J. Korean Soc Ther Radiol Oncol 1999;17(1):108 112

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Significance of Supraclavicular Lymph Node Involvement on Determination of Clinical Staging for Thoracic Esophageal Carcinoma

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Background and Purpose : Involvement of supraclavicular lymph nodes (SCL) is considered distant metastasis for thoracic esophageal carcinoma in AJCC staging system revised in 1997. We investigated significance of SCL involvement compared to other regional lymph node involvement.

Materials and Methods : Two-hundred eighty-nine patients with unresectable esophageal carcinoma were treated with radiation therapy from June of 1979 through December 1992. Of these patients, 25 were identified having SCL involvement. Survival rate and relapse patterns were compared with that of mediastinal and perigastric lymph node positive patients to evaluate prognostic significance of SCL involvement.

Results : Median survival for patients with SCL involvement was 7 months and 2- and 5-year overall survival rates were 12.0% and 4.0% respectably. Corresponding features for regional node positive patients were 9 month, 17.0% and 3.8%. There was no significant difference between two groups. There was also no difference in patterns of recurrence.

Conclusion : Results of this analysis showed that SCL involvement should be staged as nodal disease in contrast to present classification of metastatic disease.

Key Words : Esophageal neoplasm, Lymph node metastasis

INTRODUCTION

Carcinoma of the esophagus accounts 1.5% of all cancers in Korea.[1] Its incidence is continuously increasing and it presents one of the greatest challenges in the field of cancer. Accurate staging is important to assess the effectiveness of the treatment, and to advise individual patients of prognosis.

Incidence of supraclavicular lymph node (SCL) involvement is higher than 15% in patients with thoracic esophageal carcinoma.[2] SCL is considered distant metastasis for the thoracic esophagus according to current American Joint Committee on Cancer (AJCC) staging system.[3] Some investigators, however, advocated that the cervical lymph nodes should be included in the category of regional nodes in cases of thoracic esophageal cancer on the basis of the patterns of early lymph node metastases and the prognostic significance of a lymphadenectomy for metastases to these nodes.[4]

We investigated the outcome of treatment and patterns of recurrence among the patients with SCL involvement and the patients with other regional lymph nodes involvement. The purposes of this study were to reveal the prevalence of SCL involvement and to evaluate prognostic significance of SCL involvement.

MATERIALS AND METHODS

From June of 1979 through December 1992, 289 patients with unresectable esophageal carcinoma were treated with radiation therapy alone at Department of Therapeutic Radiology, Seoul National University Hospital. Detail of characteristics and outcome of these patients were published

Submitted March 29, 1999 accepted June 8, 1999
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elsewhere.[5] Of these patients, 25 (8.7%) had SCL involvement and 53 had other regional lymph node involvement. And these 78 patients were the subjects of this study.

The age of these patients ranged from 40 to 77 years (median, 60 years). There were 76 male and 2 female patients. Characteristics of the patients in each group are shown in Table 1.

After thorough history taking and physical examination, all patients with suspected esophageal cancer had a workup including esophagogram, esophagoscopy with biopsy, CT scan of chest and upper abdomen, chest roentgenogram, biochemical profile, complete blood count with differential, electrolytes, BUN, and creatinine. Computed tomography image was used to evaluate regional lymph node status.

Table 1. Comparison of Characteristics of the Patients with Supraclavicular Lymph Node Involvement and That of the Patients with Other Regional Lymph Node Involvement

Characteristic	Number (%)	
	SCL involvement	Regional node involvement
Age		
≤60	13 (52)	33 (62)
>60	12 (48)	20 (38)
Sex		
female	0	2 (4)
Male	25 (100)	51 (96)
Functional status		
ECOG 1	17 (68)	29 (54)
2	7 (28)	21 (40)
3	1 (4)	3 (6)
Histology		
squamous cell	22 (88)	48 (90)
adenocarcinoma	3 (12)	5 (10)
Location		
upper	5 (20)	8 (15)
middle	19 (76)	37 (70)
lower	1 (4)	8 (15)
Size*		
≤5cm	11 (44)	32 (60)
5 10cm	13 (52)	20 (38)
> 10cm	1 (4)	1 (2)
T-stage		
1	0	1 (2)
2	4 (16)	21 (40)
3	15 (60)	22 (42)
4	6 (24)	9 (16)
Aim of treatment		
curative	3 (12)	30 (56)
palliative	22 (88)	23 (44)

* : Longest tumor length on CT image

According to AJCC staging system, there were 21 patients with stage IIB, 32 patients with stage III, and 25 patients with stage IV. Based on TNM classification, there were 1 case of T1, 25 cases of T2, 37 cases of T3, and 15 cases of T4 tumors. All patients were pathologically confirmed, and there were 70 cases of squamous cell carcinoma and 8 cases of adenocarcinoma. Size and location of the disease is shown in Table 1. There was no statistical difference between two groups.

Under the hypothesis that SCL is regional lymph node, we restaged the patients with SCL involvement. As a result, there were 4 patients with stage IIB and 21 patients with stage III. Then comparison of survival data was done for newly staged group with originally staged group.

