The Result of Radiotherapy in Esophageal Carcinoma

Hack Joon Gil, M.D., Chul Seung Kay, M.D., Jee Young Jang, M.D., Sei Chul Yoon, M.D., Kyung Sub Shinn, M.D. and Yong Whee Bahk, M.D.

Department of Therapeutic Radiology, Catholic University Medical College, Seoul, Korea

During the period between March 1983 and December 1990, 74 patients with esophageal carcinoma (EC) were treated with radiation therapy (RT) at the Department of Therapeutic Radiology, Kangnam St. Mary's Hospital, Catholic University Medical College.

Of these, 6 patients were lost to follow-up, and 13 patients were interrupted. So the remaining 55 patients were analyzed, retrospectively. 32 patients were irradiated with curative aim, 12 patients with palliative intent, 10 patients postoperatively, and 1 patient pre- and post-operatively. Among these 55 patients, 28 patients were treated with chemoradiation modality, and 27 patients with RT alone.

All patients were followed for a minimum of 20 months or until death. Of 32 patients irradiated by curative aim, 22 patients (69%) showed partial remission (PR), 6 patients (19%) complete remission (CR). Overall mean survival and two-year survival rate were 15.6 months and 22%. With respect to sex, age, pathologic differentiation, tumor location, tumor size, stage, RT aim, RT response, RT dose, use of chemotherapy and functional categories (FC) of dysphagia at initiation of RT and at finishing RT: Tumor size, stage, RT response had great influences on prognosis and FC at finishing RT had a slight influence on prognosis. Especially, the mean survival and 2-year survival rate in patients with postoperative RT were 24.7 months and 63%, which could be compared with 29.1 months and 43% in radically treated patients with CR. And the mean survival duration and 2-year survival rate in patients irradiated with doses more than 60 Gy were 22.4 months and 29%, and 50~60 Gy were 12.2 months and 12%, respectively. However, no significant difference was shown statistically.

Among 12 patients treated with palliative intent, 9 patients (75%) had good improvement in dysphagia and the mean duration of palliative response was 10.6 months.

Key Words: Esophageal carcinoma, Radiation therapy

INTRODUCTION

Esophageal carcinoma (EC) is a relatively uncommon malignancy of the gastrointestinal tract. According to the "Cancer Registry Programme in Republic of Korea"¹⁾, the esophageal cancer constitutes 2.1% of all cancers in South Korea. However, on a global basis, EC is a major health care problem in China, South Africa, and parts of South America²⁾.

EC primarily affects older man who have used tobacco and alcohol too excess. The overwhelming majority of them present with locally advanced or metastatic disease.

In spite of technical advances in both surgery and RT, the prognosis of patients with EC remains

poor, with a median survival generally $< 1 \, \text{year}^{3,4}$. With surgery or RT alone, 5-year survival rates in most series is 2% to 17%, and even in patients with resected tumor, it is less than $30\%^{5\sim8}$. Although this low rate can be considered to be caused by the difficulty in achieving local control by RT, other major causes include the high rate of lymph node metastases⁹, and distant metastases^{10,11}. And despite aggressive local therapy, $50\sim60\%$ of patients with locoregional disease (T 1-3, N 0-1, M 0) recur²).

With all the availability of a whole new generation of chemotherapeutic agents in the last 2 decades, the prognosis of patients with EC remains dismal¹²). More recently, in an attempt to improve local control and survival, combined modality approaches have utilized a chemoradiation with or without surgery.

In this study, we analyzed the results of 44 patients irradiated with radical or palliative intent,

^{*}This paper was supported by 1992 CUMC Clinical Medical Research Fund

and those of 11 patients with postoperative RT, including 1 patient with sandwich technique. And prognostic factors influencing these results were examined to set up the role of RT and to improve survival with good quality of life.

MATERIALS AND METHODS

From March 1983 to December 1990, 74 patients with EC were irradiated at the Department of Therapeutic Radiology, Kangnam St. Mary's Hospital, Catholic University Medical College.

However, 6 patients were lost to follow-up, and 13 patients were interrupted below 30 Gy. Remaining 55 patients were entered into this study.

Among them, 32 patients were irradiated radically, 12 patients were irradiated palliatively, 10 patients postoperatively, and 1 patient pre- and post-operatively. 28 patients were irradiated with chemotherapy and 27 patients without chemotherapy.

All patients were followed for a minimum of 20 months or until death. Patients' characteristics are shown in Table 1.

Thoracic tumor sites were classified as upper, middle, and lower lesion by esophagographic findings. The upper thoracic portion extends from the thoracic inlet to the level of the tracheal bifurcation. Between the bifurcation and the esophagogastric junction was divided equally into middle and lower

Table 1. Patient Characteristics of Esophageal Cancer

		(1	(n=55)	
		No.	(%)	
Sex	Male	51	93	
	Female	4	7	
Age	40~49	9	16	
J	50~59	10	18	
	60~69	29	53	
	70~89	7	13	
Primary Site	Cervical	2	4	
,	Upper Thoracic	2	4	
	Middle Thoracic	26	47	
	Lower Thoracic	16	29	
	2 or more sites	9	16	
Tumor Length	≦5 cm	21	38	
	5~10 cm	22	40	
	≥10 cm	12	22	
Stage	1	5	9	
	II	18	33	
	III without DM	18	33	
	III with DM	14	25	

(DM = Distant Metastasis)

thirds. There were 2 patients with upper lesion, 26 patients with middle lesion, 16 patients with lower lesion, 2 patients with cervical lesions, and 9 patients with involving 2 or more lesions.

