classification divides the intrathoracic esophagus into three anatomical subsites: upper, middle, and lower. The tumor location is regarded as the point of deepest tumor invasion, which in clinical practice is the epicenter of the tumor.

The numbers and names of lymph node stations were also defined by the Japanese Classification (Table 1). The lymph nodes are designated by stations, and each station is classified into four grades (N1, N2, N3, N4) by the location of the primary tumor. The present grouping of N1–4 was designated in the 9th edition of the Japanese Classification published in 1999 [10]. Grading was estimated not from anatomical distance from the primary tumor to the lymph node station, but from the incidence of metastasis to each lymph node station and the survival rates after resection of those lymph nodes, based on clinical data collected from three institutions represented by committee members of the Japanese Classification [11]. N1–3 lymph nodes are defined as regional nodes, and N4 lymph nodes are defined as distant metastases. The lymph node groups are roughly defined as follows: N1 lymph nodes which exhibit frequent metastases and patients with metastases to these nodes have a good prognosis after lymphadenectomy; N3 lymph nodes which are characterized by rare metastases and a poor prognosis even if the lymph nodes are resected; and N2 lymph nodes which have an intermediate frequency of metastasis and prognosis.

Table 1 Numbers and naming of lymph node stations

Station number	Name of node station
103	Peripharyngeal
100L	Left superficial cervical
100R	Right superficial cervical
102upL	Left upper deep cervical
102upR	Right upper deep cervical
102midL	Left middle deep cervical
102midR	Right middle deep cervical
104L	Left supraclavicular
104R	Right supraclavicular
101L	Left cervical paraesophageal
101R	Right cervical paraesophageal
105	Upper paraesophageal
106recL	Left recurrent nerve
106recR	Right recurrent nerve
106tbL	Left tracheobronchial
106tbR	Right tracheobronchial
106pre	Pretracheal
107	Subcarinal
108	Middle paraesophageal
109L	Right main bronchus
109R	Left main bronchus
110	Lower paraesophageal
111	Supradiaphragmatic
112	Posterior mediastinum
1	Right cardiac
2	Left cardiac
3	Lesser curvature
7	Left gastric artery
9	Celiac
8	Common hepatic artery
11	Splenic artery
19	Infradiaphragmatic
16	Abdominal paraaortic

Method of analysis

To evaluate the efficacy of nodal dissection at each station, the Efficacy Index (EI) was calculated by multiplying the incidence (%) of metastases to a station and the 5-year survival rate (%) of patients with metastases to that station, and then dividing by 100 [12–14]. The EI was determined by the tumor location. Survival rates were constructed using the Kaplan–Meier method. Statistical analysis was performed using the SPSS 19.0 Statistics Software Package (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics and findings are listed in Table 2. The location of the tumors was the upper esophagus in 221 patients (17.1 %), the middle esophagus in 753 (58.1 %), and the lower esophagus in 321 (24.8 %). Histologically, most patients (97.7 %) had squamous cell carcinoma, and only 7 patients had adenocarcinoma. According to the selection criteria, most patients with junctional tumors and those with adenocarcinoma were excluded due to limited or no dissection of cervical nodes.

Neoadjuvant chemoradiotherapy was administered to 174 patients (13.4 %), and 92 patients (7.1 %) received neoadjuvant chemotherapy. Preoperative therapy was not standard for esophageal cancer in Japan during the registration period. The selection of patients, indications, and therapeutic approach to preoperative therapy depended on each institution and were not specified.

The 30-day operative mortality rate was 0.3 % (10 patients). The median follow-up duration of surviving patients was 76.8 months. The median overall survival was 75.3 months, and the 3- and 5-year survival rates were 60.3 and 52.6 %, respectively.

There were 550 patients without nodal metastases (42.5 %) and 745 patients with nodal metastases (57.5 %). The percentage of patients without nodal metastases was higher in the subjects of this study group than in all patients who underwent esophagectomy. This is because all patients

Table 2 Patients' characteristics and tumor findings

Characteristic or finding	No. (%)
Median age (range), years	61.7 (20–84)
Sex	
Male	1124 (86.8 %)
Female	171 (13.2 %)
Tumor location	
Upper	221 (17.1 %)
Middle	753 (58.1 %)
Lower	321 (24.8 %)
Histologic cell type	
Squamous cell carcinoma	1265 (97.7 %)
Adenocarcinoma	7 (0.5 %)
Others	23 (1.8 %)
Preoperative therapy	
None	1029 (79.5 %)
Neoadjuvant chemotherapy	92 (7.1 %)
Neoadjuvant chemoradiotherapy	174 (13.4 %)
Pathologic T classification	
TX	15 (1.2 %)
T0	22 (1.7 %)
T1a	115 (8.8 %)
T1b	354 (27.3 %)
T2	188 (14.5 %)
T3	578 (44.6 %)
T4	22 (1.7 %)
Pathologic positive node number (including supraclavicular node)	
N0	550 (42.5 %)
N (1–2)	290 (22.4 %)
N (3–6)	276 (21.3 %)
N (7–)	179 (13.8 %)

without nodal metastases were included, but patients with nodal metastases for whom no information about pathological metastatic lymph node location was available were excluded. The incidence of metastasis to each node station was lower in this study group than in the entire group of patients for the same reason. The number of resected nodes was not collected in this registration database.

The incidence of metastasis to a station, the 5-year survival rate of patients with metastases, and the EIs of each node station are presented according to tumor location in Tables 3, 4, and 5. Lymph node groups for grading in the Japanese Classification are added.

In patients with upper esophageal tumors, the EIs of recurrent nerve nodes (No. 106rec), cervical paraesophageal nodes (No. 101), and supraclavicular nodes (No. 104) were higher than the EI of upper paraesophageal nodes (No. 105). The EIs of the lower mediastinal and abdominal node stations were less than 1.0 (Table 3).

In patients with middle esophageal tumors, the EIs of recurrent nerve nodes (No. 106rec), right cardiac nodes (No. 1), left cardiac nodes (No. 2) were higher than, and the EIs of lower paraesophageal nodes (No. 110) and lesser curvature nodes (No. 3) were as high as the EI of middle paraesophageal nodes (No. 108). The EIs of supraclavicular nodes (No. 104), cervical paraesophageal nodes (No. 101), left gastric artery nodes (No. 7) and celiac nodes (No. 9) were higher than 1.0 (Table 4).

In patients with lower tumors, the EIs of right cardiac nodes (No. 1), left cardiac nodes (No. 2), lesser curvature nodes (No. 3), and left gastric artery nodes (No. 7) were higher than the EIs of lower paraesophageal nodes (No. 110). The EIs of recurrent nerve nodes (No. 106rec), and celiac nodes (No. 9) were higher than 1.0 (Table 5).