Although 57% of the patients were treated with palliative aim, all patients were aggressively treated. There was no clear criterion to decide curative or palliative aim, but major reason was involvement of SCL involvement.

Radiation therapy was done using high energy (6 or 10 MV) linear accelerator. Barium contrast medium was used for localizing the tumor within the esophagus during simulation and individually shaped cerrobend blocks were used for sparing the normal tissues included in radiation portal. Radiation portal included primary lesion with upper- and lower-margin of 5 cm, paraesophageal lymph nodes, and mediastinal lymph nodes. Anterior and posterior parallel opposing fields were used initially. And then computerized tomography for computer planning was taken, and a combination of anterior and oblique fields was used to spare the spinal cord. Radiation dose to spinal cord did not exceed 4500 cGy in any case. The daily dose was 180 to 200 cGy given 5 days a week, while the total dose ranged 5000 to 6660 cGy with a median of 5940 cGy 5000 to 5500 cGy, 14 patients; 5500 to 6000 cGy, 46 patients; 6000 to 6500 cGy, 18 patients. There was no difference in the distribution of radiation dose between regional lymph node involvement group and SCL involvement group.

None of the patients in this study received chemotherapy as initial treatment. Follow-up period of living patients ranged 77 to 180 months. Survival duration was measured from start of treatment to the date of death. Survival curves were calculated using the Kaplan- Meier method in the SAS procedure life test. Comparison between each group was made using log-rank test.

RESULTS

Survival data and prognostic factor analysis for 289 patients, which was treated radiation therapy alone, was presented elsewhere.[5]

Median survival, 2-year, 5-year and 10-year overall survival rate for the patients with SCL or regional lymph node involvement was 8 months, 15.1% , 4.7% and 2.3% (Fig. 1). Survival data for each group is shown in Table 2. There was no statistically significant difference between two groups.

There were 71 recurrences, 23 for SCL involvement and 48 for regional node involvement. Relapses at primary site were major component of recurrences (Table 3). There was also no statistically significant difference in patterns of relapse between two groups. Frequent metastatic sites were lung, liver and bone.

Fig. 2 shows survival curve of newly staged SCL involvement group and regional lymph node involvement group. There is no statistically significant difference stage by stage.

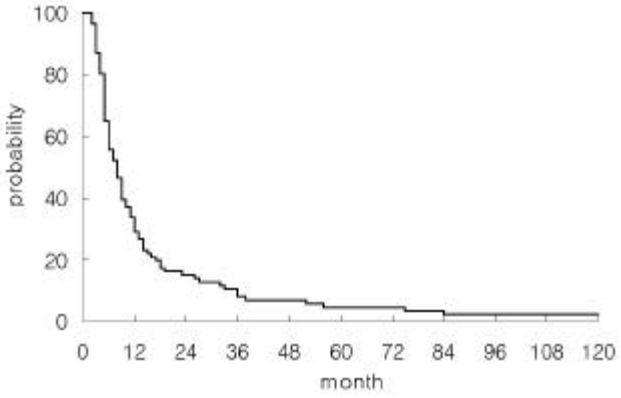

Fig. 1. Overall survival curve for the patients with supraclavicular lymph nodes and regional lymph nodes involvement.

Table 2. Survival from Radiation Therapy Alone by Lymph Node Involvement

No. of years	% Survival	
	SCL involvement	Regional node involvement
1 year	20.0	35.9
2 year	12.0	17.0
5 year	4.0	3.8
10 year	0	1.9
Median survival	7 months	9 months

p = n.s. (not significant)

DISCUSSION

The latest edition of the AJCC Cancer Staging Manual was published in 1997.[3] But there was not much changes in the case of esophageal cancer in contrast to changes

Table 3. Patterns of Relapse

Relapse pattern	SCL involvement (%)	Regional node involvement (%)
LR	11 (48)	34 (71)
DM	5 (22)	5 (10)
LR+DM	7 (30)	9 (19)
Total	23 (100)	48 (100)