Tumor length ranged between 2~18 cm with a mean of 8.0 cm. The patients were staged according to the TNM staging. 5 patients had stage I (9%), 18 patients stage II (33%), 18 patients (33%) stage III without distant metastasis, and 14 patients (25%) were stage III with distant metastasis.

Of 55 patients, 48 cases were confirmed to be squamous cell carcinoma, 1 case adenocarcinoma, 1 case papillary carcinoma, 1 case carcinosarcoma, but 4 cases were unknown histology (Table 2).

To represent the degree of dysphagia, we used functional categories of dysphagia (Table 3). All patients underwent barium swallow before starting of RT. And in most patients, esophageal biopsy and CT of chest and upper abdomen was done. Radionuclide studies of liver and bone were performed if indicated by clinical examination or biochemical profile.

All patients were irradiated with 6 MV linear accelerator. The target volume included the esophageal tumor defined by barium swallow at the

Table 2. Pathology

Cell Type	Differentiation	No.	(%)
Squamous cell carcinoma		48	87
	well-diff.	2	4
	moderately-diff.	20	36
	poorly-diff.	14	25
	undetermined	12	22
Adenocarcinoma	poorly-diff.	1	2
Papillary carcinoma		1	2
Carcinosarcoma		1	2
Unknown		4	7.

Table 3. Functional Categories of Dysphagia

	The state of the s
Category I	: Eating normally
Category II	: Requires liquids with meals
Category III	: Able to take semisolids but unable to
	take any solid food
Category IV	: Able to take liquids only
Category V	: Unable to take liquid but able to swal-
	low saliva
Category VI	: Unable to swallow saliva
Category VII	: Alimentation sustained by a surgical
	bypass procedure
Category VIII	: Alimentation sustained by gastros-
	tomy feedings of external esophagus

phageal tumor defined by barium swallow at the time of simulation, plus 5 cm margin above and below lesion, plus adjacent mediastinal structures.

The RT consisted of daily 180~200 cGy, 5 fractions per week, up to total 3000 to 6500 cGy in 4 to 8 weeks.

Initial treatment was given by anterior-posterior opposing fields. At the 20 Gy, The plan was changed to 3 portals (AP and posterior 2 oblique fields).

And at the 40 Gy, the treatment field was reduced up to 60 Gy. 8 patients were treated with postoperative RT up to $40\sim54$ Gy by fractional dose of 180 cGy.

About chemotheray, the treatment protocol had not been conformed. Different multiple regimens were used. They consisted of 5-FU (1000 $\mathrm{mg/m^2/day}$) for 4 days and cisplatin (100 $\mathrm{mg/m^2}$ IV bolus) in 12 patients, and 5-FU alone in 9 patients, and CAP, or 5-FU & MMC, or other regimens in remaining 6 patients.

Local control in our patients was defined as absence of disease in the esophagus or mediastinum determined both by absence of clinical symptoms and radiographic studies including esophagogram at one month following the completion of treatment. Survival was calculated from the first day of RT to the time of death by Kaplan-Meier method.

RESULTS

The mean age is 62 years, and male to female ratio was 12.75:1. The local response to radical RT in 34 patients was evaluated by barium swallow and esophagography.

Among 32 patients treated with radical RT, CR was achieved only in 6 patients (19%), and PR was obtained in 22 patients (69%), The remaining 4 patients (13%) showed minimal or no response. Of 9 patients who achieved CR, 6 were stage II, 2 were stage I, and 1 was stage III.

Among 12 patients treated with palliative RT, 9 patients (75%) had good improvement in dysphagia and the mean duration of palliative response was 10.6 months.

The 6 patients are still alive with the follow up period between 20 and 46 months. Of these 6 patients, 4 were treated with postopoerative RT.

Overall mean survival and 2-year survival rate were 15.6 months and 22% (Fig. 1). With respect to sex, age, pathology, tumor site, tumor length, stage, treatment aim, radiation response, radiation dose, use of chemotherapy, functional categories

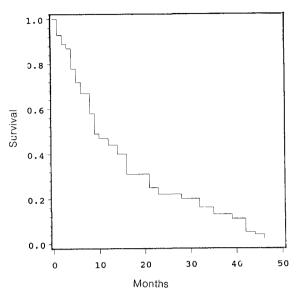


Fig. 1. Overall survival curve.

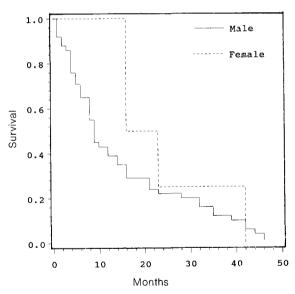


Fig. 2. Survival curve by sex.

of dysphagia, they were analysed.

Sex: The mean survival duration and 2-year survival rate in males were 14.9 months and 22%, and in females were 24.3 months and 25%, respectively (p>.05) (Fig. 2).

Age: The mean jsurvival duration and 2-year survival rate in ages below 49 were 20 months and 22%, in ages between 50 and 59 were 17.3 months and 20%, in ages between 60 and 69 were 13.3 months and 21%, and in ages above 70 were 17.1

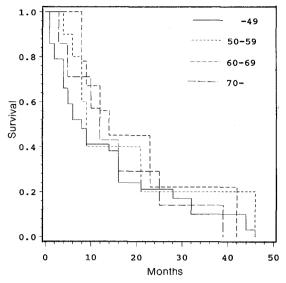


Fig. 3. Survival curve by age.