Discussion

The present study showed that EIs differed by node station. Many previous studies demonstrated that the number of lymph nodes removed is an independent predictor of survival after esophagectomy for cancer [15–20]. The extent of lymph node dissection in esophageal cancer surgery was estimated by the number of resected regional lymph nodes. In the present 7th UICC TNM Classification, it is recommended that histological examination of a regional lymphadenectomy specimen ordinarily includes 7 or more lymph nodes [1]. The 7th AJCC staging manual recommends that, for pT1, approximately 10 nodes must be resected to maximize survival; for pT2, 20 nodes; and for pT3 or pT4, 30 nodes or more [2], based on the data of the worldwide esophageal cancer collaboration [20]. In NCCN guidelines, in patients undergoing esophagectomy without induction chemoradiation, at least 15 lymph nodes should be removed to achieve adequate nodal staging [21]. The optimum number of nodes after preoperative chemoradiation is unknown, although similar lymph node resection is recommended [21, 22]. When only the node stations with low EIs are dissected, and those with high EIs are not dissected, the efficacy of node dissection is low, even if more than 20 nodes are dissected. Thus, the effective extent of node dissection should be estimated by the EIs of the dissected stations.

The present study showed that the incidence of metastasis and the calculated EI of a certain node station did not reflect the anatomical distance from the primary tumor. The conventional hypothesis is that tumor cells involve the nearby nodes first, then spread to nodes a little further, and finally reach distant nodes. The extent of node dissection has been estimated by anatomical distance from the primary tumor to the dissected node station. However, the incidence of metastasis in a certain node station did not

Table 3 Efficacy index of the lymph node stations in patients with upper thoracic esophageal cancer ($n = 221$)

Node station	No. of patients with metastases	Incidence of metastasis (%)	5-year survival rate (%)	Efficacy index	Grading of node (JES)
103	0	0.0			N4
100L	0	0.0			N4
100R	0	0.0			N4
102upL	2	0.9	0.0	0.0	N4
102upR	0	0.0			N4
102midL	5	2.3	40.0	0.9	N3
102midR	3	1.4	66.7	0.9	N3
104L	14	6.3	35.7	2.3	N2
104R	26	11.8	38.4	4.5	N2
101L	17	7.7	27.5	2.1	N1
101R	30	13.6	48.9	6.6	N1
105	11	5.0	36.4	1.8	N1
106recL	30	13.6	19.3	2.6	N1
106recR	67	30.3	25.0	7.6	N1
106tbL	15	6.8	42.9	2.9	N2
106tbR	0	0.0			N3
106pre	1	0.5	100.0	0.5	N3
107	6	2.7	33.3	0.9	N2
108	12	5.4	22.2	1.2	N2
109L	2	0.9	0.0	0.0	N2
109R	2	0.9	0.0	0.0	N2
110	6	2.7	20.0	0.5	N3
111	2	0.9	50.0	0.5	N3
112	3	1.4	33.3	0.5	N3
1	9	4.1	22.2	0.9	N3
2	7	3.2	0.0	0.0	N3
3	7	3.2	19.0	0.6	N3
7	5	2.3	0.0	0.0	N3
9	2	0.9	0.0	0.0	N4
8	0	0.0			N4
11	0	0.0			N4
16	0	0.0			N4
19	0	0.0			N4

reflect the anatomical distance from the primary tumor, but rather the lymphatic drainage system reported previously [23]. In the esophagus, long longitudinal extension of lymphatic drainage in the submucosa extends craniocaudally from the proximal esophagus and to the cardia [24]. Even with tumors located in the middle and lower esophagus, lymphatic metastasis was frequent in the upper mediastinum and perigastric area. Skip metastasis is common for this reason. Therefore, the extent of dissection should be not tailored according to the anatomical distance but according to the EI.

The EIs of certain node stations differed according to the location of the primary tumor. In the present 7th UICC TNM Classification [1] and the 7th AJCC Cancer Staging Manual [2], N grades are designated by grouping the number of involved regional nodes, irrespective of the site of the primary tumor. The extent of lymph node dissection is estimated by the number of resected regional lymph nodes, irrespective of the area of dissection [2]. The area for dissection should be modified by the location of the primary tumor. For upper esophageal tumors, the recurrent nerve nodes (No. 106rec) had high EIs and are the most important dissection target. The EIs of cervical paraesophageal nodes (No. 101) were as high as that of recurrent nerve nodes (No. 106rec). The EIs of supraclavicular nodes (No. 104) were also high. Supraclavicular nodes (No. 104) should be classified as regional nodes for tumors in the upper esophagus. Neck dissection is a must for patients with upper esophageal tumors.

Table 4 Efficacy index of the lymph node stations in patients with middle thoracic esophageal cancer ($n = 752$)

Node station	No. of patients with metastases	Incidence of metastasis (%)	5-year survival rate (%)	Efficacy index	Grading of node (JES)
103	1	0.1	100.0	0.1	N4
100L	1	0.1			N4
100R	1	0.1	100.0	0.1	N4
102upL	3	0.4			N4
102upR	2	0.3			N4
102midL	10	1.3	10.0	0.1	N4
102midR	13	1.7	18.5	0.3	N4
104L	52	6.9	15.7	1.1	N3
104R	69	9.2	22.4	2.1	N3
101L	45	6.0	32.8	2.0	N2
101R	69	9.2	27.0	2.5	N2
105	39	5.2	10.9	0.6	N2
106recL	107	14.1	28.2	4.0	N1
106recR	170	22.4	37.4	8.5	N1
106tbL	21	2.8	30.3	0.8	N2
106tbR	1	0.1	0.0	0.0	N4
106pre	1	0.1	0.0	0.0	N4
107	69	9.2	19.9	1.8	N2
108	93	12.4	25.3	3.1	N1
109L	22	2.9	22.0	0.6	N2
109R	24	3.2	28.6	0.9	N2
110	69	9.2	34.4	3.2	N2
111	12	1.6	0.0	0.0	N3
112	36	4.8	30.8	1.5	N3
1	104	13.8	26.4	3.7	N2
2	80	10.6	31.1	3.3	N2
3	79	10.5	28.6	3.0	N2
7	74	9.8	28.5	2.8	N2
9	24	3.2	30.5	1.0	N4
8	10	1.3			N4
11	11	1.5			N4
16	0	0.0			N4
19	1	0.1	0.0	0.0	N4

In patients with tumors in the middle esophagus, recurrent nerve nodes (No. 106rec) had higher EI than middle paraesophageal nodes (No. 108), and the EIs of pericardial nodes (No. 1, No. 2) were as high as EI of middle paraesophageal nodes (No. 108). Cervical paraesophageal nodes (No. 101), supraclavicular nodes (No. 104), and left gastric artery nodes (No. 7) also had high EIs. This reflects longitudinal extension of lymphatic drainage from the proximal esophagus to the cardia. For patients with tumors in the middle esophagus, the most common type of esophageal tumor in Asia, not only mediastinal and abdominal but also cervical dissection by the three-field approach is recommended.

