

An Evaluation of Surgical Problems for Carcinoma of Esophagus in view of Autopsy Findings

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By comparison of the findings in operation and those in autopsy, 9 cases of death within 30 days after esophagectomy and dissection of the lymph node for thoracic esophageal cancer were examined mainly on the influence of dissection of the lymph node. In autopsy, remained metastatic lymph node was observed in 4 of them (44.4%). Remained metastatic thoracic lymph node was to the tracheobronchial lymph node group. Metastatic abdominal lymph node was observed in many cases at the operation, but in autopsy remained cancer in this area was not observed. It is proved that remained metastatic lymph node in the abdomen at autopsy is in paraaortic lymph node in high rate.

It was examined by the experiment with the dogs that frequency of pulmonary complication will be higher if extended radical mediastinal lymph node dissection is performed. In the experiment, decrease of lung surfactant, rise in pulmonary wedge pressure, trouble in perfusion of pulmonary lymph flow in the experiment by dye solution, and interstitial edema and alveolar edema in the lung in histological examination were observed.

As described above, since direct operative death after esophagectomy is related to respiratory complications, treatments for this complications may be able to be improved, if the cause is made clear and pathological treatments are carried out. In order to improve surgical treatments for metastasis to the lymph node of esophageal cancer, these points should be given attention to.

KEY WORDS

Esophageal Cancer, Pulmonary Complication, Autopsy Findings, Operative Direct Death, Pulmonary Surfactant.

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INTRODUCTION

Although therapeutic result of esophageal cancer has been improved, its prognosis is still unfavourable compared with those of cancers of other visceral organs. Nowadays the number of the direct operative death cases has been decreasing by the improvement of pre- and postoperative managements and of method of operation (1). Therefore the most cases of death are caused by metastasis and/or recurrence (12). Consequently we studied on the operation for cancer of the intrathoracic esophagus on the basis of the findings in autopsy.

MATERIALS

By comparison of the findings in the operation and those in autopsy, 9 of the cases of death within 30 days after esophagectomy and dissection of lymph node for thoracic esophageal cancer were examined on remained metastatic lymph node, influence of lymph node dissection, and the complications. According to the "Guide line for clinical and pathologic studies on carcinoma of the esophagus" (4), location of the lesion, depth of invasion, degree of lymph node metastasis, and stage, resectability, curability, were examined.

The findings on histological diagnosis were reported in this paper.

