

The Radiotherapy Result of Esophageal Cancer

Woong Ki Chung, M.D., Sung Ja Ahn, M.D. and Byung Sik Nah, M.D.

Department of Therapeutic Radiology, Chonnam University Hospital, Kwangju, Korea

Ninety patients of esophageal cancer treated with radiation since November 1985 to June 1990 at the Department of Therapeutic Radiology, Chonnam University Hospital, were analysed retrospectively regarding survival.

Seventy five patients (94.9%) revealed squamous cell carcinoma in its histologic type, and most of patients were in advanced stage with 25 patients (27.8%) of T2 and 64 patients (71.1%) of T3.

Minimum follow up period was 12 months and median was 5 months. Overall actuarial 2 year survival rate was 11.6%. Two year survival rates according to the parameters such as treatment aim, T stage, site, length, radiation dose and response were compared and resulted that survival by tumor length only had statistically significant impact on survival of esophageal carcinoma.

Key Words: Esophageal carcinoma, Radiotherapy, Survival

INTRODUCTION

Esophageal cancer is one of the disabling illness with poor prognosis. Five year survival is less than or around 10% with radiation therapy^{1,2)}. The best result of 20% reported by Pearson et al³⁾ was not duplicated by others. The dismal failure of conventional treatment modalities (esophagectomy and radiation) to control disease has been a challenge for clinical investigations who continually look for new innovative approach⁴⁾.

We studied retrospectively 90 cases of esophageal cancer treated with radiation at the Department of Therapeutic Radiology, Chonnam University Hospital from November 1985 through June 1990 to evaluate the survival by several factors. We tried to find appropriate indicators to anticipate better survival with radiation therapy in esophageal carcinoma.

MATERIALS AND METHODS

During the 3 years and 8 months period since November 1985 to June 1990 one hundred and seventeen patients of esophageal cancer visited the Department of Therapeutic Radiology, Chonnam University Hospital for radiation therapy. Of these 13 patients who had not have planned treatment completely and 7 patients treated as adjuvant after radical esophagectomy were excluded from this analysis. Six patients who refused radiotherapy and one patient of local recurrence after operation

with distant metastases were also excluded. Ninety patients of esophageal cancer were the basis of this retrospective analysis (Table 1).

Of the ninety patients included in this analysis eighty six were male and four were female. The age ranged from 45 years to 79 years and median was 59 years. Of seventy nine histologically proven patients 75 cases (94.9%) was the squamous cell type. TNM clinical staging system was applied in these patients⁵⁾. The length of tumor involvement on esophagogram was evaluated and local extension was determined by computed tomography of chest. Of 78 patients treated with radical aim one patient had T1, 23 patients (29.5%) had T2 and 54 patients (69.2%) had T3. Twelve patients of palliative aim comprised of 2 patients of T2 and 10

Table 1. Patient Classification by Treatment Modality*

Modality	No. of Patient
Radiotherapy	90
Radical	78
Palliative	12
Radical esophagectomy + Radiotherapy	7
Incomplete treatment	13
Postoperative recurrence	1
No treatment	6
Total	117

* Patients seen in Department of Therapeutic Radiology since November 1985 to June 1990.

patients of T3.

In this study 14 patients had upper thoracic lesions and 52 patients developed in mid-thoracic region. Twenty one patients had lower thoracic lesions. Three patients had cervical lesions. The length of involvement on esophagogram of patients treated radically revealed less than 5 cm in 13 patients, 5~10 cm in 56 patients and more than 10 cm in 8 patients (Table 2).

All patients were treated with linear accelerator producing 6 MV X-ray (Mevatron, Siemens Co.). Total dose delivered to primary tumors with radical aim ranged between 3960 cGy and 7200 cGy with daily 180 or 200 cGy. The patients treated with palliative aim received 1500 to 5280 cGy with variable daily dose of 150~300 cGy. Most of patients were resimulated at 4000 cGy level to change the beam direction for sparing spinal cord. Most patients treated with radical aim received more than 5000 cGy to primary site (about 1500 ret) (Table 3). Treatment volumes included the primary tumor with minimum 5 cm margin proximally and distally, and adjacent mediastinum was covered. In case of lower thoracic esophagus celiac lymph node area was covered to radiation port.

