

Results of Radiation Therapy for Squamous Cell Carcinoma of the Esophagus

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Purpose: This study was designed to evaluate the effectiveness and prognostic factors for patients treated with postoperative radiation therapy following surgery or with radiation therapy alone for squamous cell carcinoma of the esophagus.

Materials and Methods: We retrospectively analyzed 132 esophageal cancer patients treated with postoperative radiation therapy following surgery or patients who were treated with radiation therapy alone at our institution from 1989 to 2006. Thirty-five patients had stage II disease, 88 patients had stage III disease and nine patients had stage IV disease. Tumors were located at the upper esophagus in 18 patients, the mid esophagus in 81 patients and the distal esophagus in 33 patients. Sixty patients were treated with radiation therapy alone and 72 patients were treated with postoperative radiation therapy following surgery. Eight patients received a dose less than 40 Gy and 78 patients received a dose of 40 to 50 Gy. The remaining 46 patients received a dose of 50 to 60 Gy. The majority of patients who underwent postoperative radiation therapy received a dose of 45 Gy.

Results: Actuarial survival rates for all of the patients at two years and five years were 24% and 5%, respectively. The median survival time was 11 months. Survival rates for patients who underwent postoperative RT at two years and five years were 29% and 8%, respectively. The corresponding survival rates for patients who received radiation alone were 18% and 2%, respectively. Survival rates at two years and five years were 43% and 15% for stage II disease, 22% and 2% for stage III disease and 0% and 0% for stage IV disease, respectively; these findings were statistically significant. Two-year survival rates for patients with upper, middle and distal esophageal cancer were 19, 29% and 22%, respectively. Although there was a trend of slightly better survival for middle esophageal tumors, this finding was not statistically significant. Complete response to radiation was achieved in 13 patients (22%) and partial response to radiation was achieved in 40 patients (67%) who received radiation alone. No response to radiation was noted in seven patients (12%). A statistically significant difference in survival rates was seen between patients that had a complete response and patients that had a partial response. Two-year survival rates for patients that had a complete response versus patients that had a partial response were 31% and 17%, respectively. There were no survivors for patients with no response as determined at two-year follow-up.

Conclusion: We conclude that radiation therapy is an effective treatment for esophageal cancer. Stage and response to radiation therapy were noted to be prognostic factors. A more effective treatment modality is needed to improve long term survival because of the relatively dismal prognosis for this tumor.

Key Words: Esophageal cancer, Radiation therapy

Introduction

Patients who have carcinoma of the esophagus are mainly treated with surgery, while the patients who have either advanced disease or risk for surgical procedure are preferentially treated with radiation.^{1,2)} Radiation therapy is an integral component to achieve long term local palliation in the management of the esophageal cancer. While treatment of

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choice for early stage esophageal cancer, it is not clear whether surgery is better treatment for more advanced tumor or not.^{3,4)} In general, it is reported that 5 year survival rate for esophageal cancer is approximately 10%.^{5,6)} This dismal prognosis is probably due to the fact that there is difficulty in achieving local control following surgery or radical radiation therapy. Also there is a report suggesting that result of radiation therapy for early stage esophageal cancer is not worse than that of surgery alone.¹⁾ Therefore, esophageal cancer could be treated by radiation therapy alone with curative aim.

Postoperative adjuvant radiation therapy following surgery or combined chemotherapy has been used to improve not only local control but also long term survival rate. Several studies demonstrated that postoperative radiation therapy reduces local recurrence rate and improves 5 year survival rate compared with the results which could be achieved by surgery alone.^{7~9)}

One hundred thirty two esophageal cancer patients treated with postoperative radiation therapy following surgery or radiation alone at our institution from 1989 to 2006 were retrospectively analyzed. We also evaluated the effectiveness of radiation treatment and prognostic factors affecting survival rates.

Materials and Methods

We retrospectively analyzed total of 132 esophageal cancer patients treated with postoperative radiation therapy following surgery or radiation therapy alone at our institution from 1989 through 2006. One hundred twenty six patients were male and

remaining 6 patients were female with male to female ratio of 21 (Table 1). Median age of patients was 60 years with range of 40 to 81 years. All of the patients were histologically diagnosed through endoscopic esophageal biopsy and they were squamous cell carcinoma. Patients with adenocarcinoma were excluded from this study. Patients were staged according to American Joint Committee on Cancer Staging System. Thirty five patients had stage II disease. Eighty eight patients had stage III and remaining 9 patients did stage IV disease. Location of the tumor was evaluated by esophagogram, endoscopic findings and CT of the chest. Tumor was located at upper esophagus in 18 patients, mid esophagus in 81 patients and distal esophagus in 33 patients, respectively as shown in Table 1. Fifty six patients had the tumor with 5 cm or less in length and remaining 76 patients had the tumor with more than 5 cm in length.