RESULTS

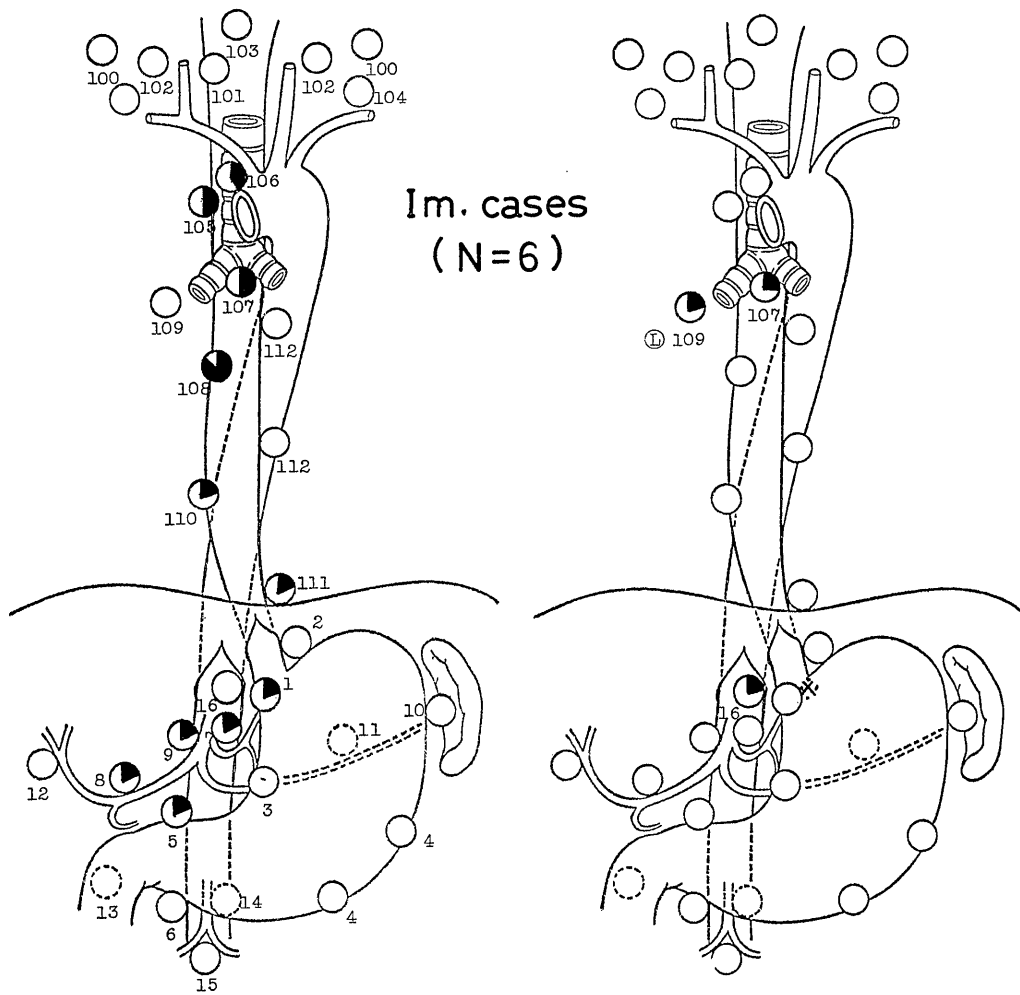
Table 1 shows sex, age, location of the lesion, radiologic, endoscopic findings, operative methods, preoperative combined treatments, histologic depth of invasion, degree of lymph node metastasis, stage, and curability in 9 study cases. Mean age among them (2 females and 7 males) was 58 years old. Their main location of the lesion were observed in Im (6 cases) and Ei (3 cases). No main lesion was observed in Iu and Ea. In spite of relatively small number of material, rates of sex, age, and regions of lesion in them were similar to those in general cases of esophageal cancer. Therefore they are seen to be regarded as standard index of the cases of esophageal cancer. In radiologic findings, the numbers of funneled type group, serrated type group, and spiral type group were 4, 3, and 2, respectively. Average length of the abnormal shadow among them was 6 cm. Therefore the number of cases of advanced cancer was in large portion in material. Transthoracic esophagectomy was performed in all cases. In 6 of them, reconstruction of the esophagus was performed in one staged operation, while it was done 2 staged operation which consist of esophagectomy and esophageal reconstruction in 3 cases, of which 2 cases died before the operation for the reconstruction. Gastric tube in major curvature and ileocolon were employed as esophageal substitute in 6 cases and 1 case respectively. The substitutive esophagus were reconstructed through antesternal route, retrosternal route, and intrathoracic route in 1, 4, and 2 cases, respectively. In other words, substitutive esophagus is, as a rule of our department of surgery, reconstruct by gastric

Table 1 Direct operative death

No.	Sex	Age	Radiologic findings			Endoscopic findings Type	Operative method	Preoperative combined treatment	D.	ly.	a	n	m	stage	c
			Location of the lesion	Type	Vertical extension										
1	M	70	Ei	Spiral	6cm	Depressed	T.T.E.R. Esophageal reconstruction by gastric roll, retrosternal route	4000R B L M 65mg	P	(-)	a1	n2	0	III	III
2	F	58	Im	Serrated	8	Depressed	T.T.E.R. //	3000R	W	(-)	a2	n1	0	III	III
3	M	49	Ei	Funnelled	7	Depressed	T.T.E.R. //		M	(+)	a3	n2	0	IV	II
4	M	44	Im	Serrated	5	Depressed	T.T.E.R. //		M	(+)	a2	n2	0	III	III
5	F	63	Im	Funnelled	2.5	Stenotic	T.T.E.R. Abdominal L, N, dissection feeding jejunostomy		W	(-)	a2	n2	0	III	III
6	M	63	Im	Funnelled	7	Stenotic	T.T.E.R. Esophageal reconstruction by ileocolon, intra-thoracic	3000R	M	(-)	a3	n3	0	IV	I
7	M	58	Im	Funnelled	8.5	Depressed	T.T.E.R. Feeding jejunostomy	5000R	M	(-)	a2	n3	0	IV	I
8	M	65	Ei	Serrated	5	Depressed	T.T.E.R. Esophageal reconstruction by jejunum interposition, intrathoracic		W	(+)	a2	n4	0	IV	I
9	M	52	Im	Spiral	7.5	Depressed	T.T.E.R. Esophageal reconstruction by gastric roll, retrosternal route		P	(+)	a3	n4	ml	IV	0

