

## The Role of Radiotherapy in Esophageal Cancer†

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A retrospective analysis was undertaken of 46 patients who were referred with squamous cell carcinoma of the esophagus during the period of March 1979 through October 1982, and who were treated by curative radiotherapy in the Department of Therapeutic Radiology Seoul National University Hospital.

The overall two-year actuarial survival rate was 20%. Survival was analyzed with respect to the site of the cancer, its size, radiation dose, and degree of response. Patients with the best two-year survival rate are the ones who had the tumor no of more than 5cm in length (39.3%) or confined to the upper third of the esophagus (29.5%). An optimum radiation dose ranged from 1600 to 1700 rets. Patients to complete response had 42.4% of two-year actuarial survival, but those to no response had 0% of survival.

Key Words: Esophageal cancer, Radiotherapy, 2 year actuarial survival rate.

### INTRODUCTION

The carcinoma of the esophagus presents challenges in the field of cancer. Because the malignant tumors in this thin anatomic tube tend to invade the surrounding vital structures and metastasize in early stage. The overall results of treatment are not also encouraging. We have carefully examined the treatments given to patients with the carcinoma of the esophagus and identified several factors that are of importance in the prognosis of patients. This study is based on the 46 patients with the carcinoma of the esophagus who received radiotherapy with curative intent during the period of March 1979 through October 1982 in the Department of Therapeutic Radiology, Seoul National University Hospital.

### METHODS AND MATERIALS

During the four year period of March 1979 through October 1982, 56 patients with squamous

cell carcinoma of the esophagus were treated in the Department of Therapeutic Radiology, SNUH. Among these patients 10 were excluded because. 2 patients had operation prior to radiotherapy, and 4 had incomplete radiotherapy. Therefore, 46 patients were available for this study (table 1).

Of these, 43 patients were male and 3 patients were female. The oldest patient in this series was 78 years old and the youngest 40 years (table 2). Diagnostic work-ups were CBC, urinalysis, liver scan and bone scan. Computed tomography and bronchoscopy were optional (table 3). The patients were staged according to the TNM staging (table 4): 7 patients had stage 1 (15%), 26 stage 2 (57%) and 13 stage 3 (28%). The majority of cases were of advanced stage (table 5). Tumor sites were classified as upper, middle or lower region by esophagography.

11 patients had the lesion in the upper part of esophagus, 25 patients in the middle, 10 patients in the lower lesion (table 6). Treatment was administered primarily with supervoltage equipment

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(Co-60, 10MV x-ray) using doses ranging from 5000 to 6000 rad in 5 to 6 weeks, delivered at 200 rad per fraction in most cases. We designed the treatment portals with a 5cm margin beyond the gross tumor based on the esophagogram and endoscopic extent. The mediastinum was included with 1 to 2cm margin. Most portals were 6 to 8cm wide. To avoid undesirable high doses to the spinal cord and heart we used combination of anterior and posterior opposed field, and a three field approach with an anterior field and right and left posterior oblique fields were used (Fig. 1).

Then 46 patients were divided into 3 groups on the basis of NSD (table 7). Over one-half of patients fall in the NSD range of 1600-1700 ret. Remission was decided by subjective symptoms and esophagogram one month after treatments. Complete remission was defined as the complete relief of

Table 1. Esophageal cancer: Treated with Radiotherapy (1979-1982)

	No. of Patients	Follow-up Period (months)
Followed	37	1-50 (8)
Lost	9	1-14 (4)
Total	46	1-50 (6)

\* Number in parenthesis is median period.