Table 2. Patient Characteristics

Characteristics	No. of patients (%)
Sex	
Male	86 (95.6)
Female	4 (4.4)
Age	
Range	45 - 79
Median	59
Histology*	
Squamous cell	75 (94.9)
Adenocarcinoma	3 (3.8)
Undifferentiated	1 (1.3)
Stage	
T1	1 (1.1)
T2	25 (27.8)
T3	64 (71.1)
Site	
Cervical	3 (3.3)
Upper thoracic	14 (15.6)
Mid-thoracic	52 (57.8)
Lower thoracic	21 (23.3)

* Information was not available in 11 patients.

The radiation response was determined by esophagogram performed after treatment. A complete remission was defined as near 100% regression of disease as seen on esophagogram. Partial remission was defined reduction of tumor but less than 100% resolution of disease as seen by esophagogram.

Sixty one patients were followed by mail, 22 patients by examination at hospital, and 7 patients by contact with relatives. Minimum follow up period was 12 months. Median follow up period was 5 months (range:1-44 months). 23 patients (25.6%) were lost to follow up (Table 4). Survival rate was calculated by Kaplan Meier method and significance between two groups was estimated with logrank test.

RESULTS

Of 58 patients evaluated regarding radiation response by esophagogram, thirty four patients (59%) showed complete remission and 21 patients (36%) showed partial remission. Two patients showed no response to radiation. One patient showed progression of disease during irradiation.

Table 3. Radiation Dose in Esophageal Cancer

Dose	No. of patients	
	Radical	Palliative
Rad		
< 5000	11	10
5000 - 6000	18	2
> 6000	49	-
Ret		
< 1500	11	6
1500 - 1700	18	3
> 1700	49	3

Table 4. Follow up of Patients

	No. of patients
Followed	67
Lost	23
period (months)	
< 2	6
2 - 4	6
4 - 6	5

Esophagogram was not performed in 32 patients and response could not be evaluated (Table 5). Overall actuarial survival rate was 11.6% at 2 years

Table 5. Radiation Response of Esophageal Cancer

Response	No. of Patients (%)			
	T1	T2	T3	Total
Complete remission	1	10	23	34 (58.6)
Partial remission	—	14	17	21 (36.2)
No response	—	—	2	2 (3.4)
Progression of disease	—	1	—	1 (1.7)

* Esophagogram was not available after completion of radiation therapy in 32 patients.

and median survival was 5.6 months (Fig. 1). Two year survival rate by radical and palliative aim was 12.3% and 10% respectively, but this difference was not significant statistically ($p > 0.05$) (Fig. 2). Two year survival rate of patients treated with radical aim by T stage had 14.9% with T2 and 11.0% with T3, and difference between two groups was not significant statistically ($p > 0.05$) (Fig. 3).

Survival rate by tumor site were 10.0%, 6.4% and 0% in upper, middle and lower thoracic esophagus respectively, and this difference was not significant statistically ($p > 0.05$) (Fig. 4). Two year survival rate according to the involved length revealed 25.4%, 14.0% and 0% in less than 5 cm, 5~10 cm and more than 10 cm respectively and this difference was statistically significant ($p < 0.05$) (Fig. 5). Survival by radiation dose group less than 1500 ret, 1500~1700

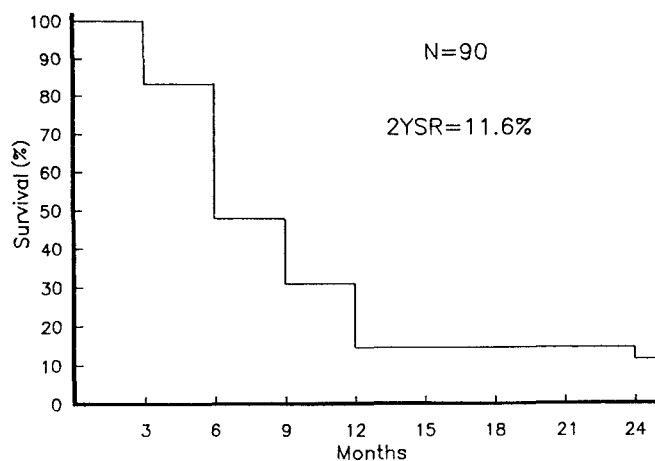


Fig. 1. Overall actuarial survival of esophageal cancer.