Sixty patients were treated with radiation therapy alone and 72 patients were treated with postoperative radiation therapy following surgery. Patients treated with radiation therapy and chemotherapy without surgery were excluded from the study. Linear accelerator producing 6 MeV or 10 MeV photons was employed to treat all of the patients. Barium swallowing was performed during the treatment planning procedure to identify the tumor location. Parallel opposed anterior-posterior fields were usually used at the initiation of the treatment. After delivering 4,000 cGy, three field technique or bilateral two fields were employed to take off the spinal cord. Eight patients received less than 40 Gy and 78 patients did 40 to 50 Gy. Remaining 46 patients received 50 to 60 Gy. Majority of postoperative radiation therapy group received 45 Gy as shown in Table 2.

Patients were followed by us or their referring physicians one month after completion of the radiation therapy and at

Table 1. Patients Characteristics (N=132)

Characteristics	No. of patients	
Sex	Male	126
	Female	6
Age	Range	40~81
	Median	60
Stage	II	35
	III	88
	IV	9
Location	Upper	18
	Mid	81
	Lower	33
Tumor size	5 cm or less	56
	more than 5 cm	76

Table 2. Distribution of Patients According to Delivered dose

Delivered dose	RT* alone	vs	Op [†] + RT	Total
Less than 40 Gy	6		2	8
40~50 Gy	8		70	78
50~60 Gy	46		0	46
Total	60		72	132

*radiation therapy, [†]operation

regular intervals thereafter. Pattern of the failure and treatment related complications were not able to be evaluated because of inadequate follow up. Survival rate was calculated by Kaplan Meyer method and statistical significance was evaluated by log rank test.

Results

Actuarial survival rates for entire patients at 2 and 5 years were 24% and 5% respectively (Fig. 1). Median survival time was 11 month. Survival rates for postoperative group at 2 and 5 years were 29% and 8%. Those for radiation alone group were 18% and 2% respectively ($p < 0.05$). More favorable results in postoperative group compared with radiation alone group is probably due to the fact that patients with more

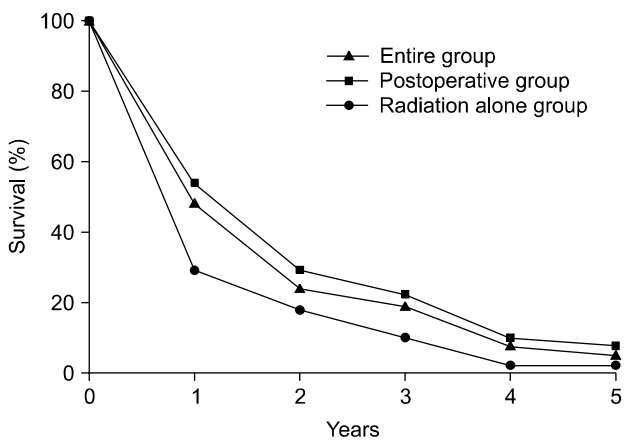


Fig. 1. Actuarial survival rates for entire, postoperative and radiation alone group.

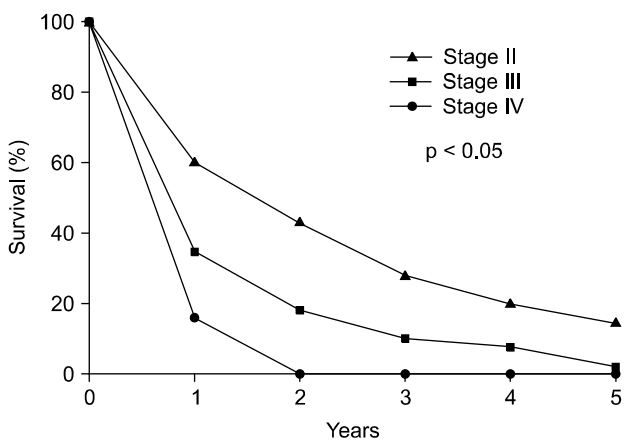


Fig. 2. Survival rates according to Stage.

advanced unresectable disease were treated with radiation alone.

Thirty five patients had stage II disease. Eighty eight patients had stage III and remaining 9 patients did stage IV disease. Survival rates at 2 and 5 years were 43% and 15% for stage II, 22% and 2% for stage III, and 0% and 0% for stage IV disease, respectively and this was statistically significant ($p < 0.05$). Survival rates according to stage are shown in Fig. 2. Two year survival rates for patients with upper, middle and distal esophageal cancer were 19, 29% and 22%, respectively. Although there was a trend of slightly better survival in middle esophageal tumor, this was not statistically significant.