Leg. T.T.E.R. : Transthoracic esophageal resection
D : Degree of differentiation
P : Poor, M : Moderately, W : Well
ly : lymphatic and/or blood vessel invasion
B.L.M. : Bleomycin

and/or the other organs. In case No. 5, dissection of the abdominal lymph node was performed with formation of feeding jejunostomy. While in case No. 7 only feeding jejunostomy was done, and in autopsy, lymph node metastasis of cancer was found in No. 1, 2, 3, and 7 lymph node. In autopsy, metastatic visceral organs were observed in the liver, left adrenal glands, and lung. On the other hand, remained metastatic lymph node observed in 5 cases in autopsy. In its classification by main location of lesion, metastatic cancer in first and second lymph node group, such as No. 108, 106, and 107 was observed in many of 6 cases in Im. Ascending metastasis was observed in relatively large number cases, while descending metastasis to to abdomen was also observed in many cases. In



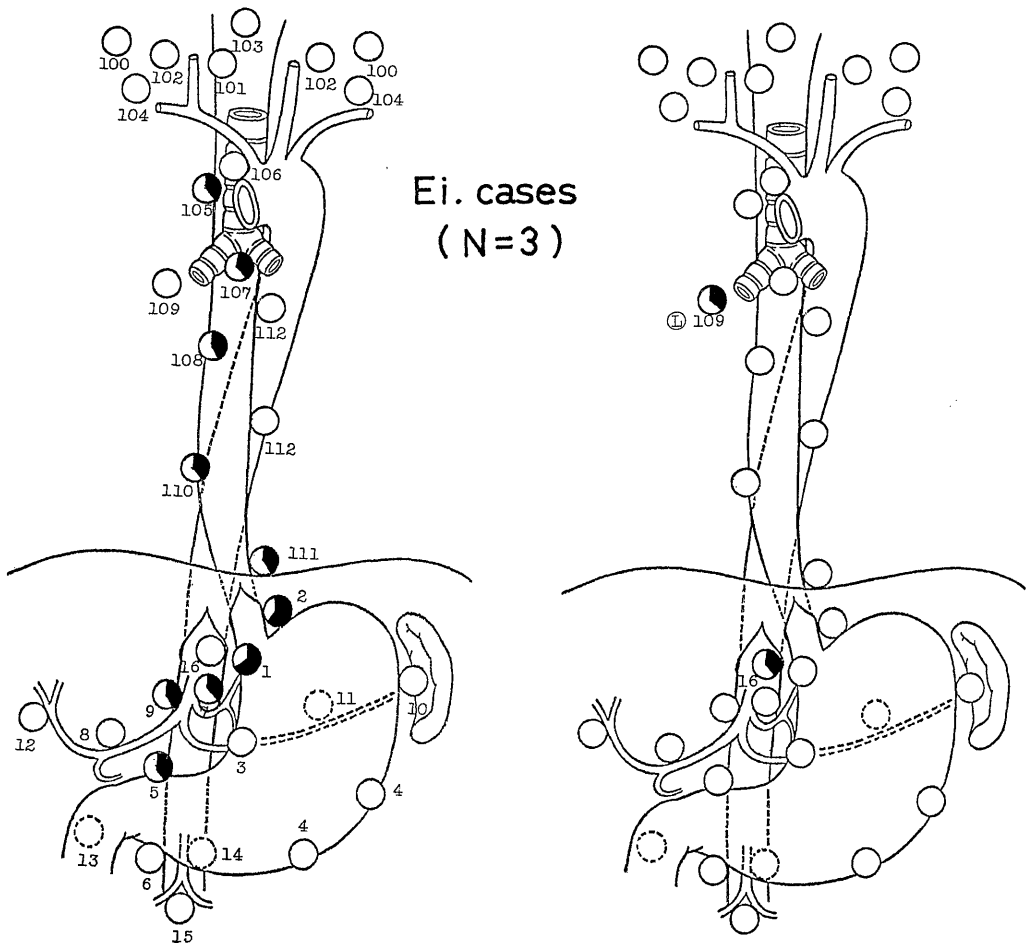
Metastatic rate in lymph node dissected during operation.

Metastatic rate in lymph node documented at autopsy. Black portion of encircled shows metastatic rate.

※(Case 7 are excluded due to no dissection performed at laparotomy.)

