the nodes along the lesser curvature of the stomach, and the parahiatal nodes.

### Follow-up after surgery

The patients with a pathological stage II or higher stage [11,12] were followed up every 2 months for the first 2 years and every 3 months thereafter in the fixed schedule shown in Fig. 1. A detailed anamnesis for history and a physical examination were performed on every clinical visit. Serum levels of tumor markers including carcinoembryonic antigen (CEA: normal range, <5 ng/ml) and squamous cell carcinoma antigen (SCC-Ag: normal range, <2 ng/ml) were measured at every clinical visit. Radiologic imaging tests including cervical, chest and abdominal computed tomography (CT), and cervical and abdominal ultrasonography (US) were performed every 4 months for the first 2 years and every 6 months thereafter. CT and US were performed at the same time to complement the limitations of each imaging modality. The follow-up for the patients with pathological stage I [11,12] was less intensively performed for the first 2 years with a clinical visit and monitoring of serum levels of tumor markers at every 3 months and radiologic imaging tests at every 6 months. In addition, bone scintigraphy and gastrointestinal endoscopy were performed once a year. Positron emission tomography with $^{18}$F-fluorodeoxyglucose (FDG-PET) was indicated when recurrence was suspected. The duration of follow-up observation is set for 5 years because of the extremely low rate of recurrence later than 5 years after the initial operation.

In total, 28 patients failed to be followed up by the regular schedule. Sixteen of these patients died of other diseases during the regular follow-up and 7 dropped out of

| Modality | Months after esophagectomy | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1st year | | | | | | 2nd year | | | | | | 3rd year | | | | 4th year | | | | 5th year | | | |
| | 2 | 4 | 6 | 8 | 10 | 12 | 14 | 16 | 18 | 20 | 22 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 | 48 | 51 | 54 | 57 | 60 |
| CV, Tumor marker | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● | ● |
| Cervical US | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● |
| Cervical–thoracic CT | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● |
| Abdominal–pelvic CT | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● |
| Abdominal–pelvic US | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● | | ● |
| Upper GI endoscopy | | | | | | ● | | | | | | ● | | | | ● | | | | ● | | | | ● |
| Bone scintigraphy | | | | | | ● | | | | | | ● | | | | ● | | | | ● | | | | ● |
| Ba enema or Colonoscopy | | | | | | | | | | | | ● | | | | | | | | ● | | | | |

**Fig. 1.** Schematic representation of the follow-up schedule after a curative esophagectomy for thoracic esophageal cancer at our institute. CV, clinical visit; US, ultrasonography; CT, computed tomography; GI, gastrointestinal

**Table 1.** (a) Mode and rate of recurrence after a curative esophagectomy for cancer and treatment for recurrence

| Mode of recurrence | No. of recurrences | Treatment (no. of patients) |
|---|---|---|
| Lymph node | 39 (22%) | CRT (23), surgery (3)<br>RT (5), CT (4), none (4) |
| Distant organ | 15 (9%) | CRT (2), surgery (2)<br>RT (5), CT (5), none (1) |
| Pleural dissemination | 4 (2%) | CT (3), none (1) |
| Combined | 14 (8%) | CRT (7), surgery (1)<br>RT (1), CT (4), none (1) |
| Total | 72 (41%) | |

CRT, chemoradiotherapy; RT, radiotherapy; CT, chemotherapy

a regular follow-up schedule for personal reasons. The median follow-up periods were 2.2 years (0.7–6.5 years) for the former and 2.0 years (0.5–2.5 years) for the latter. Only 5 among 72 cases with recurrence were found to have recurrences before the prefixed next timing of the schedule because they showed some symptoms and signs and spontaneously visited our hospital. Their first indicators were judged to be "clinical visit." All these patients were included in the analysis.