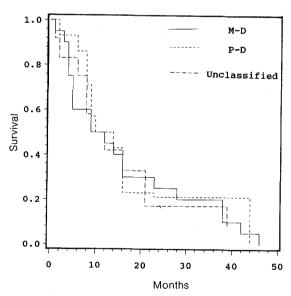


Fig. 4. Survival curve by differentiation.
(M-D=moderately differentiated, P-D=pooly differentiated)

months and 28%, respectively (Fig. 3). There were no significant differences of survival rate among age.

Pathology: In squamous EC patients, the mean survival duration and 2-year survival rate with moderately differentiated type were 15.8 months and 30%, and with poorly differentiated type were

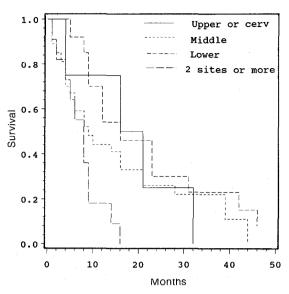


Fig. 5. Survival curve by site. (cerv=cervical)

17.0 months and 23%, and with unclassified type were 15.7 months and 17%, respectively (Fig. 4.). These showed that pathologic differentiation had no correlation with survival.

Tumor site: The mean survial duration and 2-year survival rate in cervical or upper thoracic lesion were 18.3 months and 25%, in middle thoracic lesion were 15.5 months and 26%, in lower thoracic lesion were 22.0 months and 30%, and in involving 2 or more lesions were 7.45 months and 0%, respectively (Fig. 5). The best results were obtained in the lower thoracic lesion, but there were no statistical significances (p>.05). And the worst results were achieved in involving 2 or more lesions. There were significant differences between 1 and 2 or more lesions (p<.05).

Tumor size: The mean survival duration and 2-year survival rate in patients with a tumor length of 5 cm or less were 23.4 months and 43%, with 5 \sim 10 cm were 14.9 months and 21%, and with 10 cm or above were 8.3 months and 0%, respectively (Fig. 6). A significant differences was found between the 5 cm and below, and the 5 \sim 10 cm groups (p=0.086) and those between the 5 \sim 10 cm, and 10 cm or above groups (p=0.044). These data suggest that comparatively early small-volume tumors share a significant potential for cure by RT. But, potent combined therapy is necessary for the treatment of advanced cancer.

Stage: The mean survival duration and 2-year survival rate for stage I were 28.8 months and 60%,

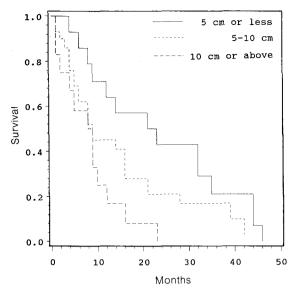


Fig. 6. Survival curve by size.

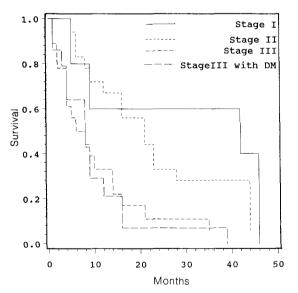
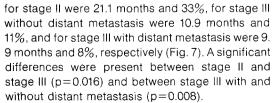


Fig. 7. Survival curve by stage.(DM = distant metastasis)



RT aim: The mean survival duration and 2-year survial rate were 14.5 months and 15% in patients

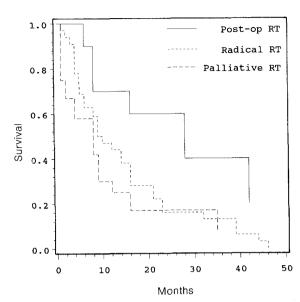


Fig. 8. Survival curve according to RT aim.

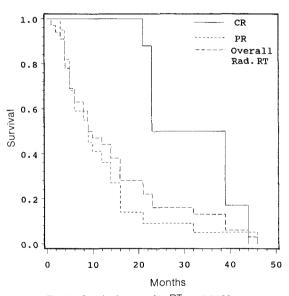


Fig. 9. Survival curve by RT response. (Rad. RT=radical radiation therapy)

treated with radical RT, 11.5 months and 18% with palliative RT, and 24.7 months and 63% with postoperative RT, respectively (Fig 8). A significant difference was shown between the postop-RT group and the palliative RT group (p=0.047). But no significant differences were present between the radical RT group and the palliative RT or postop-RT group (p>.05).

RT response: In radically treated patients, the mean survival duration and 2-year survival rate were 12.0 months and 9% in patients with PR, and 30.7 months and 43% with CR, respectively (Fig. 9) (p=0.0034).

RT dose: The mean survival duration and 2-year survival rate in patients treated with doses more than 60 Gy were 22.4 months and 29%, and treated with 50~60 Gy were 12.2 months and 12%, respec-

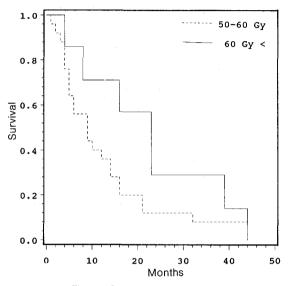


Fig. 10. Survival curve by RT dose.

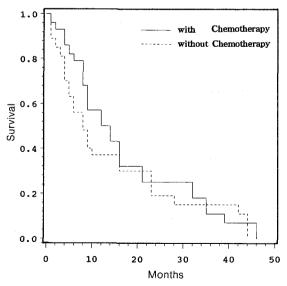


Fig. 11. Survival curve by chemotherapy.

tively (Fig. 10) (p > .05).

Chemotherapy: The mean survival duration and 2-year survival rate in patients treated with chemoradiation were 16.9 months and 25%, and without chemotherapy were 14.3 months and 19%. But there was no significant difference (Fig. 11) (p>. 05).