Fig. 1

autopsy, the remained metastatic lymph node was observed in No. 107 and left 109, i, e, tracheobronchial lymphatic group, and No. 16. (Fig. 1) (Case No. 7 without dissection of the abdominal lymph node was excluded from the materials.) Metastasis to No. 110 (+), first lymph node group, was observed in 1 of 3 cases in Ei, that to No. 1 and 2 (+) in 2 of them, and that to No. 5, No.9 (+), fourth lymph node group, in 1 of them. In autopsy, remained metastatic lymph node in No. 16 and left No. 109 were observed in one each of the cases in Ei. (Fig. 2) In the later case, 4000 Rad. Co. irradiation (by opposite double beams under 4×11 cm of irradiation field) and 65 mg of Bleomycin were used as preoperative combined treatment and at the time of the operation the mediastinal lymph node dissection showed negative in histological examination of metastasis. Only No. 2 lymph node of second abdominal lymph node group showed positive.



Metastatic rate in lymph node dissected during operation.

Metastatic rate in lymph node documented at autopsy.

Black portion of encircled shows metastatic rate.

Fig. 2

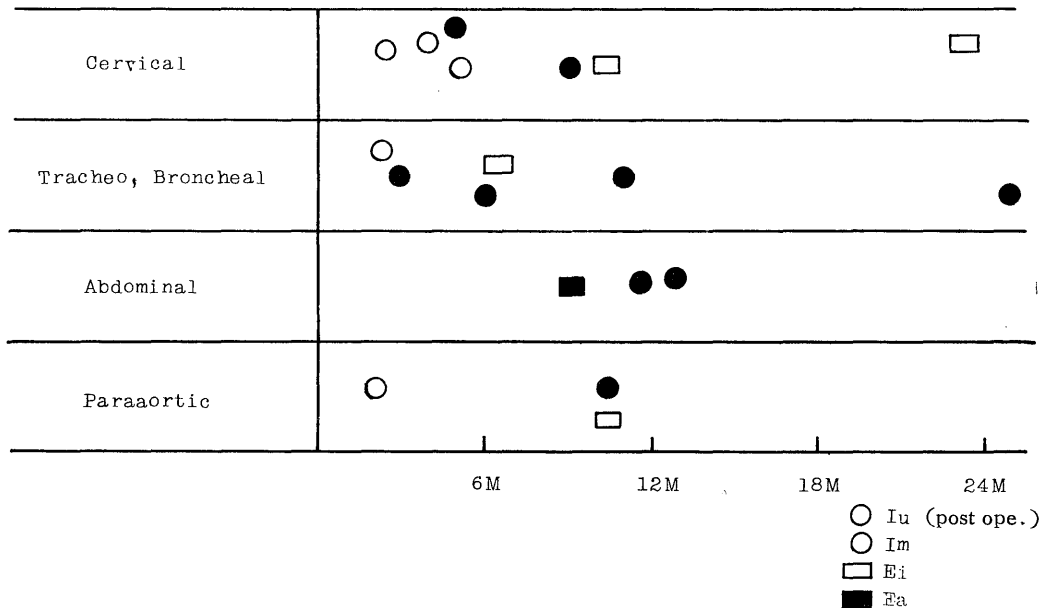


Fig. 3 Recurrent location of lymph node in 35 endured cases
(Clinical or autopsic confirmed)

In autopsy, however, lymph node at left hilum of the lung showed positive in the examination of metastasis. In brief, dissection of No. 4-13 lymph node which belong to fourth lymph node group may be performed. However, that No. 16 lymph node can not actually done and that of left No. 109 lymph node in the third lymph node group in Im, Ei, cases could not be performed completely in thoracotomy at right side. This region seems to be out of limit where dissection of lymph node can be done completely. Fig. 3 shows the recurrent location of lymph node in endures survivors after the operation. The rate of recurrence of cancer in cervical node was high, compared with that in material at the time of autopsy. This result suggests that dissection of cervical node is necessary. If dissection is not

Table 3 Cause of direct operative death

Cases No	Age	Operative death date	Causes of Death
2	58	30th	Pneumonie
3	49	7th	Pneumonie
4	44	3rd	Mediastinitis Pyohaemothorax
5	63	4th	Pyothorax Pneumonie
6	63	7th	Anastomotic leakage Sepsis
7	58	21st	Chylothorax
8	65	9th	Peritonitis Pneumonie
9	52	1st	Heart failure

performed, radiotherapy ought to be carried out. In 9 materials, all cases died of respiratory complication except that one case died of heart failure after partial resection of the liver along with the esophagectomy and one case died of chylothorax by damage of thoracic duct. (Table 3)

The Study on Causal Relation between Mediastinal
Lymph node Dissection and respiratory complication