**Table 1.** (b) Time to recurrence after a curative esophagectomy for cancer

| Months after surgery | Number of cases | Cumulative ratio |
|---|---|---|
| Earlier than 6 months | 20 | |
| From 6 to 12 months | 20 | 56% |
| From 12 to 18 months | 13 | |
| From 18 to 24 months | 9 | 86% |
| Later than 24 months | 10 | 100% |
| Total | 72 | 100% |

### Data analyses and statistics

All statistical analyses were performed using the StatView software program (version 5.0; Abacus Concepts, Berkeley, CA, USA). The relationship between recurrence and the clinicopathological features was determined using a Student's *t* test, Fisher's exact test, and a logistic regression analysis. Survival rates after recurrence were calculated by the Kaplan–Meier method for the analysis of censored data. The significance of differences in survival was analyzed with a log-rank test and a generalized Wilcoxon test in a univariate analysis and a Cox's proportional hazards model in a multivariate analysis. A $P$ value < 0.05 was considered to be statistically significant.

## Results

Recurrence occurred in 72 (41.1%) of 175 patients. Lymph node recurrence, organ metastasis, pleural dissemination, and a combination of these were observed in 39 (22.3%), 15 (8.6%), 4 (2.3%), and 14 (8.0%) patients, respectively (Table 1a). In total, 51 cases showed lymph node recurrence, 17 of which were found within the dissected area. The first choice of treatment for recurrence is also shown in Table 1a. Various kinds of treatment were indicated for each mode of recurrence, which clearly showed that there was no definite strategy for treatment of recurrence, depending on the extent of recurrent diseases, the presence or absence of pervious neoadjuvant and/or adjuvant treatments, and the patient's general status at the diagnosis of recurrence.

Forty (55.6%) and 22 (30.6%) of the 72 cases presented with recurrences in the first and second year after the initial operation, respectively, thus indicating that more than 86% of recurrences occurred within 2 years after surgery (Table 1b). However, 4 of the remaining 10 cases presented their recurrences later than 4 years after the operation (data not shown).

The relationship between recurrence and clinicopathological features at surgery is shown in Table 2a. A univariate analysis showed statistically significant associations between recurrence and the pathological depth of tumor invasion (pT), pathological lymph node metastasis (pN), pathological stage (pStage), permeation to lymphatic vessels and venous invasion, the number of fields (cervical, mediastinal, or abdominal) where lymph node metastasis was observed, and the number of metastasized lymph nodes (0–4 vs. 5 and more: this way of division yielded the statistically largest difference). The average numbers of metastasized lymph nodes were 3.84 and 0.74 in the recurrent and nonrecurrent patients, respectively, which showed a statistically significant difference ($P < 0.0001$) (data not shown). A logistic regression analysis including these factors indicated that only the presence of permeation to lymphatic vessels ($P < 0.05$, odds ratio = 5.11, 95% confidence interval = 1.34–19.45) and lymph node metastasis when observed in more than two fields ($P < 0.001$, odds ratio = 4.78, 95% confidence interval = 1.99–11.47) were selected as statistically significant factors that would predict recurrence after surgery (Table 2b).

The surveillance tools that first indicated a suspicion of recurrence (first indicator, FI) were investigated. Table 3 shows that 39 (54.2%) of 72 patients with recurrence were suspected to have recurrence by a clinical visit including anamnesis of history (symptoms) and signs observed during a physical examination. Symptoms most frequently observed were pain at metastasized sites, general fatigue, dysphagia, and appetite loss. Signs most frequently observed were fever, cough and sputum caused by pneumonia, hoarseness,

**Table 2.** Relationship between recurrence and clinicopathological factors after a curative esophagectomy for esophageal cancer

