Review

Outcomes of Extended Lymph Node Dissection for Squamous Cell Carcinoma of the Thoracic Esophagus

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Patients with thoracic esophageal carcinoma who underwent extended lymph node (LN) dissection were studied to assess the state of LN metastasis and evaluate its outcome in terms of a prognostic benefit. Pertaining to LN metastasis, it was found that depending on the location of a primary tumor, the area of choice, in which metastasis tends to develop predominantly, showed some variation. However, irrespective of the location of the tumor, the predominant growth of positive nodes was found to locate among three fields, namely the neck, mediastinum and abdomen even in patients with a single metastatic node. This suggests that extended LN dissection including the neck, mediastinum and abdomen should be considered mandatory, if a complete removal of the tumors for carcinoma of the thoracic esophagus is to be desired. Multivariate analysis revealed importance of LN dissection as a prognostic factor. A cumulative survival rate in the patients with lymphadenectomy through right thoracotomy was statistically better than that in the patients who underwent blunt extraction of the esophagus without lymphadenectomy. Furthermore, extensiveness of LN dissection could effectively serve as a prognostic factor. Consequently, three-field LN dissection yields a prognostic benefit to improve a long term survival in patients with carcinoma of the thoracic esophagus. (Ann Thorac Cardiovasc Surg 2001; 7: 325–9)

Key words: lymph node dissection, lymph node metastasis, esophageal carcinoma, prognostic factor, survival rate

Introduction

The purpose of this paper is to clarify whether lymph node (LN) dissection effectively improves the long term survival of patients with squamous cell carcinoma of the thoracic esophagus. We will be concerned in this paper mainly with questions of 1) whether lymph node dissection improves a long term survival, 2) whether the extensiveness of lymph node dissection could be a better prognostic factor and 3) whether three-field lymphadenectomy produces a survival benefit for patients with squamous cell carcinoma of the thoracic esophagus.

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Materials and Methods

We experienced 1,821 patients with esophageal carcinoma who were admitted to Toranomon Hospital during 27 years between 1972 and 1995. Of these patients, 1,510 cases were diagnosed to have squamous cell carcinoma of the thoracic esophagus and we performed esophageal resections in 1,068 cases. Four hundred and forty three cases were selected as the group of extended LN dissection, and 284 cases as the group of limited LN dissection. The extended LN dissection group includes patients who underwent three-field LN dissection which was adopted as a standard procedure for carcinoma of the thoracic esophagus since 1984. The limited LN dissection group comprises resected cases with two-field LN dissection before 1983. Until then, two-field LN dissection was the standard procedure of lymphadenectomy for thoracic esophageal carcinoma. The blunt extraction

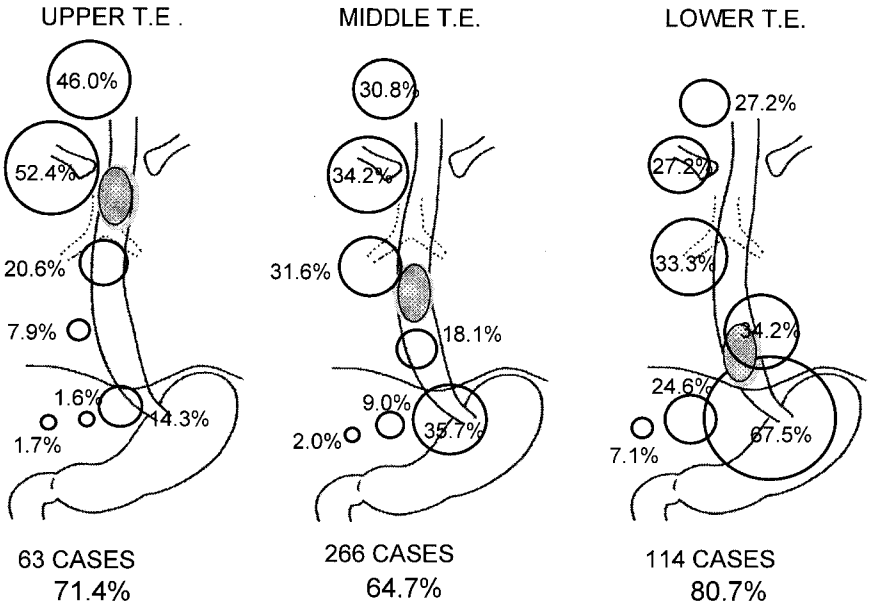

Fig. 1. State of metastastic LN according to tumor location.