The influence of lymph node dissection of mediastinal and hilar region on the lung was estimated from the surface activity of lung, experimentally. Fifteen dogs were classified into 3 groups ; Group I (5 dogs) which had undergone mediastinal lymph node dissection in only area of paratrachea ; Group II (5 dogs) which had undergone it in the area of paratrachea to bifurcation ; Group III (5 dogs) which had undergone it in the area of paratrachea, to bifurcation, to hilum of the lung. Surface activity of the lung was measured by modified Whilhelmy balance by use of washing extracts for bronchial tree 6 hours after lymph node dissection. γ min. in Group III rose greatly, but there was little difference in Group I and Group II as shown in Table 4. Stability index also decreased in Group III. After lyophilization of bronchial tree washing extracts, extraction of lipid was performed according to the method of Folch, phospholipids by thin layer chromatography and phosphorus contents of their subfraction were determined by the microquantitative method of NOJIMA (8). The amounts of phospholipids in Group II and III decreased slightly 6 hours after dissection, but the ratios of fractions of phospholipids in Group II and III were almost the same. The ratios of phosphatidyl choline in the group were almost the same (Table 6). Pulmonary lymph flow was examined by injection of sky-blue dye solution from the lung at the side of thoracotomy after dissection of hilum, bifurcation, paratracheal lymph node, flow of sky-blue dye solution was hindered at hilum of the lung. The stoppage of the lymphatic vessel on proximal side was found. Then, for the examination of pulmonary peripheral circulation, change of wedge pressure was measured under the constant flow perfusion by perfused pulmonary artery wedge method. Wedge pressure in Group III, which had undergone extended radical mediastinal lymph node dissection, rose remarkably, compared with those in Group I and II. In addition, when vagus nerves are stained by

Table 4 Influence of mediastinal dissection on surface activity

Extent of mediastinal dissection		Surface tension γ -min	Stability index
G-I (N=5)	Paratracheal	4~12 (9)	1.0~1.8 (1.6)
G-II (N=5)	Paratracheal~Bifurcation	5~15 (10)	0.8~1.8 (1.4)
G-III (N=5)	Paratracheal~Bifurcation~Hilum	9~24 (18)	0.5~1.4 (0.8)
Control (N=5)	Thoracotomy	4~16 (8)	12~20 (1.7)

Table 5 Influence of mediastinal dissection on phospholipid subfraction
(Lung washing extracts)

	P. C.	P.E.	Sph.	Lyso.	Unknown
G - II	68.9±4.5	16.6±2.0	10.4±3.8	2.8±0.5	1.3±0.7
G - III	65.5±4.0	13.5±2.3	15.0±3.3	3±0.8	3±0.9

(Values are means of 5 dogs ± standard deviation)

Legend : P.C.-Phosphatidyl Choline. P.E.-Phosphatidyl-Ethanolamin
Sph-Sphingomyelin, Lyso-Lysolecithin

vogostain, the vagus branchings are observed in adventitial layer of pulmonary artery trunk and in wall of the brouchus. However they were not observed in Group III. In the histological examination of the lung 6 hours after extended radical mediastinal lymph node dissection in Group III, leaking of blood-plasma was observed in alveolar space and interstitial edema and alveolar edema were observed. On the other hand, such a histological change was little observed in Group I and II.

DISCUSSION

The rate of direct operative death for esophageal cancer has decreased gradually (4). However, survival rate after esophagectomy has been still strikingly low (10–15%), compared with those after the operations for cancer of the other digestive organs on account of following reasons; a) difficulties in early diagnosis of esophageal cancer; b) anatomical peculiarity of esophageal cancer, that is, existance of the important organs around it and absence of serous membrane in the esophagus; location of thoracic and abdominal cavity c) high frequency of invasion of cancer cell upon the lymphatic vessels; d) possibility of skip metastasis by respiratory movement; f) high rate of disease in old patients; g) high rate of undernourished patients. So, many cases have died of metastasis and/or recurrence of cancer.