(a) Univariate analysis

| Variables | Recurrence (+) ($n$ = 72) | Recurrence (–) ($n$ = 103) | $P$ value |
|---|---|---|---|
| Age (years) | 61.8 ± 8.4 | 62.0 ± 7.8 | N.S. |
| Gender (male/female) | 64/8 | 84/19 | N.S. |
| Tumor location: Upper/Middle/Lower | 10/32/30 | 13/58/32 | N.S. |
| Depth of tumor invasion pT 0, 1/2, 3 | 16/56 | 47/56 | <0.0001 |
| Lymph node metastasis pN 0, 1, 2/3, 4 | 31/41 | 76/25 | <0.0001 |
| Pathological stage pStage 0, I, II/III, IV | 27/45 | 81/22 | <0.0001 |
| Lymph vessel permeation ly (–)/(+) | 26/46 | 83/20 | <0.0001 |
| Vascular invasion v (–)/(+) | 41/31 | 85/18 | <0.0001 |
| No. of fields of LNM 0, 1/2, 3 | 40/32 | 94/9 | <0.0001 |
| No. of metastasized LN 0–4/5 and more | 54/18 | 99/4 | <0.0001 |

pT, pN, pStage are according to references 11, 12
N.S., not significant; LN, lymph node; LNM, LN metastasis

(b) Multivariate analysis (logistic regression analysis)

| Variables | $P$ values | Odds ratio | 95% CI |
|---|---|---|---|
| pT 0, 1/2, 3 | 0.16 | 1.87 | (0.78–4.46) |
| pN 0, 1, 2/3, 4 | 0.35 | 0.54 | (0.15–1.94) |
| pStage 0, I, II/III, IV | 0.37 | 1.83 | (0.49–6.88) |
| ly (–)/(+) | <0.05 | 5.11 | (1.34–19.45) |
| v (–)/(+) | 0.27 | 2.71 | (0.46–15.91) |
| No. of fields of LNM 0, 1/2, 3 | <0.001 | 4.78 | (1.99–11.47) |
| No. of metastasized LN 0–4/5 and more | 0.98 | 1.10 | (0.39–2.63) |

CI, confidence interval

**Table 3.** First indicators to suspect recurrence and its frequency

| First indicator | No. of patients |
|---|---|
| Clinical visit | 39 (54%) |
| Symptoms | 36 (50%) |
| Signs | 22 (31%) |
| Tumor marker | 33 (46%) |
| CEA | 9 (13%) |
| SCC-Ag | 28 (39%) |
| Imaging | 49 (68%) |
| CT | 45 (63%) |
| US | 8 (11%) |
| Imaging only[a] | 19 (26%) |

CEA, carcinoembryonic antigen; SCC-Ag, squamous cell carcinoma
[a] Imaging only means the cases in which imaging was exclusive first indicator without any other first indicators such as clinical visit or tumor marker

and abnormal neurological findings such as paralysis. The FI in 33 cases (45.8%) was monitoring of tumor markers of CEA and/or SCC-Ag. Imaging including CT and/or US indicated a suspected recurrence in 49 cases (68.1%). Imaging was the exclusive FI in 19 cases (i.e., no symptoms or signs, normal levels of tumor marker; 26.4%).

The FIs were compared between 40 patients within 12 months after surgery and 32 patients more than 12 months after surgery among the recurrent patients. The FIs of them were clinical visit (65.0% and 40.6%, $P$ = 0.039), tumor marker abnormalities (55.0% and 34.4%, $P$ = 0.081), and imaging (70.0% and 65.6%, $P$ = 0.69), respectively. The rate of patients whose recurrences were found by exclusively imaging abnormalities without any symptoms, signs, or abnormal tumor marker levels was less frequent in the former group (17.5%) than in the latter one (37.5%), although this difference was statistically not significant ($P$ = 0.056).

