

Radiotherapy Results of Stage I Glottic Cancer

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Purpose : This study was to evaluate survival, failure patterns, and prognostic factors of stage I squamous cell carcinoma of the glottic larynx after curative radiation therapy.

Materials and Methods : A retrospective analysis was done for 57 patients with glottic cancer who were treated with curative radiation therapy from June 1985 to November 1992. There were 55 male and two female patients. Patients' age ranged from 17 to 71 years (median 39 years). Radiation therapy was delivered five times a week, 2 Gy daily, total 66 Gy using 6 MV X-ray.

Results : Complete response (CR) was noted in 51 out of 57 patients (89.5%) and persistent disease (PER) in six out of 57 patients (10.5%). The disease-free survival rates at 3 and 5 years were 72.9% and 63.8%, respectively. Seven failures were observed among 51 CR patients during follow-up. Salvage total laryngectomy for six recurred patients and partial laryngectomy for one recurred patient were done with successful results, i.e., all of them were actually salvaged. Among six PER patients, salvage total laryngectomy for two patients and partial laryngectomy for two patients were done and two patients refused operation. Following salvage surgery for the four PER patients, three were salvaged and one failed locoregionally. Among the 13 failures 10 (76.9%) were salvaged with surgery. The ultimate local control rate at 5 years was 92.3% and overall 47 out of 57 (82.5%) patients were able to preserve their larynx. The 5-year disease-free survival rates were 85.5% for posterior lesions, and 61.6% for anterior lesions ($p < 0.05$). Cord mobility, involvement of anterior commissure, field size, and T stage did not impact on disease-free survival.

Conclusion : Considering the high percentage of voice preservation with initial radiotherapy, radiotherapy should be the first choice in the treatment of stage I glottic carcinoma.

Key Words : Glottic cancer, Radiotherapy, Stage I

INTRODCUTION

Initial radiotherapy with surgical salvage for

local recurrence or persistence has been generally accepted as the treatment of choice for T1 glottic cancer. Voice quality is superior in the majority of patients following definitive radiation though it can be effectively treated with either surgery or radiation therapy. The treatment of T2 glottic cancer is, however, controversial because

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T2 disease comprises a heterogeneous group of tumors that respond very differently to radiation therapy.¹⁻³⁾ At our institution, patients with T1 and selected T2 lesions have been treated with definitive radiotherapy with partial laryngectomy or total laryngectomy as a salvage procedure for radiation failures. We retrospectively reviewed the patients with T1 and selected T2 glottic cancer to evaluate the efficacy of radiotherapy with surgical salvage.

MATERIALS AND METHODS

A retrospective analysis was done for 57 patients with squamous cell carcinoma of the glottic larynx, who were treated with definitive radiation therapy from June 1985 to November 1992. There were 55 male and two female patients. Patients' age ranged from 17 to 71 years (median 39 years). According to AJCC criteria,⁴⁾ 41 patients had T1a, three patients had T1b, and 13 patients had T2 lesions (Table 1). Clinical diagnostic staging work-up included medical history, physical examination, indirect and direct laryngoscopy, CBC, chest x-rays. We included T2 lesions which had a ventricular involvement or impaired cord mobility for radiotherapy and excluded those with a subglottic extension. Radiation therapy was delivered five times a week, 2 Gy daily, total 66 Gy using 6 MV X-ray. Computer-assisted planning was used and patients

were treated with opposed bilateral fields with or without wedges to insure adequate dose distribution within the tumor volume. Field sizes ranged from 4.5 cm × 4.5 cm (20.3 cm²) to 5.0 cm × 6.0 cm (30.0 cm²) with a median 5 cm × 5 cm (25.0 cm²).

One month after radiotherapy clinical evaluation of the response was done. Response was judged as complete (CR) when all clinical evidence of the tumor had disappeared, and persistent (PER) when there was any evidence of tumor masses. Follow-up period ranged from 1 to 94 months with a median 10 months.

Disease-free survival was calculated by Kaplan-Meier method and analyzed by logrank test.⁵⁾ Disease-free interval was calculated from the beginning of radiation therapy to the date of the first failure or the date of last follow-up visit. All contingency tables were evaluated by chi-square test.⁶⁾ We evaluated some prognostic factors for disease-free survival such as cord mobility, involvement of anterior commissure, field size, position of the lesion, and T stage.

RESULT

Complete response (CR) was noted in 51 out of 57 patients (89.5%) and persistent disease (PER) in six patients (10.5%). The disease-free survival rates at 3 and 5 years were 72.9% and 63.8%, respectively (Fig. 1).