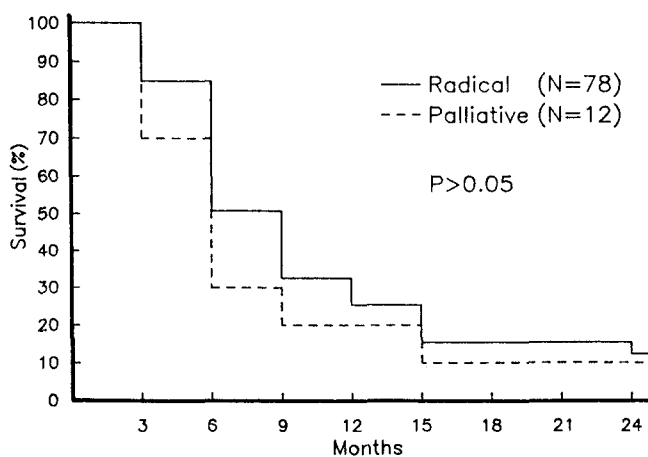


Fig. 2. Actuarial survival of esophageal cancer by treatment aim.

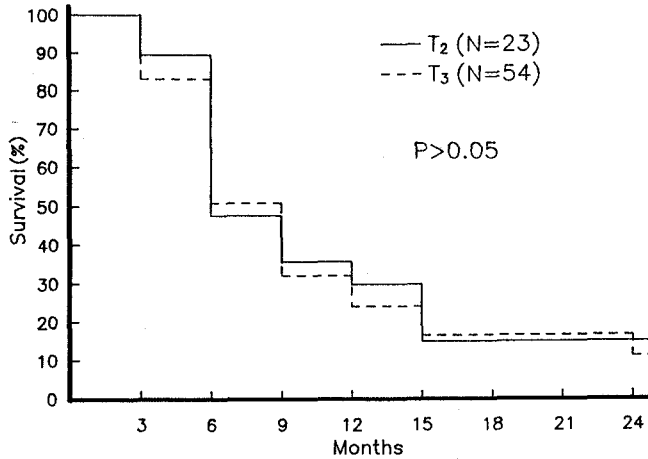


Fig. 3. Actuarial survival of esophageal cancer by T-stage.

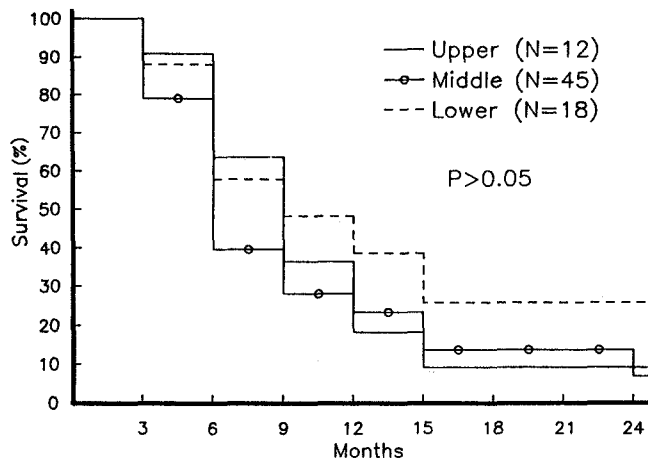


Fig. 4. Actuarial survival of esophageal cancer by site.

ret and more than 1700 ret had no significant difference (12.7%, 26.3% vs. 12.3%, $p > 0.05$) (Fig. 6). The patients with complete remission of tumor on esophagogram showed 10.8% of survival at two years and those with partial response showed 6.3% and this difference was not significant statistically ($p > 0.05$) (Fig. 7).