The overall survival rates were compared by the time to recurrence, mode of recurrence, and various FIs. The overall 1- and 3-year survival rates of all cases after the diagnosis of recurrence were 29% and 14%, and the median survival time (MST) was 7 months (data not shown). The MSTs of cases with lymph node recurrence, organ metastasis, and combined recurrence were 9, 6, and 6 months, respectively, showing no significant differences. There are 4 patients who are still alive 30 months after recurrence. The mode of recurrence, treatment modalities, and prognosis of each of these cases are solitary brain metastasis, gamma-knife radiotherapy, and 43 months (case 1); cervical lymph node metastasis, surgical resection, and 34 months (case 2); solitary lung metastasis, surgical resection, and 32 months (case

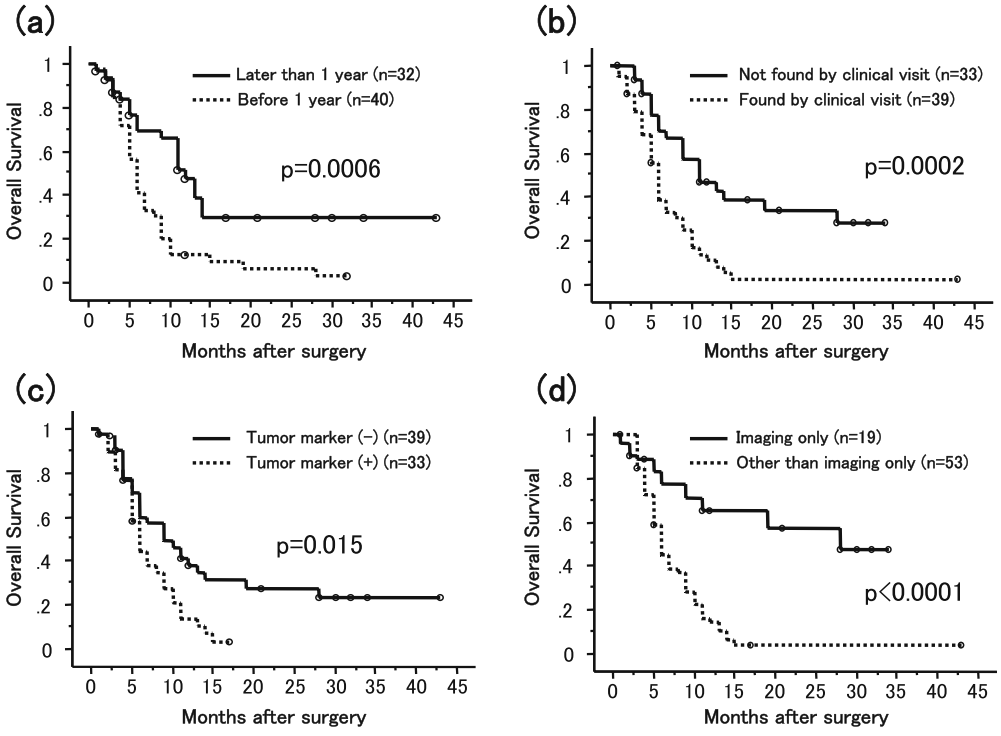


**Fig. 2.** Overall survival rates after recurrence of esophageal cancers were compared by time to recurrence [*later than 1 year* versus less than (*before*) *1 year* after surgery] (**a**), presence versus absence of symptoms and/or signs on *clinical visit* (**b**), presence versus absence of *tumor marker* abnormalities (**c**), and the cases in which *imaging* was the exclusive first indicator versus the cases that presented with any other first indicators (FIs) with or without imaging (**d**)

3); and lower mediastinal lymph node recurrence, chemoradiotherapy, and 30 months (case 4).

The patients whose recurrences were found later than 1 year after surgery showed significantly better survival rate than those within 1 year; 1- and 2-year survival rates were 47.3 % and 30.1%, respectively, in the former group and 12.8% and 6.4%, respectively, in the latter group ($P$ = 0.0006) (Fig. 2a). When the recurrence was found by a clinical visit (symptom and/or signs), the prognosis was significantly worse than in those who showed no symptoms or signs ($P$ = 0.0002; Fig. 2b). The patients who showed symptoms had a significantly poorer prognosis than those without ($P$ = 0.0008). Similarly, the prognosis of the patients who showed any signs was significantly worse than those without signs ($P$ = 0.036; data not shown). Abnormal serum tumor marker level (CEA and/or SCC-Ag) at the diagnosis of recurrence was also an unfavorable prognostic indicator (Fig. 2c). The prognosis of the patients whose FI was exclusively imaging (that is, patients who showed no symptom, sign, or abnormal tumor marker level) was significantly better than that of the patients who presented with any other FIs with or without imaging ($P$ < 0.0001) (Fig. 2d).