Patients with tumors in the lower esophagus had higher EIs in their lesser curvature nodes (No. 3) and left gastric artery nodes (No. 7) than in their mediastinal nodes. However, the EIs of recurrent nerve nodes (No. 106rec) were not negligible. Dissection of the upper mediastinum is recommended for patients with tumors in the lower esophagus.

The incidence of metastasis to certain stations is affected by the number of dissected cases of a certain station. In the present study, patients who underwent esophagectomy with three-field node dissection were selected for precise evaluation. Dissections of supraclavicular nodes and cervical paraesophageal nodes were required for cervical dissection by three-field dissection. Since this study was based on a multi-institutional, nationwide registry, the indication for dissection at each node station depended on each institution and was not specified. Dissection of all stations listed in Table 1 was not required. N4 grade stations are defined as

Table 5 Efficacy index of the lymph node stations in patients with lower thoracic esophageal cancer ($n = 321$)

Node station	No. of patients with metastases	Incidence of metastasis (%)	5-year survival rate (%)	Efficacy index	Grading of node (JES)
103	0	0.0			N4
100L	0	0.0			N4
100R	0	0.0			N4
102upL	0	0.0			N4
102upR	1	0.3	0.0	0.0	N4
102midL	2	0.6	0.0	0.0	N4
102midR	5	1.6	0.0	0.0	N4
104L	20	6.2	0.0	0.0	N4
104R	12	3.7	15.0	0.6	N4
101L	20	6.2	13.4	0.8	N3
101R	15	4.7	20.7	1.0	N3
105	11	3.4	18.2	0.6	N3
106recL	25	7.8	25.2	2.0	N2
106recR	46	14.3	21.9	3.1	N2
106tbL	8	2.5	0.0	0.0	N3
106tbR	0	0.0			N4
106pre	0	0.0			N4
107	20	6.2	7.2	0.4	N2
108	39	12.1	27.1	3.3	N2
109L	10	3.1	0.0	0.0	N2
109R	10	3.1	10.0	0.3	N2
110	57	17.8	23.9	4.2	N1
111	12	3.7	8.3	0.3	N2
112	22	6.9	26.3	1.8	N2
1	92	28.7	30.1	8.6	N1
2	79	24.6	28.9	7.1	N1
3	70	21.8	21.1	4.6	N2
7	82	25.5	23.4	6.0	N2
9	21	6.5	33.3	2.2	N3
8	14	4.4			N4
11	11	3.4			N4
16	3	0.9	0.0	0.0	N4
19	0	0.0			N3

distant metastases and are not usually dissected. The incidences of metastasis in N4 stations were very low in this study.

The incidence of nodal metastases and EI by station reported in this study were lower than in those obtained in the previous report [14]. This is because all patients without nodal metastases were included, but the patients with nodal metastases for whom no information about pathological metastatic lymph nodes locations was available were excluded.

One potential criticism of the present study is that most patients had squamous cell carcinoma, and only a few had adenocarcinoma. However, in Asian patients, including Japanese patients, squamous cell carcinoma remains the predominant type of esophageal cancer. The pattern of lymph node metastases reflects not the histological cell types but the location of the primary tumor. The present study has equivalent value to Western studies in which most patients had adenocarcinoma, and only a few had squamous cell carcinoma.

Acknowledgments This study was supported by Health and Labour Sciences Research Grants for Promotion of Cancer Control Programs (H26-Cancer Policy-General-014) from the Ministry of Health, Labour, and Welfare of Japan.

Compliance with ethical standards

Ethical statement This registry complies with the Act for the Protection of Personal Information that was promulgated in 2003, and follows the ethical guidelines for epidemiologic studies published jointly by the Japan Ministry of Education, Culture, Sports, Science and Tech-

nology and the Japan Ministry of Health, Labour, and Welfare in 2002, which was revised in 2007. The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

Informed consent This work conformed to the guidelines set forth in the Helsinki Declaration of 1975, as revised in 2000 (5), concerning Human and Animal Rights, and that they followed the policy concerning Informed Consent as shown on the following sites.

Conflict of interest All authors have nothing to disclose with regard to commercial support.

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Esophagus (2016) 13:1–7
DOI 10.1007/s10388-015-0515-3

SPECIAL ARTICLE

Efficacy of lymph node dissection by node zones according to tumor location for esophageal squamous cell carcinoma

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Received: 20 August 2015 / Accepted: 21 October 2015 / Published online: 17 November 2015

Abstract
Background The extent of node dissection in esophageal cancer surgery is usually estimated by the number of resected nodes, irrespective of the area of dissection. The efficacy of lymph node dissection by area was evaluated according to the location of the primary tumor.
Methods The study group comprised the 3827 patients who underwent R0 esophagectomy with three-field lymph node dissection for squamous cell carcinoma, registered in a nationwide registry in Japan. The areas of lymph node were classified into zones according to AJCC Staging Manual. The Efficacy Index (EI) calculating the frequency and patient survival of metastases to each zone was investigated according to tumor location.
Results The EI was high in supraclavicular and upper mediastinal zones in patients with upper esophageal tumors, highest in upper mediastinal zone followed by supraclavicular and perigastric zones in patients with middle esophageal tumors, and highest in perigastric zone followed by upper and lower mediastinal zones in patients with lower esophageal tumors. In patients with middle and lower esophageal cT1 tumors, the EIs of upper mediastinal and perigastric zones were higher than middle and lower mediastinal zones.
Conclusion The EIs of each zone were differed by tumor location. The extent of lymph node dissection should be estimated by the dissected zones and modified by the tumor location. Supraclavicular dissection is indispensable for patients with upper esophageal tumors, and recommended for patients with middle esophageal tumors. Upper mediastinal dissection is recommended for all patients with thoracic esophageal squamous cell carcinoma, irrespective of the location.

Keywords Esophageal cancer · Squamous cell carcinoma · Lymphadenectomy · Metastasis · Survival

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Introduction

Despite recent advances in multidisciplinary approaches, surgical resection remains the standard treatment for potentially resectable esophageal carcinoma. In addition to primary tumor resection, removal of all potentially involved lymph nodes is essential for achieving cure. In the present 7th UICC TNM classification [1] and the 7th AJCC Cancer Staging

manual [2], the regional nodes are not varied irrespective of the location of the primary tumor. The extent of lymph node dissection in esophageal cancer surgery is estimated by the number of resected regional lymph nodes, irrespective of the area of dissection [2]. However, many surgeons accept that the area of nodal dissection should be modified according to the location of the primary tumor in an individual patient.