Functional category of dysphagia: The mean survival duration and 2-year survival rate in patients with initial functional category (FC) I-II were 16.6 months and 24%, with initial FC III or more were 24. 5 months and 24%, respectively (Fig. 12). No significant differences were present between them. The mean survival duration and 2-year survival rate in patients with final functional category (at finishing RT) I-II were 17.3 months and 25%, with final FC III or more 9.0 months and 9%, respectively (Fig. 13) (p=0.056). These showed that final FC was more correlated with prognosis than initial FC.

Tumor length, stage, RT response, had a great influence on prognosis. Final FC of dysphagia had a slight influence on prognosis.

During RT, most of patients had radiation esophagitis. Severe complications observed were herpes zoster in 1 patient, and esophagobronchial fistula in 1 patient. 8 pateints had feeding gastrostomies due to poor oral intake.

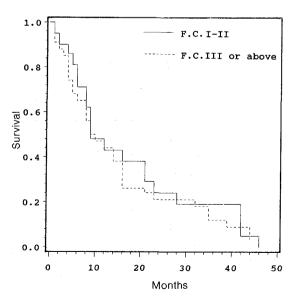


Fig. 12. Survival curve by initial F.C. (F.C.=functional category)

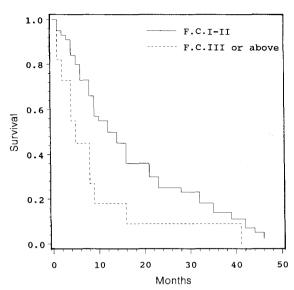


Fig. 13. Survival curve by final F.C. (F.C.=functional category)

DISCUSSION

The clinical behavior of EC supports the notion that it is a systemic disease at the outset similar to breast carcinoma. The assumption is further strengthened by autopsy series demonstrating that a great majority of patients, despite their short median survival durations, have evidence of established widespread micrometastases¹³⁾. At diagnosis, approximately 50% of patients have metastases beyond regional lymph nodes, precluding effective surgical intervantion¹⁴⁾.

Several decades of technologic improvement in surgical and RT techniques have marginally reduced the morbidity and mortality in the treatment of esophageal carcinoma, but have had virtually no impact on cure rates. The concomitant chemoradiation modality appears to offer the most consistent means of improving survival rates in EC along with minimal and acceptable increases in acute toxicity and drastic reduction in treatment-related mortality. 75~85% of patients with EC die within 1 year with surgery or RT alone. 1-and 2-year survival rates have been increased 2 fold or 3 fold with concurrent chemoradiation¹⁵⁾.

Squamous cell carcinoma is the most common type of primary tumor, accounting for 90% of all esophageal cancer. In localized adenocarcinoma of the esophagus or GE junction, the mainstay of

treatment has been surgery, either for potential cure or palliation¹⁶).

In squamous EC, the optimal treatment has remained controversial. Earlam and Cunha-Melo^{5,10)} found a 5-year survival rate of 4% with surgery only and 6% with RT alone. The results for RT were bad as those for surgery.

Pearson⁶⁾ reported that from 1949 to 1969, there had been a swing over from mainly surgery to mainly RT associated with a rise in the overall 1- and 5- year survial rates from 20% to 32% and from 7% to 9%, respectively.

The Canadian Esophageal Tumor Group¹⁷⁾ in 1985 agreed to use the tracheal bifurcation (carina) to divide the esophagus in two specific sites for the design. Patients with tumors above the carina will be allocated for RT based protocols with adjuvant programs. Patients with tumors below the carina could be considered for surgically based protocols with adjuvant programs using preoperative or postoperative RT, or chemotherapy or combined. So the comparison of the results of RT with those of surgery is difficult due to the tendency to select patients with less advanced tumors (particularly those located in the lower third of the esopohagus) for resection and to leave the more extensive and more proximal tumors for RT.

By Desa et al., ¹⁸⁾ important factors in determining the definitive treatment included the patient's age, cardiorespiratory status, the length of stricture, the presence or absence of metastases or associated malignancy and the histological type of the tumor.

When the lesion is confined to the mucosa, a 90% 5-year survival rate has been reported¹⁹⁾. Therefore the efforts have been directed toward earlier detection of the disease. A variety of methods have been used to obtain esophageal samples for cytology in mass screening programs²⁰⁾. Unfortunately, the introduction of flexible endoscopy and CT scanners does not appear to have an impact in rendering a greater portion of patients appropriate for surgical management.

Surgical resection has become standard therapy in patients whose tumors are resectable. Early diagnosis in EC increased the resectability rate to over 90%²¹⁾.

Esophagectomy can be performed with the hope of cure in patients in whom there is no apparent regional or systemic spread of disease before and during surgery. When all resections for operable squamous EC are considered, the 5-year survival rate is 10%. If only those resected for cure

are considered, the overall 5-year survival rate is $21\%^{19}$. in cases of early EC, RT also showed favorable results not inferior to those of surgery^{22,23)}.

Skinner's²⁴⁾ 5 year survival rate after en bloc resection of esophageal tumors was 18%, and Akiyama's⁹⁾ was 34.6%, but the results were not reproduced. And Moertel²⁵⁾ have not demonstrated that resection has a major impact on survival. The operative mortality rate formerly demonstrated by Earlarm and Cunha-Melo⁵⁾ was 29% fell dramatically to approximately 10% during the 1980s due to either better patient selection or improved techniques¹⁵⁾.