Table 2. Esophageal cancer: Distribution by age and sex

Age	No. of Patients	
	Male	Female
40 - 49	3	2
50 - 59	16	1
60 - 69	20	0
70 +	4	0
Total	43	3

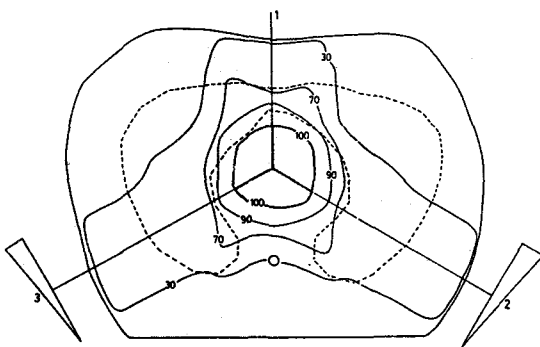


Fig. 1. Treatment plan for cancer of esophagus.

dysphagia with no evidence of obstruction by esophagogram. Partial remission was defined as partially relieved dysphagia with or without evidence of obstruction by esophagogram. No response was defined as convincing dysphagia with the evidence of obstruction by esophagogram. Survival rate was calculated from the first day of treatment to the time of death.

## RESULTS

More than 70% showed response: complete remission (22%), partial remission (56%), and no response (22%) (Fig. 2). The median survival was 7.5 months. Two year actuarial survival rates by the

Table 3. Esophageal cancer: Diagnostic Work up

History and physical exam.
Laboratory tests : CBC, LFT
Radiological study : Chest PA, Esophagography
Endoscopy and biopsy
Radioisotope scan of liver, bone
* Computed tomography
* Bronchoscopy

\*Optional

Table 4. TNM Classification and Staging

Category	Stage	Extent of lesion
T <sub>1</sub>	I	Primary lesion - 5cm long with circumference incompletely involved
T <sub>2</sub>	II	Primary lesion 5cm long or circumference completely involved
T <sub>3</sub>	III	Primary lesion any size with direct extra-esophageal spread
N <sub>0</sub>	I	Nodes not palpable with cervical primary or intrathoracic nodes biopsy negative with thoracic primary
N <sub>1</sub>	II	Ipsilateral nodes positive
N <sub>2</sub>	II	Contralateral nodes positive
N <sub>3</sub>	III	Nodes positive and fixed
N <sub>x</sub>	I	Intra-thoracic nodes not assessed with thoracic primary
M <sub>0</sub>	I	No evidence of distant metastases
M <sub>1</sub>	III	Distant metastases present

size of the tumor in its largest dimension indicated that while tumors larger than 5cm showed poor survival rates (0% with 5 to 10cm and 7.3% with over 10cm), those patients with lesions up to 5cm showed a two-year survival rate of 39.3% (Fig. 3). Two year survival rates by stage were 65.3% in stage I, 3.9% in stage II, and 26.3% in stage III (Fig. 4). The evaluation of the two-year survival rate by the location of the tumor indicated that the lesion in the lower third showed worst prognosis (9.1%), while the lesion in the upper and middle third showed survival rates of 29.5% and 21.1% respectively (Fig. 5). The relationship between the radiation dose and the survival rate was significant (Fig. 6). The patients who received higher dose did not show any addi-

tional benefit. The optimum dose range was 1600 to 1700 rats. Two-year actuarial survival rate by the degree of response indicated that complete responders had 42.4% of survival, partial responders had 16.9% of survival, erite no responders had 0% of survival (Fig. 7).

## DISCUSSION

Since the initial report of the technique of radium bouginage by Jean Giusez in 1909, there have been major technical advances in radiation therapy that have contributed to improved survival for patients with malignancies.<sup>1)</sup> Despite this, the cure of a patient with esophageal cancer remains poor. Five year survival rate for most populations generally is around 5% with surgery or radiotherapy alone and only slightly higher when a combination of the two are used in the management of local disease.<sup>2-5)</sup>

Table 5. Esophageal Cancer: Distribution by Stage

Stage	No. of Patients (%)
I	7 ( 15)
II	26 ( 57)
III	13 ( 28)
Total	46 (100)

Table 6. Esophageal Cancer: Distribution by Site


	Upper	11	( 24%)
	Middle	25	( 54%)
	Lower	10	( 22%)
	Total	46	(100%)

Table 7. Esophageal cancer: RT Dose by NSD

Rad	NSD (ret)	No. of Pts. (%)
4500 rad/4-5wk	1600 ↓	7 (15)
5000 rad/5wk	1600-1700	28 (61)
6000 rad/6wk	1700 ↑	11 (24)