The purpose of this retrospective study was to evaluate the efficacy of lymph node dissection by the area based on the location of the primary tumor, calculating the frequency and patient survival of metastases to the area in patients with thoracic esophageal squamous cell carcinoma who underwent esophagectomy with curative intent. This study was based on a large, multi-institutional, nationwide registry of esophageal cancer maintained by the Japan Esophageal Society.

Methods

Patients

A comprehensive registry of esophageal cancer in Japan has been maintained by the Japan Esophageal Society since 1976. All patient data, including demographic characteristics, symptoms, clinical stage, treatment features, and survival information, were collected. Surgical features, clinical and pathological stage, and detailed lymph node metastatic status were also collected for patients who underwent surgery.

A total of 24,748 patients with primary esophageal tumor treated in 2004, 2005 and 2006, and 2007 and 2008 were registered in 2011, 2012, and 2014, respectively, from 239 institutions in Japan [3–7]. Of the 24,748 patients, 22,667 had primary thoracic esophageal tumor, excluding cervical esophageal tumor and Siewert type II and type III esophagogastric junction cancers [8]. Of the 12,408 patients who underwent esophagectomy, 11,136 underwent R0 resection, and patients who underwent R1 and R2 resections were excluded due to limited node dissection. Of the 11,136 patients who underwent R0 resection. 4820 (43.3 %) patients underwent esophagectomy with three-field lymph node dissection [9, 10]. For the purpose of evaluating the frequency of metastasis to all regional node areas precisely, only the patients who underwent esophagectomy with three-field lymph node dissection were selected. The cervical, mediastinal, and abdominal lymph nodes were dissected. Dissections of supraclavicular nodes and cervical paraesophageal nodes were required for cervical dissection by three-field dissection in the registration. Since it was based on a multi-institutional, nationwide registry, the selection of patients and indications for three-field dissection depended on each institution and each surgeon, and were not specified. The three-field dissection

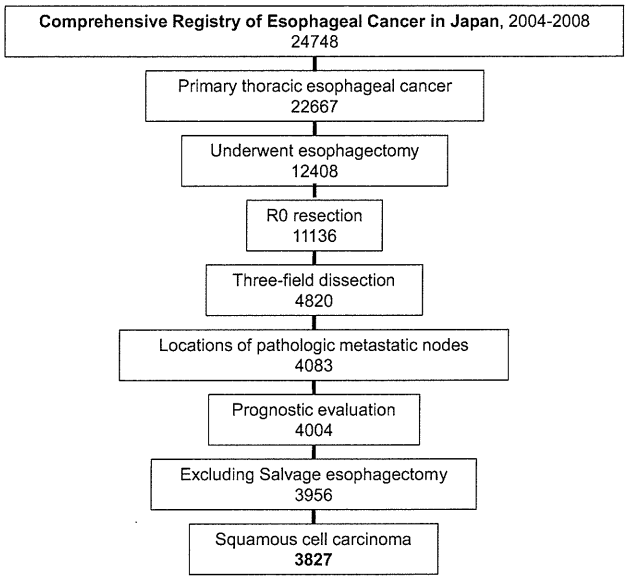

Fig. 1 Patient disposition chart

was performed in 60.5 % of patients with upper esophageal tumor, 49.5 % of patients with middle esophageal tumor, and 30.8 % of patients with lower esophageal tumor. It was performed in 36.5 % of patients with cT1 tumor and 48.2 % of patients with cT2-4 tumor. Of the 4820 patients who underwent esophagectomy with three-field lymph node dissection for R0 resection, information about the locations of pathological metastatic lymph nodes was available for 4083 patients, and outcome evaluations were available in 4004 patients. Of the 3956 patients excluding 48 patients who received definitive chemoradiotherapy and underwent salvage esophagectomy, 3827 patients (97 %) had squamous cell carcinoma including adenosquamous carcinoma and basaloid squamous carcinoma, 64 patients (1.6 %) had adenocarcinoma, and 65 patients had other tumors including undifferentiated tumor, carcinosarcoma and malignant melanoma. The total study group comprised 3827 patients who underwent R0 resection and esophagectomy with three-field lymph node dissection for squamous cell carcinoma from 155 institutions (Fig. 1).

Tumor classification

Clinical stages for all patients were recorded according to the 6th edition of the UICC TNM Classification [11]. Pathological stages for all patients were re-assessed according to the 7th edition of the UICC TNM Classification [1]. The thoracic esophagus was divided into three anatomical subsites: upper, middle, and lower. The tumor location is regarded as the point of deepest tumor invasion according to the Japanese Classification [12], which in clinical practice is the epicenter of the tumor.

Table 1 Node zones

Node zone	Station number (JES)	Name of node station (JES)	Station number (AJCC)	Name of node station (AJCC)
Supraclavicular	104R	Right supraclavicular	1	Supraclavicular
	104L	Right supraclavicular	1	Supraclavicular
	101R	Right cervical paraesophageal		(Cervical paraesophageal)
	101L	Right cervical paraesophageal		(Cervical paraesophageal)
Upper mediastinal	105	Upper paraesophageal	3p	Posterior mediastinal
	106pre	Pretracheal	2R	Right upper paratracheal
	106recR	Right recurrent nerve	2R	Right upper paratracheal
	106recL	Right recurrent nerve	2L	Left upper paratracheal
	106tbR	Right tracheobronchial	4R	Right lower paratracheal
	106tbL	Right tracheobronchial	4L	Left lower paratracheal
Middle mediastinal	107	Subcarinal	7	Subcarinal
	108	Middle paraesophageal	8 m	Middle paraesophageal
	109R	Right main bronchus	10R	Right tracheobronchial
	109L	Left main bronchus	10L	Left tracheobronchial
Lower mediastinal	110	Lower paraesophageal	8 l	Lower paraesophageal
	111	Supradiaphragmatic	15	Diaphragmatic
	112	Posterior mediastinum	9	Pulmonary ligament
Perigastric	1	Right cardiac	16	Paracardial
	2	Left cardiac	16	Paracardial
	3	Lesser curvature		
	7	Left gastric artery	17	Left gastric artery
Celiac	9	Celiac	20	Celiac
	8	Common hepatic artery	18	Common hepatic
	11	Splenic artery	19	Splenic
	19	Infradiaphragmatic		

The areas of lymph node metastasis were recorded according to the lymph node stations adopted by the Japanese Classification [12]. There are some differences in the definition of lymph node stations between the Japanese Classification [12] and AJCC Staging Manual [2] (Table 1). This difference in the anatomical definition of each lymph node station might have influenced the nodal categorization. However, with the database collected, there was no way to reasonably reconcile or amend such differences. So, lymph node stations were classified into lymph node zones according to the map in AJCC Staging Manual [2] (Table 1). The middle mediastinal zone and the lower mediastinal zone were divided by caudal margin of the inferior pulmonary vein.