The locoregional carcinoma remains the dominant cause of morbidity and mortality. In a study of autopsy findings, Mantravadi et al. 260 found that 78% of cases given RT alone has residual primary tumor, which was the cause of death in 111 (64%) among 173 of the cases. Yang et al. 270. have reported that 40% of 1,136 5-year survivors given RT died because of local recurrence. However, despite great efforts, the clinical results of RT are poor, that is, about 40~60% in terms of local control rate and 4~8 months in terms of mean survival duration. 280.

Worldwide, 50% of the EC occur in the middle third of the esophagus, 30% occur in the lower third and 20% occur in the upper third and cervical region. We achieved same results that 47% occurred in middle third, 29% in lower third, 8% in upper third and cervical region, and residual 16% in 2 or more sites. And the 2-year survival rate was 26% in middle third, 30% in lower third, 25% in upper and cervical lesions. These results show no significant differences.

And Newaishy et al. 29). showed that those with tumors less than 5 cm in length had a 12% 5-year survival rate falling to 7.5% when the tumor was 5 to 10 cm. In our study, the 2-year survival rate in cases with a tumor length of 5 cm or less was 43%, 5 \sim 10 cm was 21%, and 10 cm or above was 0%. These results are considered to reflect the fact that radiotherapy is generally more effective for tumors with a small tumor volume.

An RT dose relationship is well recognized²⁹). however, when RT is combined with Chemotherapy, the dose relationship is less clear¹²). Earle et al.³⁰) showed in a nonrandomized comparison no advatage for patients treated with 60 Gy over those treated with 50 Gy. However, John et al.'s¹⁵) study, a dose relationship appeared to exist in that 5 of 6 relapse-free survivors received more than 40 Gy in combination with chemotherapy.

Our results showed that the mean survival dura-

tion and 2-year survival rate in patients treated with doses more than 60 Gy were 22.4 months and 29%, and treated with 50~60 Gy were 12.2 months and 12%, respectively, But, there was no significant statistical difference.

Park et al.³¹⁾ reported that the degree of response was closely associated with the response rate: Patients with CR had 34.3% while PR had 9.7% of 5-year actuarial survival rate. In our study, the mean survival duration and 2-year survival rate in patients with CR were 29.1 months and 43%, and PR were 12.0 months and 9%, respectively. These results showed that RT response was very important prognostic factor.

Corn et al.³²⁾ demonstrated that spinal cord tolerance can be fully respected while optimal target volume coverage can be achieved in prone position than in supine position and the eight-field arrangement is superior to the six-field arrangement when the lung is the doselimiting organ, whereas the six-field plan is superior to the eight-field plan when the heart is dose-limiting.

Local therapy has its limitations, be it surgery, RT, or the two combined, Pearson¹¹⁾ has suggested that local therapy, even if it can totally eradicate tumor, only influences the outcome in approximately one third of all patients, because the other two thirds will fall within 2 years of intercurrent disease, age, malnutrition, or distant metastases.

Using preoperative RT, Nakayama and Kinoshita³³⁾ reported 3-, 4-, and 5-year survival rates of 27.5, 31.8, and 37.5%, respectively, with a 3. 9% operative mortality. Mandard AM³⁴⁾ found that higher than 50 Gy in preoperative RT gave 23% of sterilization of tumor, whereas 16% of sterilization of tumor was obtained by lower than 50 Gy and only 39% of esophageal cancer had no local extension to adjacent trachea, bronchus, aorta, pericardium, pleura, mediastinum and stomach.

But, Launois et al.³⁵⁾ did not find preoperative RT benefitial. Skinner^{36,37)} also abandoned this approach after very discouraging results and he insisted that there is little role in preoperative RT, in especially resectable cases.

There have been several studies using the concept of induction chemotherapy before surgery. Kelsen et al.¹²⁾ reported improved resectability and short-term survival rates accompanied with significant morbidity and perioperative mortality rates and suggested that current data did not support the routine use of induction chemotherapy.

In 1983, Franklin et al.38) at Wayne State University treated carcinoma of esophagus by using

preoperative 5-FU and mitomycin C with radiation. The median survival for the entire group was 18 months, showing marked improvement over historical group. SWOG 8037 protocol utilized preoperative RT and chemotherapy using 5-FU and cisplatin³⁹⁾. Leichman et al.¹⁵⁾ showed that median survival duration and 1 year survival rate of patients treated by a neoadjuvant program of chemotherapy (5-FU and cisplatin) and radiation (30 Gy) was 22 months and 80%, respectively.

The use of preoperative or definitive synchronous chemoradiation has consistently shown increased tumor clearance rates (at surgery or endoscoopy), acceptable toxicity, and increased 2-year survival rates. The only study with prohibitive toxicity used alteranating chemotherapy (5-FU, cisplatin, mitomycin, and bleomycin) with RT⁴⁰. However, no randomized study showing such superiority over conventional RT has been reported yet.

There is a wide range of opinions concerning the effect of postoperative RT. Pearson⁴¹⁾ claims that such treatment has very little effect because of the large areas that need to be irradiated and the limited radiosensitivity of the tissues left in place after the operation. Postoperative RT for esophageal cancer has usually been given to patients with an unresectable gross tumor left behind or a residual tumor following palliative resection¹²⁾. Generally, these patients have a very poor prognosis.

Postoperative RT in patients with resectable disease has not been systematically studied. Nishimura⁷⁾ et al. reported that 31 patients irradiated with more than 40 Gy postoperatively had a 5-year survival rate of 54%, while 26 patients treated without postoperative RT had those of 33%, revealing a significant difference (p < 0.025).