DISCUSSION

It is well known that esophageal cancer extends easily into the locoregional tissue because of its characteristic anatomical structure. Most patients have locally advanced disease when first diagnosed and poor performance status. There is no

fibrous serosa acting as a barrier to the spread of tumor beyond the confines of 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 is relatively common^{6,7}.

Despite modern technical advance in radiation therapy, the prognosis of esophageal cancer is still poor, and so five year survival figures for most population generally lower than around 10% with surgery or radiation therapy and only slightly higher when a combination of the two are used in the management of local disease^{1,2}. While most would agree that early esophageal cancer is best treated by

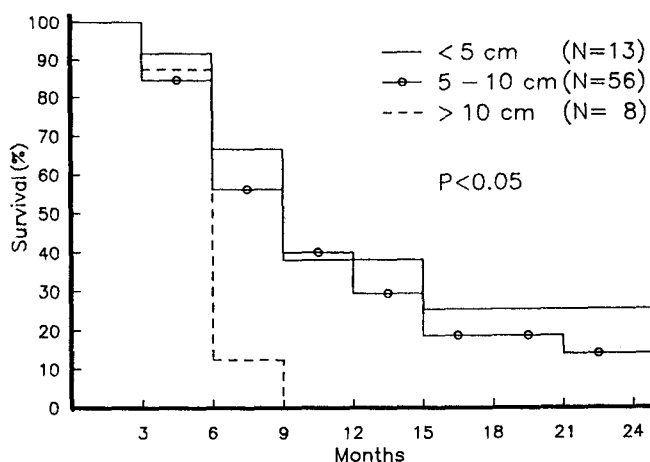


Fig. 5. Actuarial survival of esophageal cancer by length.

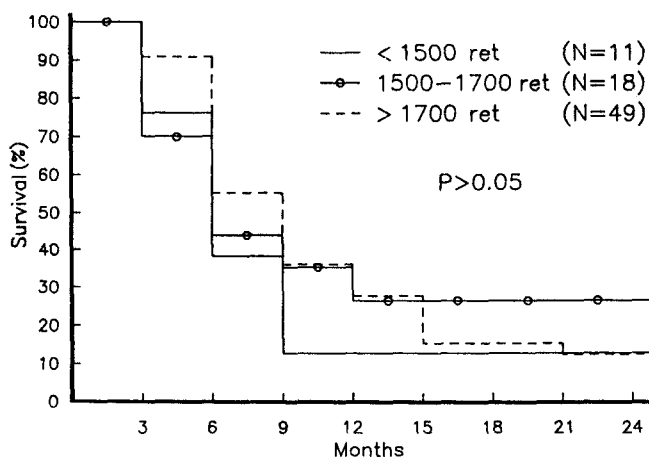


Fig. 6. Actuarial survival of esophageal cancer by dose.

surgical resection, there is no consensus on the best management for esophageal cancer that is regarded as inoperable because of its extent or the patient's fitness⁸).

Pearson reported overall 5 year survival rate of 17% for a group of 288 patients treated definitely with radiation and overall 5 year survival of 11% for a group of 432 patients treated with radical surgery⁹). The Royal Marsden experience¹⁰) showed 11% 3 year and 7% five year survival among 263 patients irradiated between 1933 and 1963 for esophageal disease. In the Princess Margaret Hospital Beatty et al¹¹) reported that none of the 176 patients treated with radical aim including radiation and surgical resection survived 5 years and suggested poor survival of esophageal carcinoma.

The modestly encouraging 20% 5 year survival reported by Pearson³) in 1969 has not been duplicated by other investigators. The authors analysed 90 patients of esophageal cancers treated by irradiation since November 1985 to June 1990 and overall 2 year survival rate revealed 11.6% and this was similar to the Royal Marsden experience in 1966. Our results was relatively lower than other reports^{2,3,9}) and this was thought to be the result of that most of patients treated were in advanced stage of T2 (27.8%) and T3 (71.1%). Radiation therapy series are generally comprised of patients with more advanced disease who are referred because of inoperability¹).