Method of analysis

To evaluate the efficacy of nodal dissection at each zone, the efficacy index (EI) was calculated by multiplying the frequency (%) of metastases to a zone and the 5-year survival rate (%) of patients with metastases to that zone, and then dividing by 100 [13–15]. The EI was investigated according to tumor location. The EI was also determined by clinical T factor: cT1 and cT2-4. Survival rates were constructed using the Kaplan–Meier method. Statistical analysis was performed using the SPSS Statistics Software Package (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics and findings are listed in Table 2. The location of the tumors was the upper esophagus in 629 patients (16.4 %), the middle esophagus in 2215 (57.9 %), and the lower esophagus in 983 (25.7 %).

Preoperative neoadjuvant chemoradiotherapy was administered to 238 patients (6.2 %), 515 patients (13.5 %) received preoperative chemotherapy, and 3 patients (0.1 %) received preoperative radiotherapy. Preoperative therapy was under clinical study [16] and not standard for esophageal cancer in Japan during the registration period. The selection of patients, indications, and therapeutic approach to preoperative therapy depended on each institution and were not specified.

Table 2 Patients' characteristics and tumor findings

Characteristic or finding	No. (%)
Median age (range), year	63.0 (30–85)
Sex	
Male	3293 (86.0 %)
Female	534 (14.0 %)
Tumor location	
Upper	983 (16.4 %)
Middle	2215 (57.9 %)
Lower	629 (25.7 %)
Preoperative therapy	
Chemotherapy	515 (13.5 %)
Chemoradiotherapy	238 (6.2 %)
Radiotherapy	3 (0.1 %)
None	3071 (80.2 %)
Clinical T classification	
T1	1160 (30.3 %)
T2	701 (18.3 %)
T3	1810 (47.3 %)
T4	156 (4.1 %)
Pathologic positive node number (including supraclavicular node)	
N0	1616 (42.2 %)
N(1–2)	843 (22.0 %)
N(3–6)	903 (23.6 %)
N(7–)	465 (12.2 %)

The 30-day operative mortality rate was 0.9 % (33 patients) and 90-day mortality was 1.8 % (69 patients). The 5-year survival rate for all patients was 57.5 %.

The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EI of each zone are presented according to tumor location in Table 3. The frequency of metastasis and the EI of each zone were different by tumor locations. In patients with upper esophageal tumors, the EIs of the supraclavicular zone and the upper mediastinal zone were high. In contrast, those of the middle mediastinal, lower mediastinal and perigastric zones were low. In patients with middle esophageal tumors, the EI of the upper mediastinal zone was the highest, followed by those of supraclavicular zone and perigastric zones. In patients with lower esophageal tumors, the EI of perigastric zone was the highest, followed by those of upper mediastinal and lower mediastinal zones. The EIs of celiac zone were the lowest among all the zones in patients with thoracic squamous cell carcinoma. Differences of the EIs between zones mostly depended on difference of the frequency of metastasis to zones. Differences of the 5-year survival rates of patients with metastases between zones were less.

The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EIs of each zone in patients with cT1 tumor are presented in Table 4. In patients with upper esophageal cT1 tumors, the EI of the upper mediastinal zone was highest. However, in patients

Table 3 The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EI of each zone according to tumor location for esophageal squamous cell carcinoma

Lymph node zone	Upper esophageal cancer			$n = 629$	Mid esophageal cancer			$n = 2215$	Lower esophageal cancer			$n = 983$
	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index
Supraclavicular zone	210	33.4	42.3	14.1	505	22.8	40.5	9.2	173	17.6	30.0	5.3
Upper mediastinal zone	270	42.9	41.1	17.6	829	37.4	40.0	15.0	249	25.3	32.6	8.2
Middle mediastinal zone	59	9.4	32.2	3.0	462	20.9	29.0	6.1	193	19.6	24.1	4.7
Lower mediastinal zone	27	4.3	33.1	1.4	254	11.5	33.5	3.9	242	24.6	34.2	8.4
Perigastric zone	62	9.9	31.1	3.1	618	27.9	33.2	9.3	479	48.7	36.5	17.8
Celiac zone	5	0.8	0.0	0.0	89	4.0	26.1	1.0	104	10.6	27.0	2.9

Table 4 The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EI of each zone according to tumor location for cT1 esophageal squamous cell carcinoma

Lymph node zone	Upper esophageal cancer			$n = 211$	Mid esophageal cancer			$n = 752$	Lower esophageal cancer			$n = 197$
	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index
Supraclavicular zone	42	19.9	60.7	12.1	94	12.5	58.9	7.4	22	11.2	39.4	4.4
Upper mediastinal zone	56	26.5	62.8	16.6	161	21.4	57.5	12.3	27	13.7	58.2	8.0
Middle mediastinal zone	2	0.9	50.0	0.5	32	4.3	34.4	1.5	12	6.1	22.2	1.4
Lower mediastinal zone	2	0.9	0.0	0.0	30	4.0	66.9	2.7	17	8.6	46.3	4.0
Perigastric zone	8	3.8	15.0	0.6	76	10.1	53.9	5.4	34	17.3	45.2	7.8
Celiac zone	0	0.0			11	1.5	36.4	0.5	5	2.5		

with middle and lower esophageal cT1 tumors, the EIs of the middle and lower mediastinal zones were lower than those of the upper mediastinal and perigastric zones. In 22 patients with lower esophageal cT1 tumors and metastasis to the supraclavicular zone, 9 patients had the proximal margin of the tumor in the middle esophagus. In 27 patients with lower esophageal cT1 tumors and metastasis to the upper mediastinal zone, 14 patients had the proximal margin of the tumor in the middle esophagus.

The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EIs of each zone in patients with cT2-4 tumors are presented in Table 5. In patients with middle esophageal cT2-4 tumors, frequency of lymph node metastasis and the EI of the middle mediastinal zone was increased dramatically compared with patients with cT1 tumors, but still lower than those of the upper mediastinal and perigastric zones. In patients with lower esophageal cT2-4 tumors, the EI of the upper mediastinal zones was as high as that of the lower mediastinal zones.

Discussion

The present study showed that the efficacies of node dissection differed by zone of lymph node. Many previous studies demonstrated that the number of lymph nodes removed is an independent predictor of survival after esophagectomy for cancer [17–22]. The extent of lymph node dissection in esophageal cancer surgery was estimated by the number of resected regional lymph nodes. In the present 7th UICC TNM Classification, it is recommended that histological examination of a regional lymphadenectomy specimen ordinarily include 7 or more lymph nodes [1]. The 7th AJCC staging manual recommends that, for pT1, approximately 10 nodes must be resected to maximize survival; for pT2, 20 nodes; and for pT3 or pT4, 30 nodes or more [2], based on the data of the worldwide esophageal cancer collaboration [22]. In NCCN guideline, in patients undergoing esophagectomy without induction chemoradiation, at least 15 lymph nodes should be removed to achieve adequate nodal staging [23]. However, when only the node zones with low EI are dissected, and those with high EI are not dissected, the efficacy of node dissection is low, even more than 20 nodes are dissected. Thus, the effective extent of node dissection should be modified by the EIs of node zones.