LR : locoregional recurrence, DM : distant metastasis

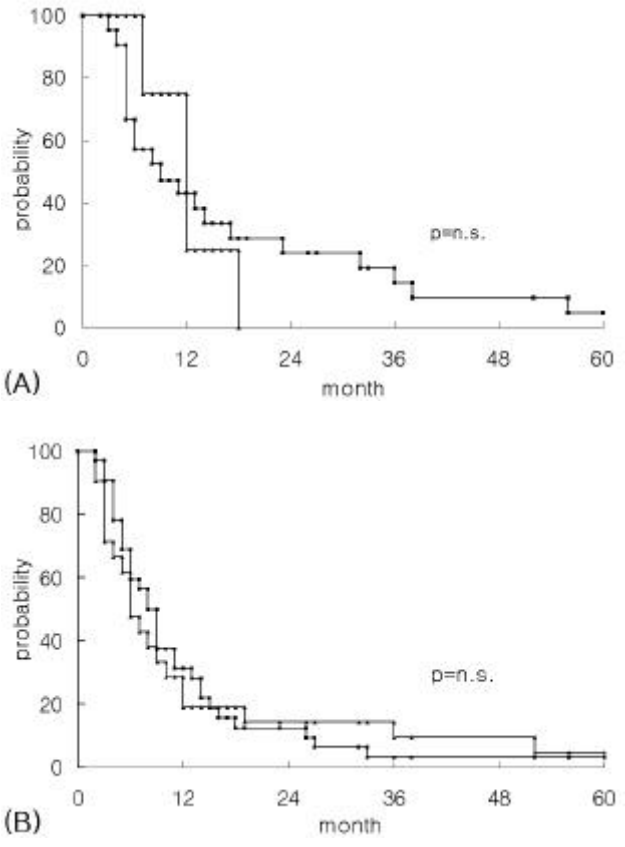

Fig. 2. Comparison of overall survival for re-staged patients with supraclavicular lymph node involvement and patients with regional lymph node involvement.
(A) Stage IIB (square, n=21) vs. re-staged IIB (triangle, n=25).
(B) Stage III (square, n=32) vs. re-staged III (triangle, n=53).

occurred between 1983 and 1988.[6] The current system is based on depth of wall penetration and lymph node involvement.

Involvement of SCL is considered distant metastasis for intrathoracic lesions. This implies a poor prognosis with positive SCL. In the large Japanese cohort data, the location of involved lymph nodes correlated with survival. The Japanese Committee reported retrospective data that the patients with paraesophageal, mediastinal, and perigastric metastases had similar long-term survivals, whereas patients with other involved abdominal nodes and further distant nodes, such as supraclavicular and cervical lymph nodes, had a much worse prognosis.[7]

However, controversy exists about whether this system is practical for most patients, and whether it properly stratifies groups by prognosis. The presence of involved regional lymph node is correlated with a less favorable prognosis than when the lymph nodes are negative. Some Japanese investigators examined all part of surgical specimens and all of the dissected lymph nodes, and analyzed survival rate by current staging system. Cervical node groups were anatomically as closely located to the thoracic esophagus as the abdominal node groups, and they were frequently involved by metastases from the primary tumors, occasionally in a jumping fashion in the early stage of the lymphatic spread. And there were no survival differences in patients with positive cervical nodes as compared with patients with positive mediastinal or abdominal lymph nodes. They finally suggested that the cervical node group should be considered as a part of the regional nodes of the thoracic esophagus.[4] Although all patients were clinically staged, our data support this suggestion. Kato et al. also reached the same conclusion based on their data that cervical nodes were frequently involved with metastases from thoracic esophageal cancer and the 5-year survival rate for patients with positive cervical nodes was 30.0%.[8]

Another controversy on lymph node staging is the significance of the number of positive regional lymph nodes. Abe et al. found that no patients with two or more regional nodal metastases lived for 4 years after surgery, whereas the 5-year survival for patients with no or only one metastatic node was 50.9%.[9] Siewart also reported the significance of the number of involved lymph.[10] There was no survivor greater than 25 months for the patients with five or more lymph nodes involved compared with 35% 5-year survival for patients with fewer than five lymph nodes involved.

Most of previously reported studies about controversies on lymph node staging consisted of patients treated with extensive radical surgery. Study population of our study was patients with unresectable esophageal carcinoma. Although different study population, the result reached same conclusion. SCL involvement should be considered as a part of regional lymph node involvement for patients with thoracic esophageal cancer.

ACKNOWLEDGEMENTS

Supported by grant no. 96-182 from the Seoul National University Hospital Research Fund

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J. Korean Soc Ther Radiol Oncol 1999;17(2):108 112

국문 초록

흉부 식도암의 병기 결정에 있어서 쇄골상 림프절 전이의 의미

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목 적 : 1997년에 개정된 AJCC 병기분류법에 의하면 흉부식도암의 쇄골상림프절전이는 원격전이로 분류된다. 연구자들은 다른 국소림프절전이와 쇄골상림프절전이의 임상적 양상의 차이에 대하여 연구하였다.

대상 및 방법 : 1979년 6월부터 1992년 12월 사이에 임상적으로 절제가 불가능한 식도암 환자 289명이 방사선치료를 받았다. 이 중 25명의 환자에서 쇄골상림프절전이가 관찰되었다. 쇄골상림프절의 임상적 중요성을 평가하기 위하여, 국소림프절전이 환자와 생존율 및 재발양상에 대한 결과를 비교 분석하였다.

결 과 : 쇄골상림프절전이 환자의 생존중앙치는 7개월이었으며 2년 및 5년 생존율은 각각 12.0% 및 4.0% 였다. 국소림프절전이 환자에서는 9개월, 17.0% 및 3.8% 였다. 두 군 사이에 통계적 유의성은 관찰할 수 없었다. 또한 재발양상에 있어서도 두 군 사이에 차이가 없었다.

결 론 : 본 연구의 결과 흉부식도에서 발생한 식도암에서 쇄골상림프절로의 전이는 현재의 분류인 원격전이이기 보다는 국소림프절전이로 분류되어야 할 것이며, 향후 이에 대한 다기관공동연구가 필요할 것이다.

핵심용어 : 식도암, 림프절 전이