The most important pretreatment factors in identifying patients who responded treatment were

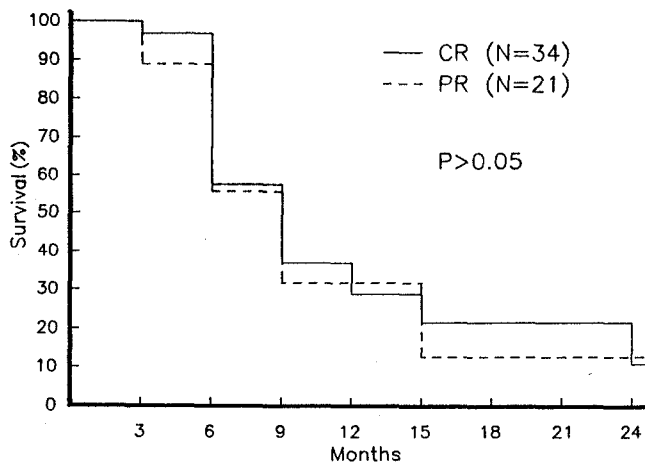


Fig. 7. Actuarial survival of esophageal cancer by response.

the size of the primary lesion and the degree of obstruction¹¹. By Beatty et al's report¹¹ patients with primary lesion less than 5 cm in length responded to treatment in 100% of cases and the incidence of response decreased to 29% survival for lesions over 10 cm in length. The authors analysed survival rate by involved length.

As a result the patients who had developed local tumor infiltration less than 5 cm in length on esophagogram showed 25.4% and those with 5 to 10 cm had 14% of survival at the end of 2 years and the patients more than 10 cm revealed 12.5% of survival at 6 month ($p < 0.05$). This result suggested the impact of tumor size on survival.

10% to 33% of reported esophageal cancer arise in the cervical region, and traditionally the majority of these lesion have been managed with irradiation^{12,13}. Pearson¹⁴ reported 29% 5 year survival (5 of 17) in patients presenting with post-cricoid region tumors treated with orthovoltage irradiation and 25% 5 year actuarial survival in 43 patients treated with megavoltage irradiation.

In this study only 3 patients of cervical esophagus lesion were seen. According to the Beatty et al's report¹¹ only 22% of cervical primary esophagus lesion responded to irradiation compared with 66% response in the thorax and abdomen, and no difference was observed between upper, middle and lower thoracic or abdominal esophagus lesion¹¹. This study showed 10%, 6.4%, 0% in upper, mid and lower thoracic esophageal carcinoma and best results in upper esophageal lesion, but had no statistical significance.

Treatment volume, total tumor dose and

fractionation are major determinants of response and cure in radiation therapy and are issues that remain unsettled in the management of patients with esophageal cancer¹¹. Foci of tumor involvement have been documented 4~8 cm beyond the margins of primary tumor despite microscopically uninvolved intervening regions of esophagus¹⁴. Many authors report the use of limited volume as advocated by Pearson in which the primary esophageal lesion is irradiated with approximately 5 cm of margin⁹.

The patients included in this study were treated with limited volume in 82 cases covering the primary tumor with 5 cm margin and adjacent mediastinal structure. 8 patients were treated with large field including the both supraclavicular lymph nodes. Most of patients tolerated well to radiation. At the Princess Margaret Hospital¹¹ both large and small field areas were compared to survival and both showed an optimum area of about 120 cm², but neither of these findings was statistically significant. Because of the wide variation in radiation dosage, only patients receiving 5000 rads in 5 weeks were considered and it was then noted that the large field correlated well with survival. An optimum size of 100~140 cm² was identified.

Normally one would expect to see an increasing survival with increasing dosage as more tumor cells were killed and eventual decrease in survival as the incidence of fatal complication increased. Rider and Mendosa¹⁵ in 1969 reported the incidence of pulmonary fibrosis as high as 80% radiologically, while the dosage of radiation used was 5000~7000 rads. Beatty et al¹¹ reported the

incidence of pulmonary fibrosis as high as 7% radiologically and the radiation dosage was 4000~6000 rads.