Overall 13 failures (22.8%) were observed including 6 PER lesions after initial radiotherapy. All failures were progression or recurrence at the primary site (Table 2). During follow-up seven failures were noted among 51 CR patients for whom salvage total laryngectomy for six patients and partial laryngectomy for one patient were done with successful salvage. Among six PER patients, total laryngectomy for two patients and partial laryngectomy for two patients were done and two patients refused operation. Following salvage surgery for the four PER lesions, three were salvaged and one failed locoregionally. Among the 13 failures ten (76.9%) were salvaged

Table 1. Patient Characteristics

Characteristics	
No. of Patients	57
Age (in years)	
Median	61
Range	33-79
Sex	
Male	55
Female	2
Stage	
T1a	41
T1b	3
T2	13
Follow-up (months)	
Median	10
Range	1-94

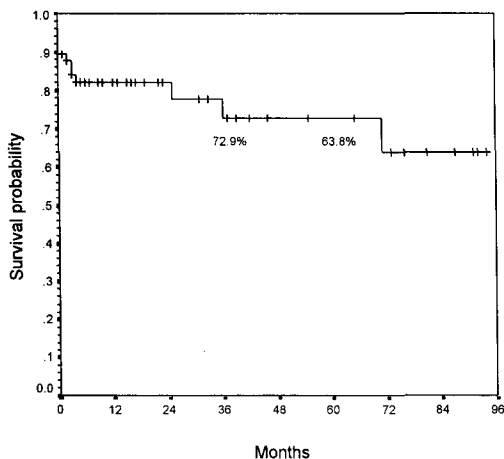


Fig. 1. Disease-free survival for all patients.

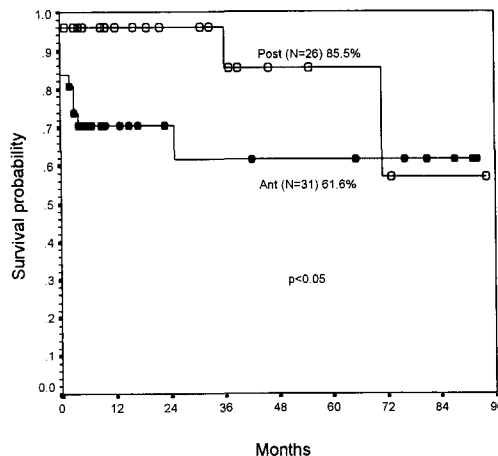


Fig. 2. Disease-free survival by location of the tumor (Ant: anterior, Post: posterior).

Table 2. Failure Pattern and Type of Salvage Surgery

	No. of Failure		Salvage Surgery		
	T1	T2	PL	TL	Refused
Persistent disease	4	2	2	2*	2
Vocal cord	5	2	1	6	—

PL : Partial laryngectomy

TL : Total laryngectomy

*Failed at neck after total laryngectomy

with surgery (Table 2). If we exclude two patients who refused surgery, only one patient failed after salvage surgery. The ultimate local control rate at 5 years was 92.3% and 47 out of 57 patients (82.5%) were able to preserve their larynx.

The 5-year disease-free survival rates were 85.5% for posterior lesions, and 61.6% for anterior lesions ($p < 0.05$, Fig. 2). Cord mobility, involvement of anterior commissure, field size, and T stage did not impact disease-free survival (Table 3).

DISCUSSION

Local control in stage I glottic cancer ranges from 80 to 90%. With surgical salvage of failures, overall local control improves to approximately 90 to 100%, and the voice preservation rates are

Table 3. Prognostic Factors Predicting Disease-Free Survival

Variables	No. of patients	5YDFS (%)	p value
Position			
Posterior	26	85.5	$p < 0.05$
Anterior	31	61.6	
T stage			
T1	44	69.6	N.S.
T2	13	51.3	
Cord mobility			
Normal	53	72.8	N.S.
Impaired	4	75.0	
Field size			
$\leq 25 \text{ cm}^2$	35	71.4	N.S.
$> 25 \text{ cm}^2$	22	75.6	
Anterior commissure			
Free	43	67.5	N.S.
Involved	14	85.1	

5YDFS : 5-year disease-free survival

N.S. : Not significant

around 80 to 90%.^{1-3, 9-19, 21)} Our local control rate of 63.8% is much lower compared with these results. One possibility is that our staging procedures were not adequate to select T1 lesions and some higher stage cases may have been understaged. Larynx CT or MRI were not routinely checked for staging. Fletcher et al.⁷⁾ indicated that the major causes of radioresistance of laryngeal cancer were the inappropriate evaluation of tumor extension or deep invasion and the problem of radiation technique such as

insufficient dose or field. The extent of bulky lesion tends to be inappropriately evaluated because it is sometimes difficult to obtain detailed information by laryngoscopy or even by fiberoptic. Ultimate local control rate of 92.3% in our study is, however, comparable with those results because our results of salvage surgery were good.