In 9 materials very small metastatic cancers (in the lung, liver, and adrenal glands), which could not be found before and during operation, were observed in 4 of them in autopsy. To diagnose metastasis to the lung before the operation, simple X-ray examination and tomography of the lung, bronchial arteriography, lung scintigram have been carried out as our routine pre-operative examinations. Exact diagnosis of lung metastasis was impossible even by these examinations. Since diameter of tumor which can be identified on chest x-ray is more than 0.5 cm, the size of very small metastatic cancer seems to be out of limit to be identified. When the liver shows positive in the examination of metastasis by its scintigram and selective cealiac angiogram before the operative indication for esophageal cancer is, of course, far beyond. These methods has also a limit for exact diagnosis (8). On the other hand, the examination on adrenal glands metastasis, which was observed in one in autopsy, was not included in our preoperative routine exami-

nation to determine the operative indication for esophageal cancer. In addition, the examination on bone metastasis, although such a case was not observed in materials, ought to be ordinarily carried out by general bone X-ray and Ga scintillationgram of bone. However, frequent use of preoperative examination gives not only unnecessary financial and mental distress to the patients, but also advancing time to cancer. Therefore, various preoperations examinations ought to be carried out properly, taking into consideration with clinical symptoms.

In the materials most of whom had advanced cancer in stage III or IV, both Im and Ei cases spread to the lymph node mainly horizontally and also proximal or peripheral. Especially many cases of paradoxical metastasis to the abdominal lymph node were observed (7). These results were almost the same as those reported before by us (13). But because of reconstruction of the esophagus by gastric tube at major curvatura, first, second, and third lymph node in abdominal cavity are, of course, excised. In addition, mobilization of stomach by Kocher method is performed for easy anastomosis of the gastric tube at left neck side. Consequently dissection of the lymph node in No. 1-13 is performed almost completely. Actually remained metastatic lymph node in the area were not observed in autopsy. Paraaortic lymph node causes bottleneck for dissection of the abdominal lymph node.

In regard of the metastatic lymph node in thoracic cavity, remained metastatic lymph node in the left pulmonary hilar was observed in 2 cases by autopsy. Dissection of this area seems to be difficult by ordinary thoracotomy at right side. Moreover, remained bifurcation lymph node metastasis was observed in one cases. And also, it is said that dissection at the left 0-3° thoracic paratracheal lymph node can not be performed completely. So, the lymph node in the tracheal system is difficult to dissect completely. Since extended radical lymph node dissection had been performed thoroughly to the opposite side to raise curability by dissection of the lymph node, so hoarseness by paralysis of recurrent laryngeal never was observed in some cases.

In the experiment on the influence of lymph node dissection in dogs, stoppage of the pulmonary lymphatic vessel caused by dissection in large area resulted in stagnation of pulmonary lymph, cutting of branches of nerve to the pulmonary artery trunk and bronchus, dysfunction of vasomotor, and then spasm of the pulmonary artery. Those may related to surfactant loss and hypoxemia. On the other hands, from the point of clinical view, high rate of this disease in old patients, more cases with obstructive lung disease and higher permeability of the blood vessel by hypoalbuminemia along with malnutrition, and taking long time for the operation are important factors to give rise easily to lung complications by dissection of the lymph node over large area.

To improve prognosis of esophageal cancer, primary and metastatic focuses of cancers need to be excised completely, especially radical dissection of the lymph node is needed. On the other hands, taking into consideration with complications accompanied with them, especially lung complications (2) (10), extent of dissection is important. Moreover the lymph node which is free from metastasis of cancer should be left for immunological point of view (11). However, old patients, especially those with esophageal

cancer, have antracosis in the tracheal lymph node according with aging of the lung, so differential macroscopic diagnosis of antrocosis and cancer is generally difficult (7). What is worse, metastatic cervical lymph node have been observed in many endured cases, although they were not observed in our materials. Therefore the cervical node are important region to be dissected, whether this one is caused by metastasis or recurrence after dissection. Moreover prognosis of esophageal cancer depend on degree of differentiation and invasion upon the blood and/or lymphatic vessels as other cancers. In accordance with advance in pathology (14), pre and post operative care techniques have been improved. In other words, postoperative treatment by antibiotic with wide range spectrums for pulmonary infections, intubation and respiratory care by respirator in time, suction of sputum by use of bronchoscope, oxygen therapy with blood gas analysis, nutrition care by intravenous hyperalimentation, application of membrane oxygenator support in respiratory crisis have been carried out, so temporary respiratory complications may be controled. In conclusion, it is important to dissect remained cancer completely in surgical treatment, although esophageal cancer has still a limit in curability (6). Moreover, by combination of local medicine administration in retromediastinal portion (3), X-ray irradiation, and chemotherapeutic therapy as a general treatment as reported by various researchers, the prognosis after operation for esophageal cancer may improved.

As described above, some problems on operation of esophageal cancer, especially on dissection of the lymph node were studied clinically and experimentally.

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