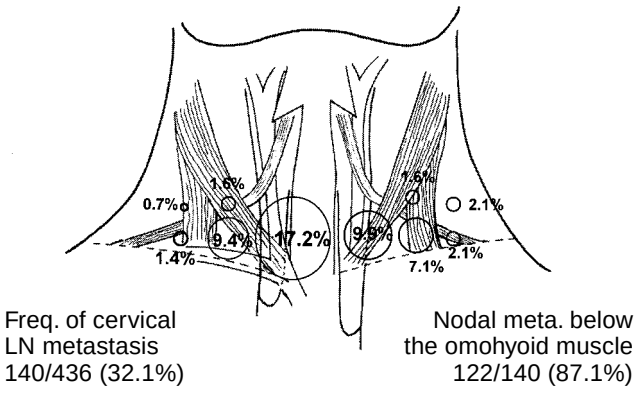

Fig. 2. State of metastastic nodes in the neck.

group contains 22 cases with a tumor of submucosal invasion who underwent blunt extraction of the esophagus without thoracotomy and systematic LN dissection.

Long term survival rates were calculated according to the Kaplan-Meier method and statistical differences were assessed using the log-rank test. The Cox proportional hazard model was used to adjust confounding prognostic variables. Statistical significances were set at the 5% level. All statistical analysis were performed on a personal computer using SPSS statistical software.

States of lymph node metastases

We analyzed frequencies and distributions of metastastatic LN according to the location of the main tumor (Fig. 1). The frequency of the positive node was calculated as the number of patients with positive nodes per number of overall patients. In the patients with carcinoma of the upper thoracic esophagus, 71.4% developed the metastatic nodes predominantly in the superior mediastinum and/or in the neck. In patients with cancer of the middle thoracic esophagus, 64.7% showed a nodal involvement which developed equally in the neck, mediastinum and abdomen. We also noted that 80.7% of patients with carcinoma of the lower thoracic esophagus developed LN metastasis mostly in the abdomen. However, cervical LN metastasis developed even in the cases with lower esophageal carcinoma.

When we investigated the extent of the positive nodes in the neck (Fig. 2), cervical LN metastasis was found to develope at a rate of 32.1% in overall cases. The most frequent site of positive nodes was located along the right recurrent laryngeal nerve at a rate of 17.2%. The metastatic cervical LN were confined below the omohyoid muscle in about 90% of the patients with positive nodes in the neck.

Figure 3 shows a state of LN metastasis in cases with only a single node metastasis. Even a single metastasis developed in wide areas from the abdomen to the neck. The state of LN metastasis in 134 five-year survivors is demonstrated in Fig. 4, which shows the incidence of positive nodes was 53.7%. More than 10% of five-year survivors had node metastasis in the neck.

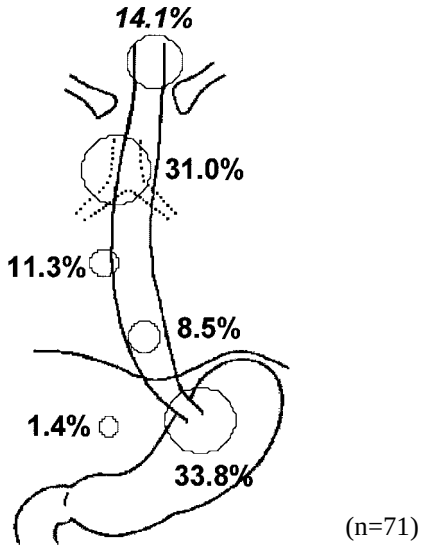

Fig. 3. State of LN metastasis in cases with a single metastatic node.

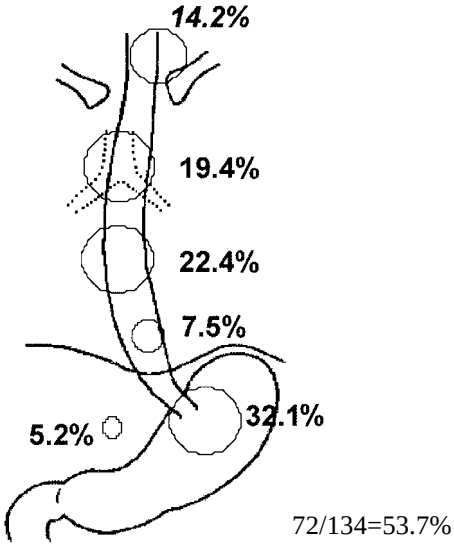

Fig. 4. State of LN metastasis in five-year survivors.