The prognostic values of FIs for 40 patients who showed recurrences within 12 months after surgery were also analyzed. Importantly, the patients whose recurrences were found by exclusively imaging abnormalities without any symptoms, signs, or abnormal tumor marker levels (7 cases) showed a significantly longer survival rate than the remaining 33 cases ($P$ = 0.0027 by log-rank test) (MST: 19.0 months vs. 6.0 months, $P$ = 0.037 by a generalized Wilcoxon test).

Table 4 summarizes the results of a multivariate analysis to identify independent prognostic factors using a Cox's proportional hazards model. Subsequently, recurrences later than 1 year after surgery and when imaging was the exclusive FI were indicated to be independent factors for a favorable prognosis after recurrence (Table 4).

## Discussion

The primary aim of the follow-up after a curative resection of an esophageal cancer is to detect local recurrence, distant metastasis, or metachronous primary cancers at an early stage when curative treatments are still possible, thus leading to an improvement of the prognosis. Follow-up is also important to evaluate and administrate the general condition and the quality of life of the patients, because an esophagectomy is associated with a significant level of surgical stress. However, achieving a successful cure of patients with recurrence is extremely rare even after multimodality therapies. The MST after a diagnosis of recurrence is about 5–8 months [2–4,8,9]. Nevertheless, it is also obvious that there are a few patients who could be cured if their recurrence were diagnosed at an early stage [13–15]. Furthermore, even when a curative treatment is impossible, early detection of recurrence could possibly provide patients with a better compliance for various treatments and with an opportunity to obtain a more prolonged survival and a better quality of life. The fact that patients whose FI was exclusively imaging (that is, patients who showed no symptoms, signs, or abnormal tumor marker levels) had a significantly longer survival rate clearly indicates the usefulness of a regular follow-up, and this is also true among the patients whose recurrences were found within 12 months after surgery. Thus, these data strongly suggest that the

**Table 4.** A Cox's proportional hazards model for factors predictive of prognosis after recurrence

| Variables | *P* value | Hazards ratio | 95% CI |
|---|---|---|---|
| Time of recurrence | | | |
| <1 year vs. >1 year | 0.002 | 3.04 | (1.51–6.12) |
| Symptoms (–) vs. (+) | 0.27 | 2.08 | (0.57–7.59) |
| Signs (–) vs. (+) | 0.12 | 1.87 | (0.85–4.10) |
| Clinical visit[a] | | | |
| (–) vs. (+) | 0.28 | 0.39 | (0.071–2.19) |
| Tumor marker[b] | | | |
| (–) vs. (+) | 0.78 | 1.18 | (0.36–3.86) |
| Imaging[c] | | | |
| (–) vs. (+) | 0.30 | 0.49 | (0.13–1.86) |
| Imaging only[d] | | | |
| (–) vs. (+) | 0.011 | 5.22 | (1.46–18.68) |

CI, confidence interval
[a] Clinical visit: symptom and/or signs
[b] Tumor marker: CEA and/or SCC-Ag
[c] Imaging: CT and/or US
[d] Imaging only: the cases in which imaging was exclusive first indicator without any other first indicators such as clinical visit or tumor marker

patients whose recurrences could be found before appearance of any symptoms, signs, or tumor marker abnormalities can expect a better chance of longer survival.