They noted that the optimum range of radiation was 4000~6000 rads in which the survival was maximized and the complication rate was minimized and no correlation between total dose and survival. We usually planned total dose 6000~6500 cGy in case of curative aim with 180 cGy daily over 7 to 8 weeks and around 3000 cGy with 150~300 cGy daily in case of palliative aim. During irradiation no serious radiation complication was observed except one patient developed massive esophageal hemorrhage after 2160 cGy irradiation and died of. Survival by radiation dose groups who received less than 1500 ret, 1500~1700 ret and more than 1700 ret had no significant difference in this analysis.

Most investigators consider radical therapy to be any dose regimen equivalent to or exceeding the administration of 5000~6000 rad to the tumor in standard, 180 or 200 rad fraction, over 5~6 wks period¹¹.

Among 78 patients treated radically 58 patients performed esophagography after radiation. Of these 34 patients revealed complete remission and 21 patients showed partial remission. Two year survival of patients showing complete remission was slightly higher than partial remission group.

Curability of esophageal cancer is limited because of its special anatomical features, and so various treatment modality was studied. Combined modality therapy of esophageal cancer involving preoperative radiation has been employed by a number of investigators. Some preoperative irradiation series^{16,17} have improved substantial local tumor resection rate, but overall result is poor as seen in 5 year survival rate less than 20%. Launois et al¹⁸) noted that preoperative irradiation did not improve survival over esophagectomy alone in randomized prospective trial.

Postoperative radiotherapy improved local control, but did not improve survival for patients with lymph node involvement^{19,20}. Kelson et al²⁰) compared one hundred ten patients treated at the Memorial Sloan-Kettering Center with combined modality technique involving preoperative radiotherapy and surgery, and with preoperative chemotherapy with surgery and radiation. They concluded that resection rate seems to be higher (54% vs. 76%), neither preoperative radiation nor chemotherapy (with cisplatin and bleomycin) have had a major impact on long term survival.

The authors think that local irradiation of esophageal cancer will not suffice to improve the long term survival of patients, and effective chemotherapy in combination with surgery or radiation, or both is more promising approach to the treatment of esophageal carcinoma.

CONCLUSION

Ninety cases of esophageal cancer treated with radiation at the Department of Therapeutic Radiology, Chonnam University Hospital, since November 1985 to June 1990 were analysed retrospectively. The results are as follows:

1) Of ninety patients treated with radiation 75 patients (83.4%) revealed squamous cell carcinoma in its histologic type.

2) Most of patients were in advanced stage with 25 patients (27.8%) of T2 and 64 patients (71.1%) of T3.

3) Among 58 patients who have had esophagography after completion of radiotherapy complete and partial remission was observed in 34 patients (58.6%) and 21 patients (36.2%) respectively.

4) Overall 2 year survival rate was 11.6%.

5) Two year survival of radically treated patients (12.3%) was higher than palliative group (10%) ($p > 0.05$). The patients of T2 stage revealed better survival than those of T3 stage (14.9% vs 11.0%, $P > 0.05$). The upper thoracic lesion revealed best result in comparison with mid and lower thoracic lesion (10%, vs. 6.4% vs. 0%, $P > 0.05$). Survival rate according to tumor length revealed 25.4%, 14.0% and 0% in less than 5 cm, 5~10 cm and more than 10 cm respectively ($P < 0.05$).

Survival by radiation dose had no significant difference between groups received less than 1500 ret, 1500~1700 ret and more than 1700 ret (12.7% vs. 26.3% vs. 12.3%, $p > 0.05$). The patients with complete response showed better survival than partial response (10.8% vs 6.8%, $p > 0.05$).