Akine et al.²⁰⁾ reported anterior commissure involvement was associated with lower control rates. However, Fletcher et al.⁷⁾ showed this not to be the case. We did not find anterior commissure involvement to impact local control. Poor local control rates in some series for lesions with anterior commissure extension might be secondary to understaging or inadequate radiation dose at the anterior commissure due to improper treatment technique. A prominent feature of 6 MV X-rays is the longer distance of secondary electrons to attain an electronic equilibrium in comparison with photons of lower energies. Inadequate build-up of electrons may be found beneath the skin of the neck and at the surface of the vocal cord. The vocal cords are located on the surface of an air cavity within the soft tissue. At our institution all early stage vocal cord lesions were treated with adequate dose distribution and build-up at the anterior commissure. As stated previously, patients were contoured and computer-assisted planning was used with or without wedges to insure adequate dose distribution within the tumor volume. Doses were prescribed to a gross tumor volume plus adequate margin with a minimum daily dose of 2 Gy. In our analysis patients with posterior lesions had a superior disease-free survival than those with anterior lesions. We could not find any reasonable explanation for this. One thing we would like to comment is that no patient with posterior cord involvement failed, which might mean that there was no underdose.

Geographic miss may, of course, be the cause of local failure. Lustig et al.²³⁾ reported no correlation between increasing field size and local control in the Patterns of Care study. Horwood et

al.^{8, 22)} reported that field size was an important prognostic factor for local control in early glottic cancer. It did not appear that field size impacted local control in our patients. All initial recurrences noted were in field and recurred 2-71 months after initial radiotherapy.

T stage or cord mobility in our analysis was not found to influence local control. Other authors^{17, 18)} have demonstrated vocal cord mobility to be significantly related to local control with irradiation. We thought there might be selection factors in T2 disease, that is, we had selected relatively early T2 lesions for radiotherapy. We included T2 lesions which had a ventricular involvement only or impaired cord mobility for radiotherapy and excluded those with a subglottic extension. Again some T1 lesions might be understaged due to inadequate staging procedures.

In conclusion, considering the high percentage of voice preservation with initial radiotherapy, radiotherapy should be the first choice treatment of stage I glottic carcinoma.

REFERENCES

1. Mendenhall WM, Parsons JT, Mancuso AA, Stringer SP, Cassisi NJ. Larynx. In Principles and Practice of Radiation Oncology, 3rd ed, Perez CA, Brady LW, Philadelphia, JB Lippincott, 1998; pp 1069-1093
2. Sessions RB, Harrison LB, Forastiere AA. Cancer of the Head and Neck. In Cancer: Principles and Practice of Oncology, 5th ed, DeVita VT, Hellman S, Rosenberg SA, Philadelphia, JB Lippincott, 1997; pp 802-829
3. Wang CC. Carcinoma of the larynx: In Radiation Therapy for Head and Neck Neoplasms, New York, Wiley-Liss Inc, 1997; pp 221-228
4. American Joint Committee on Cancer (AJCC). Larynx. In Manual for Staging of Cancer, 5th ed., Philadelphia, JB Lippincott, 1997; pp 41-46
5. Lee ET. Statistical methods for survival data analysis. California: Belmont 1980;75-131
6. Armitage P. Statistical methods in medical research. Oxford: Blackwell 1971;131-138
7. Fletcher GH, Goeptfert H. Larynx and pyriform