Although Kasai et al.⁴²⁾ reported that postoperative RT was not effective for patients with lymph node metastases, according to Nishimura et al⁷⁾., postoperative RT significantly improved the survival of those with regional lymph node metastases, and it also improved substantially the survival of patients without lymph node metastases. N 0 and N 1 cases, including perigastric lymph node metastases, are the candidates for postoperative RT.

Kasai et al⁴²⁾, reported that the rate of relapse in the locoregional area was 14% in patients who received postoperative RT compared with 78% in those treated with surgery alone. The lowering of the local recurrence rate is attributable to the improvement in survival by postoperative RT. Pro-

phylactic postoperative RT of 50 Gy can safely and effectively be combined with surgical resection of esophageal cancer. In our study, the mean survival duration and 2-year survival rate in patients with postoperative RT were 24.7 months and 63%, which could be compared with 29.1 months and 43% in radically treated patients with CR.

Patients with widespread lymph node metastases (i.e. celiac or lower neck lymph node metastases) are far from being candidates for regional adjuvant RT. Chemotherapy following surgical resection is required for them.

Investigation from several centers have recently reported partial response rates approaching 50% for cisplatin-based combination chemotherapy regimens, with or without concomitant irradiation^{43,44}. Multicentric trials using concurrent RT and chemotherapy with or without surgery, such as SWOG and RTOG^{40,45}, confirmed these observations

The inclusion of surgery to various chemoradiation regimens does not increase (consistently) either the median survival or the 2-year survival in several groups of patients¹⁵. With increasing evidence of dose-response to RT and the need for more effective and/or prolonged chemotherapy, the addition of a surgical procedure to vigorous chemoradiation protocols may pose the risk of increased morbidity and mortality¹⁵.

The combination of interferon and FU is an active regimen in the treatment of advanced esophageal cancer with a response rate similar to that reported for cisplatin containing combinations²⁾.

Mukai et al⁴⁶). reported that combination of RT and local administration of OK-432 (a BRM) for carcinoma of the esophagus. CR was obtained in all 8 patients with tumors less than 5 cm in length and in 11 of 14 patients (78.6%) with tumors 5~10 cm in length. In the group with tumors more than 10 cm in length, CR was observed only in 37.5%. And the 1-year, 2-year, and 3-year survival rates were 67. 9%, 40.8% and 29.0%. This combination therapy had a great advantage not only in local control rate, but also in survival rate, compared with photon therapy alone.

The majority of patients die from aspiration pneumonia due to obstruction caused by the persisting local cancer. Reassessment of palliative procedures is indicated in the light of recent surgical and technological developments⁴⁷⁾. Almost all published reports agree that resection of the tumor provides the best form of palliation. Surgical bypass offers an effective alternative.

Palliative RT can be used either solely or in combination with any of the previous methods. And it is certainly superior to surgery in metastatic or unresectable conditions and since it does not increase the morbidity or mortality usually associated with esophagectomy, it provides a better selection by limiting its use to only potentially curable disease.

Wara et al⁴⁸⁾, reported that of 103 patients completing a course of irradiation, 11% achieved no palliation, whereas 66% had an improvement in symptoms that lasted longer than 2 months. In our study, 75% had a good improvement in dysphagia and the mean duration of palliative response was 10.6 months.

Intracavitary irradiation may offer superior palliation⁴⁹⁾. Radiotherapy is frequently chosen as a means of palliation but its effectiveness may be marred by serious complications. If the tumor is adherent to a bronchus a fistula may occur.

The combination of intracavitary and external RT for EC has several advantages over the conventional external beam X rays, either as a primary form of treatment for upper esophageal lesions, or as an adjuvant program to potentially operable cases, particularly in the lower esophagus below the tracheal bifurcation.

And intracavitary RT is superior to external RT alone, as it improves the therapeutic ratio by delivering higher doses to the more exophytic, more hypoxic, intraluminal portion of the esophageal disease while sparing normal tissues¹⁷).

Heyden et al²¹). began to study the effect of intraluminal microwave hyperthermia in combination with brachytherapy for patients with unresectable EC. Kai et al²⁸), reported that a combination of hyperthermia, RT and chemotherapy not only improved local control rate, but also achieved good palliation.

Since advent of the treatments TEM MS 90 which consist of multiple adjacent arcs, conformational therapy has enabled to deliver higher doses to the tumor volume while reducing the volume of normal tissue⁵⁰. Because it has a great advantage when the treatment volume has an irregular tubular shape rather than cubic, we think conformational therapy may be very appropriate for the treatment of the esophageal carcinoma.

CONCLUSION

1) From March 1983 to December 1990, 74 patients with esophageal carcinoma were treated

- with RT: 55 patients were analyzed.
- 2) Most of patients were in advanced stage: Stage II were 33%, stage III were 58%.
- 3) Among 32 patients treated with radical RT, CR was obtained in 6 patients (19%) and PR in 22 patients (69%).
- 4) Overall mean survival duration and 2-year survival rate were 15.6 months and 22%.
- 5) Tumor size, stage, RT response had great influences on prognosis.
- 6) The mean survival duration and 2-year survial rate in patients with a tumor length of 5 cm or less were 23.4 months and 43%, $5\sim10$ cm were 14.9 months and 21%, and 10 cm or above were 8.3 months and 0% (p=0.086) (p=0.044), respectively.
- 7) A significant differences between stage II and stage III (p=0.016), and between stage III with and without distant metastasis (p=0.008) were present.
- 8) The mean survival duration and 2-year survival rate were 12.0 months and 9% in patients with PR, and 30.7 months and 43% with CR, respectively (p=0.0034).
- 9) In palliative purposed treatment, 75% had a good improvement in dysphagia, and the mean duration of response was 10.6 months.