Table 8. Esophageal Cancer: Response Rate

Response	No. of Patients (%)
Response	36 ( 78)
CR	10 ( 22)
PR	26 ( 56)
No Response	10 ( 22)
Total	46 (100)

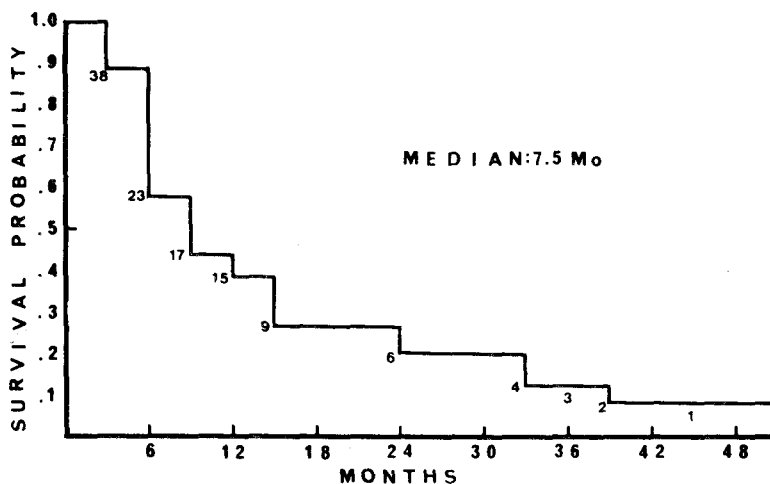


Fig. 2. Esophageal cancer: Actuarial overall survival

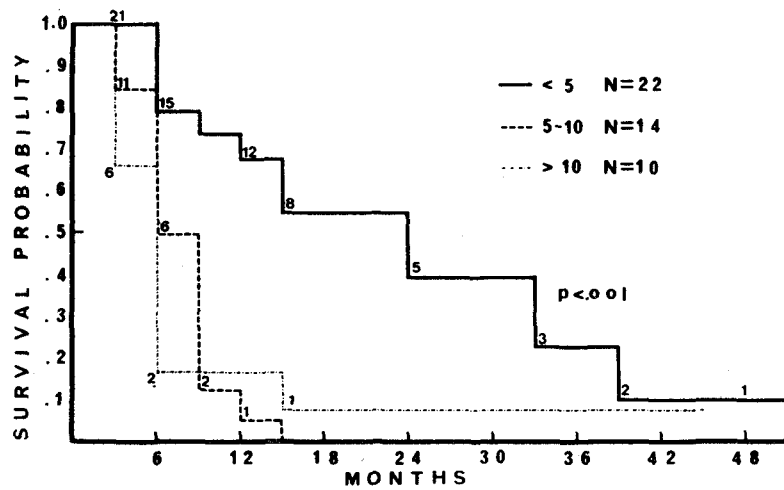


Fig. 3. Esophageal cancer: Actuarial survival by size

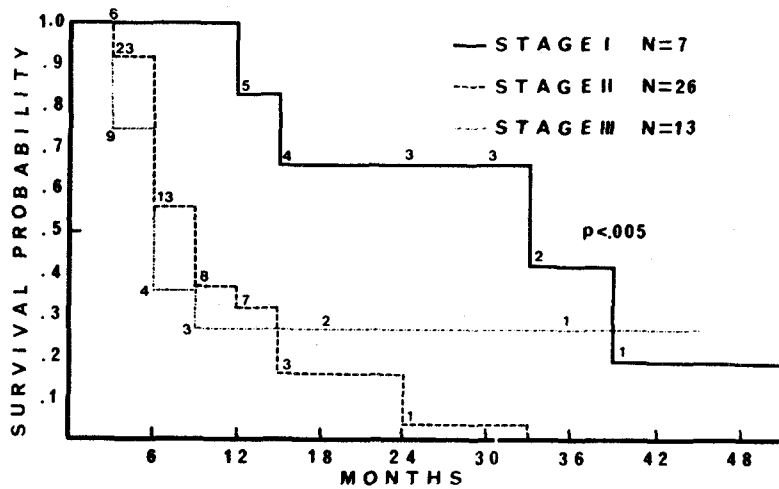


Fig. 4. Esophageal cancer: Actuarial survival by stage

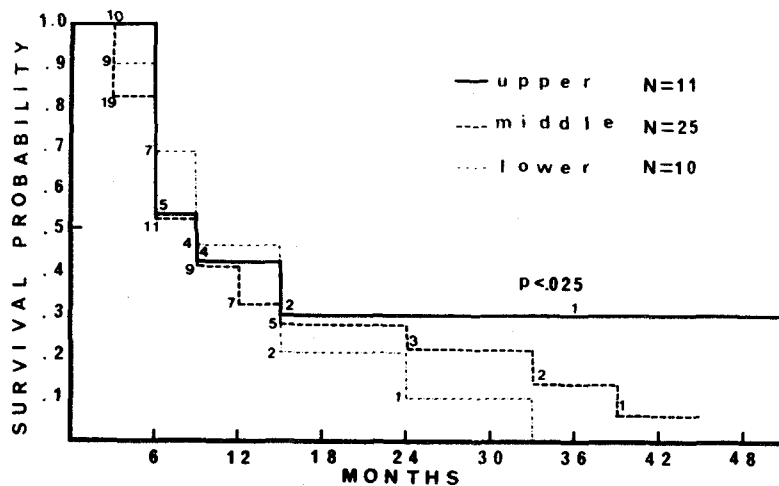


Fig. 5. Esophageal cancer: Actuarial survival by site

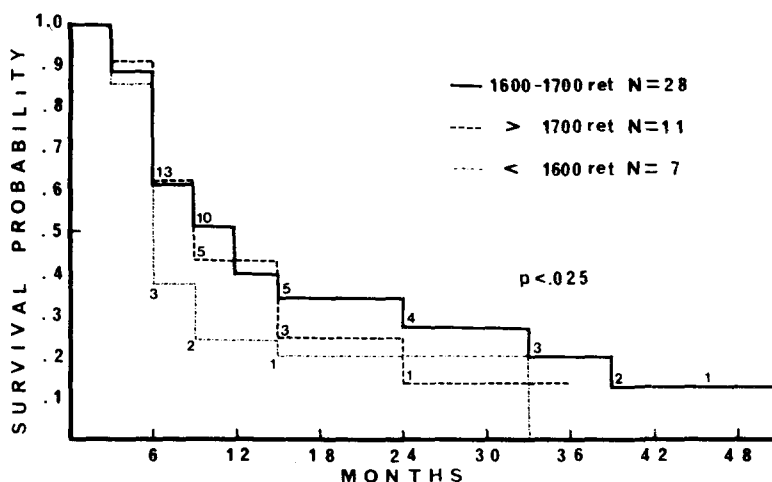


Fig. 6. Esophageal cancer: Actuarial survival by RT dose

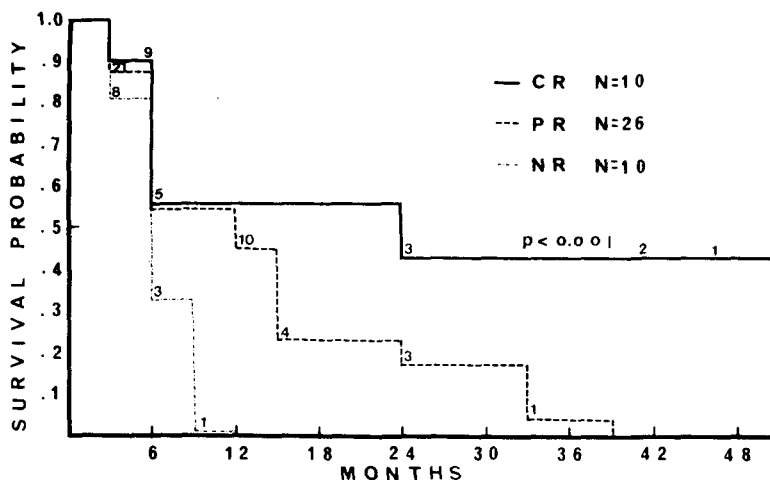


Fig. 7. Esophageal cancer: Actuarial survival by response

The selection of the patients strongly influences the results of any individual series: Nakayama et al. (37.5%) and Pearson (20%).<sup>6)</sup> This study showed 20% of two-year actuarial survival rate. The curability of the esophageal cancers is impaired by the special anatomic features of the organ since there is no fibrous serosa acting as a barrier to the spread of tumor beyond the confines of the esophageal wall. Rich lymphatic networks in the submucosa and muscularis facilitate the spread of tumor circumferentially, transmurally, and longitudinally. Distant spread of tumor within the esophagus itself is relatively common. Surgery and radiotherapy can cure only localized esophageal cancer, although there are differences in the extent of tumor which can be encompassed by either method.<sup>6)</sup>