EIs of each node zone were differed by tumor location. The zones for dissection should be modified according to the location of the tumor. For upper esophageal tumors, the upper mediastinal zone had the highest EI and is the most important dissection target. The EI of supraclavicular zone was also high and supraclavicular node dissection is indispensable for patients with upper esophageal tumor. Supraclavicular nodes should be classified as regional nodes for tumors in the upper esophagus. In patients with

Table 5 The frequency of metastasis, the 5-year survival rate of patients with metastases, and the EI of each zone according to tumor location for cT2-4 esophageal squamous cell carcinoma

Lymph node zone	Upper esophageal cancer			$n = 418$	Mid esophageal cancer			n = 1146	Lower esophageal cancer			n = 786
	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index	Positive patients	Positive rate (%)	5-year survival rate (%)	Efficacy index
Supraclavicular zone	168	40.2	37.8	15.2	411	28.1	36.6	10.3	151	19.2	27.7	5.3
Upper mediastinal zone	214	51.2	34.6	17.7	668	45.7	36.2	16.5	222	28.2	27.8	7.8
Middle mediastinal zone	57	13.6	31.8	4.3	430	29.4	28.4	8.3	181	23.0	23.8	5.5
Lower mediastinal zone	25	6.0	34.5	2.1	224	15.3	28.9	4.4	225	28.6	33.2	9.5
Perigastric zone	54	12.9	33.8	4.4	542	37.0	30.3	11.2	445	56.6	35.7	20.2
Celiac zone	5	1.2	0.0	0.0	78	5.3	24.6	1.3	99	12.6	25.3	3.2

tumor in the middle esophagus, upper mediastinal zone had the highest EI followed by perigastric and supraclavicular zones. For patients with tumor in the middle esophagus, the most common type of esophageal tumor in Asia, not only mediastinal and abdominal, but also cervical dissection by the three-field approach is recommended. Patients with tumor in the lower esophagus had the highest EI in perigastric zone. However, the EI of upper mediastinal zone was as high as that of lower mediastinal zone. Upper mediastinal dissection is recommended for all patients with thoracic esophageal squamous cell carcinoma, irrespective of the location.

The present study showed that the frequency of metastasis and the EI did not reflect the anatomical distance from the primary tumor, but rather the lymphatic drainage system reported previously [24, 25]. Even with tumors located in the middle and lower esophagus, lymphatic metastasis was frequent in the upper mediastinal and perigastric zones. The conventional hypothesis is that tumor cells involve the nearby nodes first, then spread to nodes a little further, and finally reach distant nodes. The extent of node dissection has been estimated by anatomical distance from the primary tumor to the dissected node area. However, in patients with middle and lower esophageal cT1 tumors, the EIs of the middle and lower mediastinal zone were lower than those of upper mediastinal zone and perigastric zone. Therefor extent of dissection in patients with cT1 tumors should be not tailored according to the anatomical distance from the tumor, but according to the EI.

Many patients with lower esophageal cT1 tumors and the proximal margin of the tumor in the middle esophagus had metastasis to the supraclavicular zone and the upper mediastinal zone. It suggests that the proximal nodal spread to the supraclavicular and upper mediastinal nodes is reflect to the location of proximal margin of the tumor. The attention to the proximal margin of tumor should be paid in planning the extend of node dissection. The proximal margin of squamous cell carcinoma tends to be more proximal than those of adenocarcinoma. Supraclavicular and upper mediastinal node metastasis are not neglected.

In this study, lymph node stations were classified into lymph node zones according to the map in AJCC Staging Manual. In surgical dissection and in identification and labeling during pathological examination of specific lymph node, and also in planning of irradiation field, lymph node zones are more practical than small neighboring lymph node stations.

The present study was based on patients with squamous cell carcinoma, and patients with adenocarcinoma were not included. However, in Asian patients, including Japanese patients, squamous cell carcinoma remains the predominant histological cell type of esophageal cancer, and more than half of tumors locates in the upper and middle esophagus.

In conclusion, the EIs of each zone were differed by tumor location. The extent of lymph node dissection should be estimated by the dissected lymph node zones and modified by the tumor location. Supraclavicular dissection is indispensable for patients with upper esophageal tumors and recommended for patients with middle esophageal tumors. Upper mediastinal dissection is recommended for all patients with thoracic esophageal squamous cell carcinoma, irrespective of the location.

Acknowledgments This registry complies with the Act for the Protection of Personal Information that was promulgated in 2003, and follows the ethical guidelines for epidemiologic studies published jointly by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Japan Ministry of Health, Labour, and Welfare in 2002, which was revised in 2007. This study was supported by Health and Labour Sciences Research Grants for Promotion of Cancer Control Programs (H26-Cancer Policy-General-014) from the Ministry of Health, Labour, and Welfare of Japan. The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

Compliance with ethical standards

Ethical Statement This work conforms to the guidelines set forth in the Helsinki Declaration of 1975, as revised in 2000, concerning Human and Animal Rights. This article does not contain any studies with human or animal subjects performed by any authors.

Conflict of interest There are no financial or other relations that could lead to a conflict of interest.

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Esophagus (2015) 12:101–129
DOI 10.1007/s10388-015-0488-2

SPECIAL ARTICLE

Comprehensive Registry of Esophageal Cancer in Japan, 2007

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Published online: 1 March 2015

Preface 2007

We deeply appreciate the great contributions of many physicians in the registry of esophageal cancer cases. The Comprehensive Registry of Esophageal Cancer in Japan, 2007, was published here, despite some delay. The registry complies with the Act for the Protection of Personal Information. The encryption with a HASH function is used for ''anonymity in an unlinkable fashion''.

These data were first made available on December 25, 2014, as the Comprehensive Registry of Esophageal Cancer in Japan, 2008. Not all the pages are reprinted here; however, the original table and figure numbers have been maintained.

The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

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We briefly summarized the Comprehensive Registry of Esophageal Cancer in Japan, 2007. Japanese Classification of Esophageal Cancer 10th and UICC TNM Classification 6th were used for cancer staging according to the subjected year. A total of 5216 cases were registered from 257 institutions in Japan. Tumor locations were cervical: 4.4 %, upper thoracic: 12.7 %, middle thoracic: 49.5 %, lower thoracic: 25.1 % and EG junction: 5.9 %. Superficial carcinomas (Tis, T1a, and T1b) were 35.7 %. As for the histologic type of biopsy specimens, squamous cell carcinoma and adenocarcinoma accounted for 90.1 % and 3.9 %, respectively. Regarding clinical results, the 5-year survival rates of patients treated using endoscopic mucosal resection, concurrent chemoradiotherapy, radiotherapy alone, chemotherapy alone, or esophagectomy were 88.1, 25.1, 16.0, 9.4, and 52.8 %, respectively. Esophagectomy was performed in 2834 cases. Concerning the approach used for esophagectomy, 19.8 % of the cases were treated thoraco-

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scopically. The operative mortality (within 30 days after surgery) was 0.67 % and the hospital mortality was 1.27 %.