REFERENCES

- Ministry of Health and Social Affairs, Republic of Korea: Cancer registry programme in republic of Korea. July 1, 1989–June 30, 1990
- Kelsen D, Lovett D, Wong J, et al: Interferon alfa-2a and fluorouracil in the treatment of patients with advanced esophageal cancer. J Clin Oncol 10:269 -274, 1992
- Coia LR, Engstrom PF, Paul A: Nonsurgical management of esophageal cancer: Report of a study of combined radiotherapy and chemotherapy. J Clin Oncol 5:1783-1790, 1987
- Morstyn G, Thomas R, Mullerworth M, et al: Improved surival in esophageal cancer in the period 1978-1983. J Clin oncol 4:1062-1067, 1986
- Earlam R, Cunha-Melo JR: Oesophageal squamous cell carcinoma: I. A critical review of surgery. Br J Surg 67:381-390, 1980
- Pearson JG: The present status and future potential of radiotherapy in the management of esophageal cancer. Cancer 39:882-890, 1977
- Nishimura Y, One K, Imamura M, et al: Postoperative radiation therapy for esophageal cancer. Radiation Medicine 7:88-94, 1989
- 8. Skinner DB: Surgical treatment for esophageal carcinoma. Sem Oncol 11(2):136-143, 1984
- Akiyama H, Tsurumaru M, Kawamura T, Ono Y: Principles of surgical treatment for carcinoma of

- the esophagus: Analysis of lymph node involvement. Ann Surg 194:438-446, 1981
- Earlam R, Cunha-Melo JR: Oesophageal squamous cell carcinoma: II. A critical review of radiotherapy. Br J Surg 67:457-461, 1980
- Pearson JG: The value of radiotherapy in the management of esophageal cancer. AJR 105:500 -513, 1969
- Kelsen D, Bains M, Hilaris B, Martini M: Combinedmodality of esophageal cancer. Sem Oncol 11(2): 169-177, 1984
- Anderson LL, Lad TE: Autopsy findings in squamous-cell carcinoma of the esophagus. Cancer 50:1587-1590, 1982
- 14. Ajani JA, Roth JA, Ryan B, et al: Evaluation of preand postoperative chemotherapy for resectable adenocarcinoma of the esophagus or gastroensophageal junction. J Clin Oncol 8:1231-1238, 1990
- John MD, Flam MS, Mowry PA, et al: Radiotherapy alone and chemoradiation for nonmetastatic esophageal carcinoma: A critical review of chemoradiation. Cancer 63:2397-2403, 1989
- Fein R, Kelsen DP, Geller N, et al: Adenocarcinoma of the esophagus and gastrointestinal junction: Prognostic factors and results of therapy. Cancer 56:2512-2518, 1985
- 17. 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
- Desa L, Raghunath AS, Chawla SL, et al: Treatment policy for the management of carcinoma of the esophagus. Br J Surg 75:275-278, 1988
- DeMeester TR, Barlow AP: Surgery and current management for cancer of the esophagus and cardia. Curr Probl Cancer 12:241-327, 1988
- Lightadale CJ, Winawer SJ: Screening diagnosis and staging of esophageal cancer. Semin Oncol 11(2):101-112, 1984
- Hyden EC, Langholz B, Tilden T, et al: External beam and intraluminal radiotherapy in the treatment of the esophagus. J Thorac Cardiovase Surg 96:237-241, 1988
- Okawa T, Kita M, Tanaka M, Ikeda M: Results of radiotherapy for inoperable locally advanced esophageal cancer. Int J Radiat Oncol Biol Phys 17:49 -54, 1989
- Nakano T, Sudro H, Ito J, et al: Radicality of radiotherapy alone for esophageal cancer. Jap J Cancer Clin 31:236-239, 1985
- 24. Skinner DB: En bloc resection for neoplasms of the esophagus and cardia. J Thorac Cardiovasc Surg 85:59-71, 1983
- Moertel CG: The case against surgery. Dig Dis 23: 735-736, 1978

- Mantravadi RVP, Lad T, Briele H, Lieber EJ: Carcinoma of the esophagus: Sites of failure. Int J Radiat Oncol Biol Phys 8:1897-1901, 1982
- 27. Yang ZY, Gu XZ, Zhao S, et al: Long term survival of radiotherapy for esophageal cancer: Analysis of 1136 patients survivig for more than 5 years. Int J Radiat Oncol Biol Phys 9:1769–1773, 1983
- Kai H, Matsufuji H, Okudaira Y, et al: Heat, drugs, and radiation given in combination is palliative for unresectable esophageal cancer. Int J Radiat Oncol Biol Phys 14:1147-1152, 1988
- Newaishy GA, Read GA, Duncan W, Kerr GR: Results of radical radiotherapy of squamous cell carcinoma of the esophagus. Clin Radiol 33:347 -352, 1982
- Earle JD, Gelber RD, Moertel CG, Hahn RG: A controlled evaluation of combined radiation and bleomycin therapy for squamous cell carcinoma of the esophagus. Int J Radiat Oncol Biol Phys 6(7):821-826, 1980
- Park CI, Choi EK, Chung WK, et al: The result of radiotherapy in esophageal cancer. J Korean Soc Ther Radiol 6(2):227-233, 1988
- Corn BW, Coia LR, Chu JCH, et al: Significance of prone positioning in planning treatment for esophageal cancer. Int J Radiat Oncol Biol Phys 21: 1301-1309, 1991
- Nakayama K, Kinoshita Y: Surgical treatment combined with preoperative concentrated irradiation. JAMA 227:178, 1974
- Mandard AM, Chasle J, marnay J, et al: Autopsy findings in 111 cases of esophageal cancer. Cancer 48:329-335, 1981
- Launois B, Delarue D, Campion JP, and Kerbaol M: Preoperative radiotherapy for carcinoma of the esophagus. Surg Gynecol Obstet 153:690-692, 1981
- 36. **Skinner DB:** Esophageal malignancies: Experience with 110 cases. Surg Clin N Am 56:137, 1976
- 37. Ellis FH Jr, Gibb SP, Watkins E Jr: Esophagectomy: A safe, widely applicable, and expeditious form of palliation for patients with carcinoma of the esophagus and cardia. Ann Surg 198:531-540, 1983
- Franklin R, Steiger Z, Vaishampayan G, et al: Combined modality therapy for esophageal squamous cell carcinoma. Cancer 51:1062-1071, 1983
- Austin JC, Postier RG, Elkins RC: Treatment of esophageal cancer: The continued need for surgical resection. Am J Surg 152:592-595, 1986
- Leichman L, Herskovic CG, Leichman PB, et al: Nonoperative therapy for squamous-cell cancer of the esophagus. J Clin Oncol 5:365-370, 1987
- 41. Giuli R, Sancho-Garnier H: Diagnostic, therapeutic, and prognostic features of cancers of the esophagus: Results of the international prospec-