The most important pretreatment factors in identifying patients who would respond to the treatment

were the size of the primary lesion and the degree of obstruction. Newaishy et al.<sup>7)</sup> reported the five-year survival rate of 12.6% for lesions up to 5cm in length. In our study the two-year actuarial survival rate was 39.3% for lesions up to 5cm in length. 78% of patients had relief of dysphagia in our study. Improvement of dysphagia with radiation therapy has been reported as 60-79%.<sup>8)</sup>

Relief of symptoms was closely associated with the survival rate: patients with complete response had 42.4% while partial response had 16.9% of two-year actuarial survival rate. The first radiation parameter examined was radiation dose. The optimum dose range reported was 1600-1700 ret. The patients who received the higher dose did not show any additional benefit. Preoperative irradiation did not improve the survival rate, although there were substantial local tumor responses.<sup>9,15)</sup> Postoperative

irradiation also did not improve survival for patients with lymph node involvement but did improve local control.<sup>16,19)</sup>

The major late complication which occurred after radical radiotherapy were fibrous stricture formation, the development of fistulae and massive hemorrhage from the erosion of large intrathoracic blood vessels.<sup>20)</sup> In our study two cases of tracheoesophageal fistula formation during the course of radiation treatment occurred.

## CONCLUSION

The retrospective analysis was carried out with of 46 patients who were referred with squamous cell carcinoma of the esophagus during the period of March 1979 through October 1982. They treated with curative radiotherapy in the Department of Therapeutic Radiology, Seoul National University Hospital.

The results were as follows:

1. 78% (36 cases) of the patients showed the relief of symptoms, and 22% (10 cases) showed no response. The relationship between the degree of response and the survival rate was significant. ( $p < 0.01$ )
2. Two-year survival rates of stage, 1, 2 and 3 disease was 65.3%, 3.9% and 26.3% respectively. ( $p < 0.01$ )
3. Two-year survival rates by the location of tumor were 29.5% for the upper third, 21.1% for the middle third, and 9.1% for the lower third lesion. ( $p < 0.05$ )
4. The size of primary lesion had a significant effect on the survival rate: 39.3% for the lesion up to 5cm in length, 0% for the lesions between 5cm and 10cm, and 7.3% for those over 10cm in length. ( $p < 0.05$ )
5. The relationship between the radiation dose and the survival rate was significant. The optimal dose range was 1600-1700 ret ( $p < 0.05$ )

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**=국문초록=**

**식도암에 있어서 방사선치료의 역할**

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1979년 3월부터 1982년 10월까지 식도의 편평상피암으로 진단되어 서울대학교병원 치료방사선과에서根治적 목적으로 방사선치료를 받았던 46례에 대한 후향성 분석을 시행하여 다음과 같은 결과를 얻었다.

전체 환자의 2년 생존율은 20%이었으며 식도암의 위치, 크기, 병기, 방사선조사량 그리고, 관해정도에 따라 생존율에 차이가 있었다.

식도 촬영상 5 cm 이하(39.3%) 또는 식도의 상부 1/3에 종양이 있는 경우(29.5%)에 가장 좋은 2년 생존율을 보였으며 최적방사선 조사량은 1,600~1,700 ret였다. 관해정도에 따른 생존율은 완전관해를 보인 경우의 2년 생존율이 42.2%인 반면 전혀 반응이 없던 경우의 2년 생존율은 0%이었다.