We hope that this Comprehensive Registry of Esophageal Cancer in Japan for 2007 will help to improve all aspects of the diagnosis and treatment of esophageal cancer in Japan.

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Asahikawa Medical College Hospital
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Chiba Cancer Center
Chiba Medical Center
Chiba Prefectural Sawara Hospital
Chiba University Hospital
Chibaken Saiseikai Narashino Hospital
Dokkyo Medical University Hospital
Fujioka General Hospital
Fujisawa Shounandai Hospital
Fujita Health University
Fukui Prefectural Hospital
Fukui University Hospital
Fukuoka Dental College and Dental Hospital
Fukuoka Saiseikai General Hospital
Fukuoka University Hospital
Fukuoka Wajiro Hospital
Fukushima Medical University Hospital
Gifu Prefectural General Medical Center
Gifu University Hospital
Gunma Central General Hospital
Gunma Prefectural Cancer Center
Gunma University Hospital
Gunmaken Saiseikai Maebashi Hospital
Hakodate Goryokaku Hospital
Hakodate National Hospital
Hamamatsu University School of Medicine, University Hospital
Health Insurance Naruto Hospital
Heartlife Hospital
Higashiosaka City General Hospital
Hino Memorial Hospital
Hiratsuka City Hospital
Hiratsuka Kyosai Hospital
Hiroshima City Asa Hospital
Hiroshima University Research Institute for Radiation Biology Medicine
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Hokkaido P.W.F.A.C Obihiro-Kosei General Hospital
Hokkaido University Hospital
Hyogo Cancer Center

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Ida Municipal Hospital
Iizuka Hospital
Imazu Surgical Clinic
Inazawa City Hospital
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Ishikawa Prefectural Central Hospital
Iwakuni Medical Center
Iwate Medical University Hospital
Japanese Red Cross Kyoto Second Hospital
Japanese Red Cross Shizuoka Hospital
Jichi Medical University Hospital
Juntendo University Hospital
Junwakai Memorial Hospital
Kagawa Prefectural Central Hospital
Kagawa Rosai Hospital
Kagawa University Hospital
Kagoshima Kenritsu Satsunan Hospital
Kagoshima University Hospital
Kanazawa Medical University Hospital
Kanazawa University Hospital
Kansai Medical University Hirakata Hospital
Kansai Rosai Hospital
Kashiwa Kousei General Hospital
Kawakita General Hospital
Kawasaki Hospital
Kawasaki Medical School Hospital
Kawasaki Municipal Hospital
Keio University Hospital
Keiyukai Sapporo Hospital
Kikuna Memorial Hospital
Kinki Central Hospital
Kinki University Hospital
Kiryu Kosei General Hospital
Kishiwada City Hospital
Kitakyushu Municipal Medical Center
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Kitasato University Kitasato Institute Medical Center Hospital
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Kobe University Hospital
Kochi University Hospital
Kokura Memorial Hospital
Kumamoto City Hospital
Kumamoto University Hospital
Kurashiki Central Hospital
Kurume First Social Insurance Hospital

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Kyusyu Medical Center
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Matsuda Hospital
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Matsushita Memorial Hospital
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Oita University Hospital
Okayama Saiseikai General Hospital
Okayama University Hospital
Omuta City Hospital
Onomichi Municipal Hospital
Osaka City General Medical Center
Osaka City University Hospital
Osaka Hospital of Japan Seafarers Relief Association
Osaka Koseinenkin Hospital
Osaka Medical Center for Cancer and Cardiovascular Diseases
Osaka Medical College Hospital
Osaka Prefectural Hospital Organization Osaka General Medical Center
Osaka Red Cross Hospital
Osaka University Hospital
Otsu Red Cross Hospital
Rinku General Medical Center
Ryukyu University Hospital
Saga University Hospital
Saga-Ken Medical center Koseikan
Saiseikai Utsunomiya Hospital
Saiseikai Yahata General Hospital
Saitama City Hospital
Saitama Medical Center
Saitama Medical Center Jichi Medical University
Saitama Medical University Hospital
Saitama Medical University International Medical Center
Saitama Prefectural Cancer Center
Saitama Social Insurance Hospital
Sakai Municipal Hospital
Saku Central Hospital
Sano Kousei General Hospital
Seirojika National Hospital University Hospital
Sendai City Hospital
Sendai Medical Center
Shiga Medical Center for Adults
Shiga University of Medical Science Hospital
Shikoku Cancer Center
Shimada Hospital
Shimane University Hospital
Shimizu Welfare Hospital

continued

Institution
Shinshu University Hospital
Shizuoka Cancer Center
Shizuoka City Shizuoka Hospital
Shizuoka General Hospital
Showa University Hospital
Social Insurance Omuta Tenryo Hospital
Social Insurance Tagawa Hospital
Social Insurance Yokohama Central Hospital
Sonoda First Hospital
Sugita Genpaku Memorial Obama Municipal Hospital
Suita Municipal Hospital
Suwa Red Cross Hospital
Syowa University Hospital
Syowa University Toyosu Hospital
Takaoka Hospital
Takasago Municipal Hospital
Takatsuki Red Cross Hospital
Tenri Hospital
The Cancer Institute Hospital of JFCR
The Jikei University Hospital
The Research Center Hospital for Charged Particle Therapy of the NIRS
Tochigi Cancer Center
Toho University Hospital
Toho University Omori Medical Center
Tohoku Kosai Hospital
Tohoku University Hospital
Tokai University Hospital
Tokushima Municipal Hospital
Tokushima Red Cross Hospital
Tokushima University Hospital
Tokyo Dental College Ichikawa General Hospital
Tokyo Jikeikai Medical

continued

Institution
Tokyo Medical and Dental University Hospital
Tokyo Medical University Hospital
Tokyo Metropolitan Cancer and Infectious Center Komagome Hospital
Tokyo Metropolitan Health and Medical Corporation Toshima Hospital
Tokyo University Hospital
Tokyo Women's Medical University Hospital
Tokyo Women's Medical University Medical Center East
Tonan Hospital
Tone Central Hospital
Toranomon Hospital
Tottori Prefectural Central Hospital
Tottori University Hospital
Toyama Prefectural Central Hospital
Toyama University Hospital
Tsuchiura Kyodo Hospital
Tsukuba University Hospital
University Hospital, Kyoto Prefectural University of Medicine
University of Miyazaki Hospital
Wakayama Medical University Hospital
Yamagata Prefectural and Sakata Municipal Hospital Organization
Yamagata Prefectural Central Hospital
Yamagata Prefectural Shinjo Hospital
Yamaguchi-ken Saiseikai Shimonoseki General Hospital
Yamanashi Prefectural Central Hospital
Yamanashi University Hospital
Yokohama City Municipal Hospital
Yokohama City University Hospital
Yokohama City University Medical Center
Yuri General Hospital