- tive study conducted by the OESO group (790 patients). Surgery 99:614-622, 1986
- 42. Kasai M, Mori S, Watanabe T: Follow-up results after resection of thoracic esophageal carcinoma. World J Surg 2:543-551, 1978
- 43. Carey RW, Hilgenberg AD, Wilkins EW, et al:
 Preoperative chemotherapy followed by surgery
 with possible postoperative radiotherapy in
 squamous cell carcinoma of the esophagus: Evaluation of the chemotherapy component. J Clin
 Oncol 4:697-701, 1986
- 44. Kelsen D, Hilaris B, Coonley C, et al: Cisplatin, vindesine, and bleomycin chemotherapy of localregional and advanced esophageal carcinoma. Am J Med 75:645-652, 1983
- 45. **Byfield JE, Barone R, Mendelsohn J, et al**: Infusional 5-fluorouracil and x-ray therapy for non-resectable esophageal cancer. Cancer 45:703

- -708, 1980
- 46. Mukai M, Morita S, Tsunemoto H, et al: Combination therapy of local administration of OK-432 and radiation for esophageal cancer. Int J Radiat Oncol Biol Phys 22:1047-1050, 1992
- 47. Hennessy TPJ: Choice of treatment in carcinoma of the oesophagus. Br J Surg 75:193-194, 1988
- 48. Wara WM, Mauch PM, Thomas AN, et ak: Palliation for carcinoma of the esophagus. Radiology 121: 717-720, 1976
- Rowland CG, Pagliero KM: Intracavitary irradiation in palliation of carcinoma of the esophageal and cardia. Lancet 2:981–982, 1985
- Tate T, Brace JA, Morgan H, Skeggs DBL: Conformation therapy: A method of improving the turnour treatment volume ratio. Clin Radiol 37:267, 1986

= 국문초록 =

식도암의 방사선치료 성적

가톨릭의과대학 강남성모병원 치료방사선과학교실

길학준 · 계철승 · 장지영 · 윤세철 · 신경섭 · 박용휘

가톨릭의대 강남성모병원 치료방사선과에서는 1983년 3월부터 1990년 12월까지 74명이 식도암으로 진단되어 방사선치료를 받았다. 이중 6명은 추적소실되었고, 13명은 치료중단되어 55명에 대한 후향적 분석을 했다.

이중 32명은 근치적 방사선치료를 받았고, 12명은 대증적 방사선치료를 받았으며, 10명은 수술후 방사선치료를 받았다. 나머지 1명은 수술 전후로 방사선치료를 실시했다. 55명중 28명은 방사선치료 단독으로, 27명은 방사선과 약물 병용요법으로 치료했다.

근치적 방사선치료받은 32명중 88%의 환자에서 관해를 얻었으며, 이중 완전관해는 19%, 부분관해는 69%였다. 전체 환자의 평균생존기간과 2년 생존율은 15.6개월과 22%였다. 성별, 나이, 병리학적 분화도, 종양 위치, 크기, 병기, 방사선치료목적, 관해정도, 방사선 치료선량, 약물요법 병용유무, 치료시작시와 치료종결시의 연하곤란정도가 생존율에 미치는 영향을 조사했다.

이중 종양의 크기, 병기, 관해정도가 가장 큰 예후인자였으며, 특이한 점은 수술후 방사선치료의 평균생존기간과 2년 생존율은 24.7개월과 63%로 근치적 방사선치료후 완전관해를 얻었을 때의 평균 생존기간과 2년 생존율 29.1개월과 43%에 유사한 좋은 결과를 보여줬다. 이는 아마도 수술받은 환자의 선별된 선택에 기인한 것으로 생각되고, 또한 연하곤란의 정도는 치료시작 때보다 치료종결시의 연하곤란정도가 예후에 약간의 영향을 주었다.

또한 근치적 방사선 치료의 경우 60 Gy이상 줬을 때가 그 이하로 치료했을 때보다 좋은 생존율을 얻었으나 통계적 의의는 없었다. 대증적 방사선치료의 경우, 75%에서 연하곤란의 개선을 보였고, 평균지속기자은 10.6개월이었다.