In radiation alone group, response to radiation therapy was evaluated. Complete response to radiation was achieved in 13 patients (22%) and partial response was achieved in 40 patients (67%). No response to radiation was noted in 7 patients (12%). There was statistically significant difference in survival rates between complete response group and partial response group as shown in Fig. 3. Two year survival rates for complete vs partial group were 31% and 17% ($p < 0.05$). No survivors were noted in no response group at 2 year follow up.

Discussion and Conclusion

Although the esophageal cancer is not a very popular tumor, mortality rate is remarkably high. Recently multi-disciplinary approach including surgery, radiation and

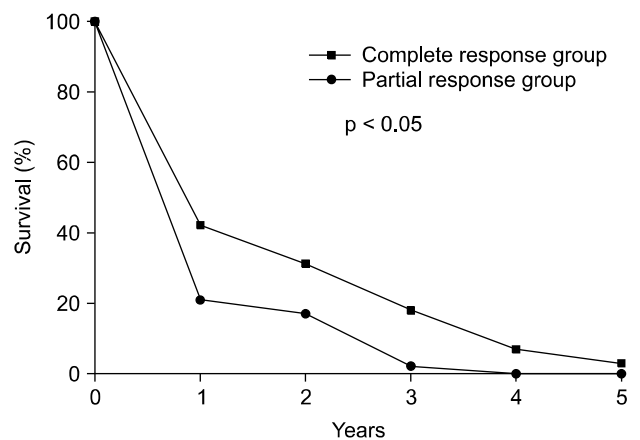


Fig. 3. Survival rates for complete response group vs partial response group in patients treated with radiation alone.

chemotherapy has been preferred. However, approximately 20% of patients with esophageal cancer were noted to have the distant metastases at the time of diagnosis.^{1,3)} Postoperative radiation therapy has been employed to eradicate remaining microscopic or gross residual tumor after surgery or to palliate patients following surgery. In literature review done by Earlam and Cunhamelo, they reviewed 8,400 patients treated with radical radiation therapy.¹⁰⁾ For entire group of patients, 1, 2 and 5 year survival rates were 18, 8% and 6%, respectively. Also they documented results of postoperative radiation therapy and range of 1, 2 and 5 year survival rates were 42~46%, 8~27% and 6~20%, respectively.

Several reports demonstrated that surgery followed by postoperative radiation therapy could result in promising long term survival rate.^{11~15)} DeMeester et al. showed that surgery and radiation therapy resulted in 35% of 5 year survival rate compared with 16% in surgery alone.¹¹⁾ They suggested high dose postoperative radiation therapy following surgery might eradicate microscopic residual tumor and eventually improve survival for those patients. Also Harrison et al. showed improved survival in patients treated with combined modality.¹³⁾ They reported that 1 and 2 year survival rates in postoperative group were 65% and 35% and corresponding survival rates in radiation alone group were 19% and 15%, respectively. In our study, survival rates for postoperative group at 2 and 5 years were 29% and 8%. Those for radiation alone group were 18% and 2% respectively. More favorable results in postoperative group compared with radiation alone group is probably due to the fact that patients with more advanced unresectable disease were treated with radiation alone.

Petrovich et al. reported that 2 year survival rates for Stage I, II, III and IV were 29, 24, 5% and 3%, respectively ($p < 0.001$). In that study, median survival for entire patients was 12 month and 5 year survival rate was 4.2%.¹⁶⁾ In our study, survival rates at 2 and 5 years were 43% and 15% for stage II, 22% and 2% for stage III, and 0% and 0% for stage IV disease, respectively and this was statistically significant. Also several reports documented that prognostic factors affecting treatment results are age, stage, tumor size, hemoglobin level and response to radiation.^{13,14,17,18)} There was statistically significant difference in survival rates between complete response group and partial response group in this study. Two year survival rates for complete vs partial group were 31%

and 17%. No survivors were noted in no response group at 2 year follow up.

Based on this study, we conclude that radiation therapy is an effective treatment for esophageal cancer. Stage and response to radiation therapy were noted to be prognostic factors in our study. Further effective treatment modality would be needed to improve long term survival because of relatively dismal prognosis in this tumor.