Statistical analysis of the prognosis

The prognosis of patients in the three groups was analyzed and assessed statistically to clarify the efficacy of lymph node dissection. As for the patients with carcinoma of sm invasion, the 5-year survival rate was found to be 72.0% for patients who underwent systemic LN dissection through right thoracotomy, while that for the blunt extraction group(without systematic LN dissection) was 38.1% (Fig. 5). The difference was statistically significant ($p<0.01$) on the log-rank test. In order to adjust different background factors between these two groups, multivariate analysis was used to investigate the effect of LN dissection on long term survival. LN dissection, together with gender, age, tumor location and cell differentiation were entered into the Cox regression Model, and as a result, LN dissection was selected as a prognostic factor with less than 5% of significance level (Table 1). Risk ratio was 0.4724.

Survival curves were compared between the extended LN dissection group and the limited LN dissection group to determine whether the extent of LN dissection can serve effectively as a prognostic factor. The 5-year sur-

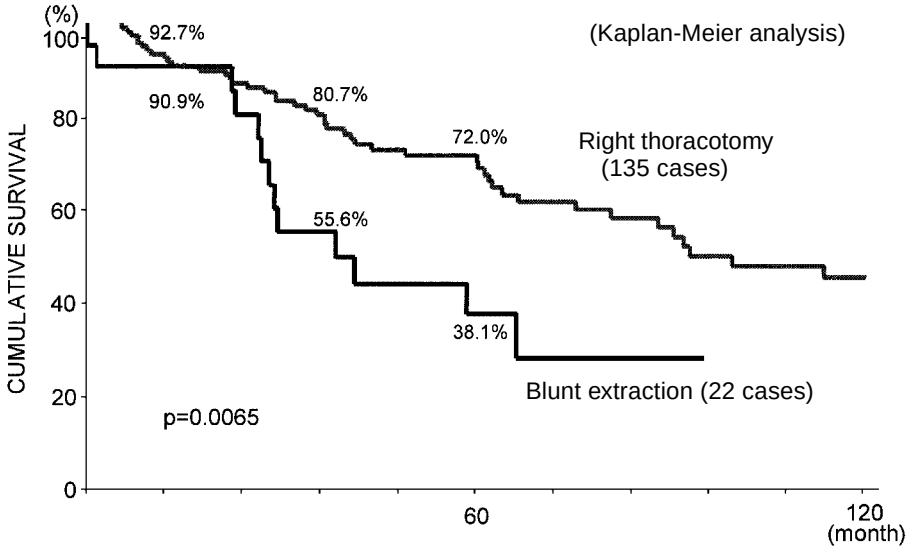

Fig. 5. Cumulative survival of the patients with sm invasion according to the approaches.

Table 1. Multivariate analysis: Cox regression analysis

Covariates	Significance	Risk ratio
Gender	0.6791	0.930
Age	0.0502	
40 : 50	0.5524	0.6853
40 : 60	0.4233	1.6297
40 : 70	0.5903	1.4151
Tumor location	0.1915	
low : mid	0.0779	
low : upp	0.6791	
LN dissection	**0.0269**	**0.4724**
Cell diff.	0.2536	

vival rate for the extended LN dissection group was 50.5%, whereas the limited LN dissection group showed 37.0% (Fig. 6). Thus, the extended LN dissection group was found to yield a rate statistically better than the limited LN dissection group ($p<0.001$). The effect of extensive lymph node dissection upon long term survival was also examined using Cox regression analysis. Ten factors such as age, the number of metastatic nodes, gender, tumor location, cellular differentiation, curability, the extent of lymph node dissection, pT category, pN category, pM category were entered into the model as covariates. Consequently, the extent of LN dissection was selected as one of the prognostic factors together with pM category and pT category whose risk ratio was 0.5501 (Table 2).