No standard method for postoperative follow-up observation after a curative esophagectomy for esophageal cancer has been established. The clinical practice guidelines for esophageal cancer established by NCCN [6] state a brief follow-up: (1) for asymptomatic patients, complete history and physical examination every 4 months for 1 year, then every 6 months for 2 years, and annually thereafter, and (2) circulating blood cell count and serum chemistry evaluation, endoscopy, and imaging studies as clinically indicated. However, no evidence or references are cited in this guideline. The clinical recommendations for esophageal cancer by ESMO show no method for postoperative follow-up and note that there is no evidence that regular follow-up after initial therapy influences the outcome [7]. The Japanese guidelines [5] briefly discuss the follow-up procedures, including imaging modalities, to be used, but again no definite data or evidence is presented.

This report documented the follow-up method used in this institute. This method identified the FIs that suggested recurrence and the factors predictive of prognosis after recurrence. More than half (54%) of the recurrences were suspected merely by clinical visits (symptom and/or sign), indicating that complete anamnesis and the history and physical examination of the patient are extremely important on every clinical visit. Measurement of the serum level of tumor markers, including CEA and SCC-Ag, is also effective to find recurrences. In particular, the SCC-Ag level was increased in about 40% of the patients with recurrence. Imaging including CT and/or US was also shown to be effective for follow-up. CT and US were performed at the same time because the use of both these imaging methods sometimes complemented the deficiencies of the other. Four patients were suspected to have recurrence by only US but not by CT (data not shown).

These FIs could therefore be factors predictive of the prognosis after recurrence. A univariate analysis indicated the presence of symptoms and/or signs, and abnormal tumor maker levels at the diagnosis of recurrence would predict more unfavorable prognosis after recurrence. In contrast, the patients whose recurrences were identified by imaging only (i.e., no symptoms or signs, and normal level of tumor markers) could therefore expect a significantly better prognosis after recurrence. A multivariate analysis also demonstrated that this factor could be an independent predictor of a favorable prognosis. This finding clearly showed that recurrence should be found as early as possible before appearance of any symptoms, signs, or tumor marker abnormalities. Furthermore, patients with recurrence later than 1 year after the initial operation were shown to have significantly better prognosis than those before 1 year in both the univariate and multivariate analyses, which may mean that recurrent lesions found within a year after surgery consisted of tumor cells with more aggressive potential than those after 1 year. However, even in such cases, earlier detection of recurrence would give a greater possibility for cure by multimodality treatments including surgery and chemoradiotherapy. Considering that most recurrences occurred within 2 years after the operation, postoperative follow-up should be more intensive for the first 2 years and less intensive for the following 3 years.

Recently, FDG-PET has been shown to be effective in detecting recurrence of esophageal cancer after surgical resection. FDG-PET seems to be more accurate that conventional CT for detection of both locoregional recurrence and distant metastases, except small lung metastasis [16,17]. The fact that FDG-PET has a larger field of imaging than CT can be another merit for detecting recurrences. However, FDG-PET is not always facilitated in most hospitals, including this one, and is reserved for patients with suspected recurrence detected by the conventional follow-up system.

It is also mandatory to check for the development of either asynchronous remnant esophageal cancer or asynchronous multiple cancers of other organs such as of the stomach (gastric tube used for reconstruction) or head and neck region. Sato et al. reported that a second malignancy was the major cause of death among the patients without any lymph node metastasis who underwent an esophagectomy for thoracic esophageal cancer [18]. Therefore, endoscopic examinations are conducted for the head and neck region, remnant esophagus, stomach, and colorectum (see Fig. 1).

## Conclusions

No standard follow-up method after a curative esophagectomy for esophageal cancer has yet been established. Furthermore, so far few studies have investigated the effectiveness of any follow-up schedules including the frequency and modalities used. The efficacy and suitability of the schedule shown in this article for the cure of patients with recurrence of esophageal cancer are not known. A nationwide accumulation of larger-scale clinical data based on a fixed schedule with a consensus is necessary to obtain evidence for the diagnosis and treatment of recurrent esophageal cancer. In the future, the performance of meta-analyses using the findings of many reports on postoperative follow-up are absolutely required.

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