(Total 257 institutions)

Patient background

Table 1 Age and gender

Age	Male	Female	Unknown	Cases (%)
~29	9	0	0	9 (0.2 %)
30~39	9	7	0	16 (0.3 %)
40~49	122	36	4	162 (3.1 %)
50~59	911	158	8	1077 (20.6 %)
60~69	1800	238	18	2056 (39.4 %)
70~79	1298	206	9	1513 (29.0 %)
80–89	277	63	2	342 (6.6 %)
90~	11	7	0	18 (0.3 %)
Unknown	17	5	1	23 (0.4 %)
Total	4454	720	42	5216 (100 %)

Table 15 Histologic types of biopsy specimens

Histologic types	Cases (%)
Not examined	63 (1.2 %)
SCC	4702 (90.1 %)
SCC	3062 (58.7 %)
Well diff.	301 (5.8 %)
Moderately diff.	1015 (19.5 %)
Poorly diff.	324 (6.2 %)
Adenocarcinoma	205 (3.9 %)
Undifferentiated	17 (0.3 %)
Carcinosarcoma	14 (0.3 %)
Malignant melanoma	12 (0.2 %)
Other tumors	51 (1.0 %)
Unknown	152 (2.9 %)
Total	5216 (100 %)

SCC squamous cell carcinoma

Table 11 Primary treatment

Treatments	Cases (%)
Surgery	2892 (55.4 %)
Esophagectomy	2834 (54.3 %)
Palliative	58 (1.1 %)
Chemotherapy/radiotherapy	1366 (26.2 %)
Endoscopic treatment	782 (15.0 %)
Others	13 (0.2 %)
None/unknown	163 (3.1 %)
Total	5216 (100 %)

Table 12 Tumor location

Location of tumor	Endoscopic treatment (%)	Chemotherapy and/or radiotherapy (%)	Palliative surgery (%)	Esophagectomy (%)	Other (%)	None/Unknown (%)	Total (%)
Cervical	13 (1.7 %)	127 (9.3 %)	1 (1.7 %)	77 (2.7 %)	0	9 (5.5 %)	227 (4.4 %)
Upper thoracic	76 (9.7 %)	238 (17.4 %)	14 (24.1 %)	312 (11.0 %)	1 (7.7 %)	20 (12.3 %)	661 (12.7 %)
Middle thoracic	439 (56.1 %)	652 (47.7 %)	31 (53.4 %)	1380 (48.7 %)	7 (53.8 %)	73 (44.8 %)	2582 (49.5 %)
Lower thoracic	171 (21.9 %)	281 (20.6 %)	11 (19.0 %)	808 (28.5 %)	1 (7.7 %)	36 (22.1 %)	1308 (25.1 %)
E > G	35 (4.5 %)	29 (2.1 %)	1 (1.7 %)	199 (7.0 %)	0	3 (1.8 %)	267 (5.1 %)
E = G	0	3 (0.2 %)	0	25 (0.9 %)	0	1 (0.6 %)	29 (0.6 %)
G > E	0	1 (0.1 %)	0	10 (0.4 %)	0	0	11 (0.2 %)
Unknown	48 (6.1 %)	35 (2.6 %)	0	23 (0.8 %)	4 (30.8 %)	21 (12.9 %)	131 (2.5 %)
Total	782 (100 %)	1366 (100 %)	58 (100 %)	2834 (100 %)	13 (100 %)	163 (100 %)	5216 (100 %)

EG esophago-gastric

Table 16 Depth of tumor invasion, cT (UICC TNM 6th)

cT	Cases (%)
cTX	152 (2.9 %)
cT0	10 (0.2 %)
cTis	128 (2.5 %)
cT1	245 (4.7 %)
cT1a	579 (11.1 %)
cT1b	906 (17.4 %)
cT2	703 (13.5 %)
cT3	1840 (35.3 %)
cT4	653 (12.5 %)
Total	5216 (100 %)

Table 17 Lymph node metastasis, cN (UICC TNM 6th)

cN	Cases (%)
cNX	236 (4.5 %)
cN0	2433 (46.6 %)
cN1	2547 (48.8 %)
Total	5216 (100 %)

Table 18 Distant metastasis, cM (UICC TNM 6th)

cM	Cases (%)
cMX	178 (3.4 %)
cM0	4208 (80.7 %)
cM1	189 (3.6 %)
cM1a	167 (3.2 %)
cM1b	474 (9.1 %)
Total	5216 (100 %)

Table 20 Clinical Stage (UICC TNM 6th)

Location of tumor	Endoscopic treatment (%)	Chemotherapy and/or radiotherapy (%)	Palliative surgery (%)	Esophagectomy (%)	Other (%)	None/unknown (%)	Total (%)
0	95 (12.1 %)	5 (0.4 %)	0	13 (0.5 %)	0	4 (2.5 %)	117 (2.2 %)
I	555 (71.0 %)	181 (13.3 %)	3 (5.2 %)	673 (23.7 %)	3 (23.1 %)	21 (12.9 %)	1436 (27.5 %)
IIA	10 (1.3 %)	128 (9.4 %)	7 (12.1 %)	571 (20.1 %)	2 (15.4 %)	18 (11.0 %)	736 (14.1 %)
IIB	3 (0.4 %)	77 (5.6 %)	4 (6.9 %)	361 (12.7 %)	0	6 (3.7 %)	451 (8.6 %)
III	29 (3.7 %)	469 (34.3 %)	31 (53.4 %)	831 (29.3 %)	3 (23.1 %)	32 (19.6 %)	1395 (26.7 %)
IV	4 (0.5 %)	114 (8.3 %)	3 (5.2 %)	34 (1.2 %)	0	20 (12.3 %)	175 (3.4 %)
IVA	2 (0.3 %)	73 (5.3 %)	2 (3.4 %)	87 (3.1 %)	0	2 (1.2 %)	166 (3.2 %)
IVB	11 (1.4 %)	255 (18.7 %)	3 (5.2 %)	165 (5.8 %)	1 (7.7 %)	25 (15.3 %)	460 (8.8 %)
Unknown	73 (9.3 %)	64 (4.7 %)	5 (8.6 %)	99 (3.5 %)	4 (30.8 %)	35 (21.5 %)	280 (5.4 %)
Total	782 (100 %)	1366 (100 %)	58 (100 %)	2834 (100 %)	13 (100 %)	163 (100 %)	5216 (100 %)