- sinus, In *Textbook of Radiotherapy*, 3rd ed, Fletcher GH, Philadelphia, Lea & Febiger, 1980; pp 330-363
8. **Horwood AR, Hawkins NV, Rider WD, Bryce DP.** Radiotherapy of early glottic cancer-I. *Int J Radiat Oncol Biol Phys* 1979; 5:473
 9. **Amornmarn R, Prempre T, Viravathana T, Donavanik V, Wizenberg MJ.** A therapeutic approach to early vocal cord carcinoma. *Acta Radiol Oncol* 1985; 24:321
 10. **Woodhouse RJ, Quivey JM, Fu KK, Sien PS, Dedo HH, Phillips TL.** Treatment of carcinoma of the vocal cord: A review of 20 years experience. *Laryngoscope* 1981; 91:1155
 11. **Mendenhall WM, Parsons JT, Million RR, Fletcher GH.** T1-T2 squamous cell carcinoma of the glottic larynx treated with radiation therapy: Relationship of dose-fractionation factors to local control and complications. *Int J Radiat Oncol Biol Phys* 1988; 5:1267
 12. **Wang CC.** Treatment of squamous cell carcinoma of the larynx by radiation. *Radiol Clin North Am* 1978; 16:209
 13. **Mills ED.** Early glottic carcinoma: Factors affecting radiation failure, results of treatment and sequelae. *Int J Radiat Oncol Biol Phys* 1979; 5:811
 14. **Pene F, Fletcher GH.** Results in irradiation on the in situ carcinomas of the vocal cords. *Cancer* 1976; 37:2586
 15. **Schwaibold F, Scariato A, Nunno M, et al.** The effect of fraction size on control of early glottic cancer. *Int J Radiat Oncol Biol Phys* 1988; 14:451
 16. **Teshima T, Chatani M, Inoue T.** Radiation therapy for early glottic cancer (T1N0M0): I. Results of conventional open field technique. *Int J Radiat Oncol Biol Phys* 1989; 17:1199-1202
 17. **Sakata K, Aoki Y, Karasawa K, et al.** Radiation therapy in early glottic carcinoma: Uni- and multivariate analysis of prognostic factors affecting local control. *Int J Radiat Oncol Biol Phys* 1994; 30:1059-1064
 18. **Fein DA, Mendenhall WM, Parsons JT, Million RR.** T1-T2 squamous cell carcinoma of the glottic larynx treated with radiotherapy: A multivariate analysis of variables potentially influencing local control. *Int J Radiat Oncol Biol Phys* 1993; 25: 605-611
 19. **Rudoltz MS, Benammar A, Mohiuddin M.** Prognostic factors for local control and survival in T1 squamous cell carcinoma of the glottis. *Int J Radiat Oncol Biol Phys* 1993; 26:767-772
 20. **Akine Y, Tokita N, Ogino T, et al.** Radiotherapy of T1 glottic cancer with 6 MeV X-rays. *Int J Radiat Oncol Biol Phys* 1991; 20:1215-1218
 21. **Cellai E, Chiavacci A, Olmi P.** Causes of failure of curative radiation therapy in 205 early glottic cancers. *Int J Radiat Oncol Biol Phys* 1990; 19: 1139-1142
 22. **Harwood AR, Beale FA, Cummings BJ, Keane TJ, Payne D, Rider WD.** T2 glottic cancer: An analysis of dose-time volume factors. *Int J Radiat Oncol Biol Phys* 1981; 7:1501
 23. **Lustig RA, Maclean CJ, Hanks J, Kramer S.** The Patterns of Care Outcome Studies: Results of the national practice in carcinoma of the larynx. *Int J Radiat Oncol Biol Phys* 1984; 10:2357-2362

= 국문 초록 =

조기 성문암의 방사선 치료 결과

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목적 : 조기 성문암의 방사선 치료 후 생존율, 실패 양상, 그리고 예후 인자에 대해 분석하였다.

대상 및 방법 : 1985년 6월부터 1992년 11월까지 방사선 치료를 위해 의뢰된 57례의 성문암 환자를 대상으로 후향적 분석을 실시하였다. 연령 분포는 17세부터 71세까지 광범위했고 (중앙값 39세), 남자 55례와 여자 2례로 남성에서 호발하였다. 방사선 치료는 6 MV X-ray를 이용하여 1회 선량 2 Gy씩, 주 5회, 총선량 66 Gy를 조사하였다.

결과 : 방사선 치료에 대한 반응은 완전 관해 89.5% (51/57), 부분 관해 혹은 무반응 10.5% (6/57) 였다. 51례의 완전관해 환자 중에서 7례의 재발이 관찰되었고 7례 모두 수술로 구제되었다. 부분 관해 혹은 무반응 6례 중 4례에 대하여 구제수술을 시행하였고 2례에서는 수술을 시행하지 못하였다. 구제수술을 시행한 4례 중 3례가 구제되었고 1례는 다시 국소재발하였다. 3년 및 5년 무병생존율은 각각 72.9% 및 63.8%였다. 병소의 위치에 따른 5년 무병생존율은 후방인 경우 85.5%, 전방인 경우 61.6%였다 ($p < 0.05$). 방사선치료에 대해 부분 관해 혹은 무반응을 보인 5례를 포함하여 13/57 (22.8%) 례의 치료 실패가 관찰되었고 그 중 10/13 (76.9%) 례가 수술로 구제되었다. 최종 5년 국소제어율은 92.3%였고 전체적으로 47/57 (82.5%) 례에서 음성을 보존할 수 있었다.

결론 : 높은 음성 보존율을 고려하면 초기 성문암에서 방사선치료가 우선적으로 고려되어야 한다.