REFERENCES

1. Hancock SL, Glastein E: Radiation therapy of esophageal cancer. *Semin Oncol* 11:144-158, 1984
2. Earlam R, Cunha-Melo JR: Esophageal squamous cell carcinoma: II, A critical review of radiotherapy. *Br J Surg* 67:457-461, 1980
3. Pearson JH: The value of radiotherapy in the management of esophageal cancer. *Am J Roentgenol* 105:500-513, 1969
4. Flores AD, Nelems B, Evans K, et al: Impact of new

- radiotherapy modalities on the surgical management of cancer of the esophagus and cardia. *Int J Radiat Oncol Biol Phys* 17:937-944, 1989
5. **Perez CA, Brady LW:** Principles and practice of radiation oncology: Carcinoma of the esophagus. Philadelphia, J.B.Lippincott Co, 1987, pp 706-707
 6. **Soga J, Tanaka O, Sasaki K, et al:** Superficial spreading carcinoma of the esophagus. *Cancer* 50:1641-1645, 1982
 7. **Jennings FL, Arden A:** Acute radiation effect in the esophagus. *A.M.A. Arch of Pathology* 59:407-412, 1959
 8. **Mckewon KC:** The surgical treatment of carcinoma of the esophagus in the elderly: 20 years experience. *Br J Surg* 72:28-30, 1985
 9. **Pearson JG:** The present status and future potential of radiotherapy in the management of esophageal cancer. *Cancer* 39:882-890, 1977
 10. **Lederman M:** Carcinoma of the esophagus, with special reference to the upper third; Part 1. Clinical considerations. *Br J Radiol* 39:193-294, 1966
 11. **Beatty JD, DeBoer G, Rider WD:** Carcinoma of the esophagus: Pretreatment assessment, correlation of radiation treatment parameters with survival, and identification and management of radiation treatment failure. *Cancer* 43:2254-2267, 1979
 12. **Mendenhall WM, Million RR, Bova FJ:** Carcinoma of the cervical esophagus treated with radiation therapy using a four-field box technique. *Int J Radiat Oncol Biol Phys* 8:1435-1439, 1982
 13. **Newaishy GA, Read GA, Duncan W, et al:** Results of radical radiotherapy of squamous cell carcinoma of the esophagus. *Clin Radiol* 33:347-352, 1982
 14. **Pearson JG:** Radiotherapy of carcinoma of esophagus and post cricoid region in South East Scotland. *Clin Radiol* 17:242-257, 1966
 15. **Rider WD, Mendoza RD:** Some opinions on treatment of cancer of the esophagus. *Am J Roentgenol* 55:514-517, 1969
 16. **Akakura 1, Nakayama Y, Kakegawa T, et al:** Surgery of carcinoma of the esophagus with preoperative radiation. *Chest* 57:47-57, 1970
 17. **Nakayama K, Kinishita Y:** Surgical treatment combined with preoperative concentrated irradiation. *JAMA* 227:178-181, 1974
 18. **Launois B, Delarue D, Campion JP, et al:** Preoperative radiotherapy for carcinoma of the esophagus. *Surg Gynecol Obstet* 153:690-692, 1981
 19. **Kasai M, Mori S, Watanabe T:** Follow-up results after resection of thoracic esophageal carcinoma. *World J* 2:543-551, 1978
 20. **Kelsen DP, Ahuja R, Hopfans, et al:** Combined modality therapy of esophageal carcinoma. *Cancer* 48:31-37, 1981

== 국문초록 ==

식도암의 방사선 치료 성적

전남대학교 의과대학 치료방사선과학교실

정 응 기 · 안 성 자 · 나 병 식

1985년 11월부터 1990년 6월까지 전남대학교병원 치료방사선과에서 방사선 치료를 받은 90명의 식도암 환자를 대상으로 생존율에 관하여 후향적 분석을 시행하였으며 다음과 같은 결과를 얻었다.

조직학적으로 75예(94.9%)가 편평상피 세포암으로 관찰되었으며, 병기는 25예(27.8%)가 T2, 64예(71.1%)가 T3로 대부분 진행된 암이었다. 최소 추적기간은 12개월 이었으며 중앙값은 5개월이었다. Kaplan Meier 법에 의한 2년 생존율은 11.6%이었다.

치료목표, T병기, 병변부위, 병변길이, 방사선량, 관해정도에 따른 2년 생존율을 구하여 비교하였으며, 이들중 중앙의 침범길이만 생존율에 영향을 미쳤다.