Discussion

Three-field lymph node dissection is now widely adopted as a standard procedure for carcinoma of the thoracic esophagus.[1)] However, it is still encountering criticism suspicious of its efficacy on survival benefit.[2)] In order to investigate outcomes of extensive LN dissection, we analyzed the extent and frequency of LN metastasis and long term survivals. Pertaining to LN metastasis, it was found that depending on the location of the primary tumor, the area of choice, in which metastasis tends to develop predominantly, showed some variation. On the other hand, however, irrespective of the location of the tumor, the predominant growth of positive nodes was found to locate almost equally among three fields, namely the neck, mediastinum and abdomen. Recently, the LN which is the first site of nodal metastasis is called a sentinel node and is reported possible to be detected by means of a sentinel node navigation system.[3)] When we consider the distribution of a single LN metastasis, a sentinel node of thoracic esophageal cancer might be located widely in the neck, mediastinum and abdomen. A metastatic lymph node in the neck had been thought to be distant metastasis and evidence of uncurability. However, I would like to emphasize that some of the patients with cervical node metastasis could be cured by its dissection. Extended LN dissection including the neck, mediastinum and abdomen should be considered mandatory, if complete removal of tumors of carcinoma of the thoracic esophagus is desired.

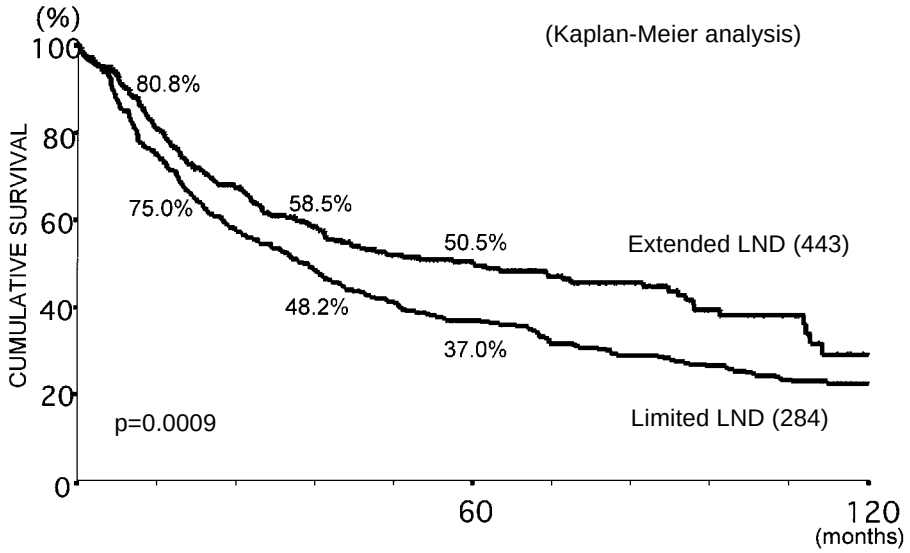

Fig. 6. Cumulative survival for extended and limited LN dissection.

Table 2. Prognostic factors by Cox regression analysis

Covariates	Significance	Risk ratio
Age	< 0.0001	1.0308
No. of positive nodes	< 0.0001	1.0539
Cellular difference	0.0056	
MQ : PQ	0.0051	1.4999
MQ : WQ	0.1615	0.7935
Gender	< 0.0001	2.3296
Curability	0.0466	
C1 : C2	0.9444	0.9795
C1 : C3	0.0175	0.7265
TNM pM	0.0008	
pM0 : pM1 (hep)	0.0089	14.7106
pM0 : pM1 (lym)	0.0042	1.5600
TNM pT	< 0.0001	
pT1 : pT2	0.0004	1.9575
pT1 : pT3	< 0.0001	2.3917
pT1 : pT4	< 0.0001	3.1654
pT1 : pTis	0.7062	0.7969
Extent of LND.	**< 0.0001**	**0.5501**

Analysis on long term survival rates provides evidence that extensive LN dissection yields better survival rates compared to limited node dissection.[4)] Multivariate analysis concerning efficacy of LN dissection revealed that the estimated risk of dying, after adjusting for other factors in the model, is 0.4724 times less in the group who underwent right thoracotomy which comprises systematic LN dissection than in the blunt extraction group without systematic lymphadenectomy. Furthermore, the extensiveness of LN dissection was selected as one of the independent prognostic factors with a risk ratio of 0.5501. This means that systematic LN dissection contributes to improve the long term survival of squamous cell carcinoma of the thoracic esophagus.

Conclusion

1) A cumulative survival rate in the patient group with LN dissection through a right thoracotomy was statistically better than in the blunt extraction group without LN dissection and thoracotomy.
2) An analysis using the Cox regression model showed extensiveness of the LN dissection can effectively serve as a prognostic factor.
3) Three-field LN dissection is essential for improvement of the long term survival in patients with squamous cell carcinoma of the thoracic esophagus.

References

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