References

1. Okawa T, Kita M, Tanaka M, et al. Result of radiotherapy for inoperable locally advanced esophageal cancer. *Int J Rad Oncol Biol Phys* 1989;17:49-54
2. Muller JM, Erasmi H, Stelzner M, Zieren U, Pichelmaier H. Surgical therapy of esophageal carcinoma. *Br J Surg* 1990;77:845-857
3. Drucker MH, Mansour KA, Hatcher CR, et al. Esophageal carcinoma, an aggressive approach. *Ann Thorac Surg* 1979;28:133-138
4. Hancock SL, Glatstein E. The radiotherapy result of esophageal cancer. *Semin Oncol* 1984;11:144-158
5. Nishimura Y, One K, Imamura M, et al. Postoperative radiation therapy for esophageal cancer. *Radiat Med* 1989;77:88-94
6. Sykes AJ, Burt PA, Slevin NJ, Stout R, Marrs JE. Radical radiotherapy for carcinoma of the esophagus: an effective alternative to surgery. *Radiother Oncol* 1998;48:15-21
7. Wu HK, Park SW, Park CI. Long term follow up after radiation therapy alone for esophageal carcinoma. *J Korean Soc Ther Radiat Oncol* 1998;16:441-446
8. Stahl M, Stuschke M, Lehmann N, et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. *J Clin Oncol* 2005; 23:2310-2317
9. Graham AJ, Shrive FM, Ghali WA, et al. Defining the optimal treatment of locally advanced esophageal cancer: a systemic review and decision analysis. *Ann Thorac Surg* 2007; 83:1257-1264
10. Earlam R, Cunhamelo JR. Esophageal squamous cell carcinoma: a critical review of radiotherapy. *Br J Surg* 1980;67: 457-461
11. Demeester TR, Barlow AP. Surgery and current management for cancer of the esophagus and cardia. *Curr Probl Cancer* 1988;12:241-247
12. Goodner J. Surgical and radiation treatment of cancer of the thoracic esophagus. *Am J Roentgenol* 1969;105:523-528
13. Harrison L, Fohel T, Picone J, et al. Radiation therapy for squamous cell carcinoma of the esophagus. *J Surg Oncol* 1988;37:40-43
14. Pearson JG. The value of radiotherapy in the management

- of squamous esophageal cancer. Br J Surg 1971;58:794-798
15. **Earlam R, Johnson L.** 101 Esophageal cancer: a surgeon uses radiotherapy. Ann R Coll Surg Engl 1990;72:32-40
16. **Petrovich Z, Langholz B, Formenti S, et al.** Management of carcinoma of the esophagus: the role of radiotherapy. Am J Clin Oncol 1991;14:80-86
17. **Rades D, Lang S, Schild SE, Alberti E.** Prognostic value of haemoglobin levels during concurrent radiochemotherapy in the treatment of esophageal cancer. Clin Oncol 2006;18:139-144
18. **Ahn SJ, Chung WK, Nah BS, Nam TK.** External beam radiotherapy alone in advanced esophageal cancer. J Korean Soc Ther Radiol Oncol 2000;18:11-16

국문초록

식도 편평세포암의 방사선치료 결과

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목적: 식도암에서 수술 후 방사선치료 및 방사선 단독 치료의 효과를 검증하고 예후 인자를 알아보고자 하였다.

대상 및 방법: 1989년부터 2006년까지 방사선치료를 받은 132명의 환자를 후향적으로 분석하였다. 35명은 제2병기 88명은 제3병기 9명은 제4병기 환자였다. 상부 식도암이 18명, 하부 식도암이 33명이었으며 중등부 식도암이 81명이었다. 60명에서는 방사선 단독 치료를 시행하였고 72명은 수술 후 방사선치료를 받았다. 8명에서는 40 Gy 이하를 조사하였으며 78명에서는 40내지 50 Gy를 조사하였다. 나머지 46명은 50내지 60 Gy를 조사 받았으며 수술 후 방사선치료를 받은 대부분의 환자는 45 Gy를 조사받았다.

결과: 전체 환자의 2년 및 5년 생존율은 24% 및 5%이었고 중앙 생존기간은 11개월이었다. 수술 후 방사선치료군의 2년 및 5년 생존율은 19% 및 8%, 방사선 단독치료군의 2년 및 5년 생존율은 18% 및 2%이었다. 제2병기, 제3병기 및 제4병기 환자의 2년 및 5년 생존율은 각각 43% 및 15%, 22% 및 2%, 0% 및 0% 이었으며 이는 통계적으로 유의하였다. 상부, 중등부, 하부 식도암의 2년 생존율은 각각 19, 29, 22%이었으며 통계적으로 유의한 차이는 나타나지 않았다. 방사선 단독치료군에서 13명(22%)은 완전관해를, 40명(67%)은 부분관해를 보였고 7명(12%)은 반응을 보이지 않았다. 완전관해를 보인 환자군이 부분관해를 보인 환자군보다 더 나은 2년 생존율을 나타내었다 (31% vs 17%).

결론: 식도암에서 방사선치료는 효과적이고 유용한 치료 방법이었으며 병기 및 방사선치료에의 반응 정도가 유의한 예후인자이었다. 그러나 식도암의 장기 생존율 및 예후가 만족스럽지 못하므로 더욱 효과적인 치료 방법의 개발이 향후 필요하리라 사료된다.

핵심용어: 식도암, 방사선치료