

The Result of Radiotherapy in Glottic Cancer

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A retrospective analysis of 29 patients with glottic cancer, treated at the Department of Therapeutic Radiology, Seoul National University Hospital. 97% of the patients was male. Of the 29 patients, stage T₁N₀M₀ comprised 31%, T₂N₀M₀ 52%, and stage T₃N₀M₀ 14%. Local control rate with radical radiotherapy was 78% for stage T₁N₀M₀, 60% for stage T₂N₀M₀, and 50% for stage T₃N₀M₀. 57% of the patients with the radiation failure was salvaged by surgery.

The overall 3 year survival rate was 89% for the T₁N₀M₀, 80% for stage T₂N₀M₀, and 50% for stage T₃N₀M₀. Among the survivors: 88% of T₁N₀M₀, 75% of T₂N₀M₀, and 50% T₃N₀M₀ had an intact larynx and natural voice.

It is concluded that radiotherapy is a highly effective method as the primary treatment of the early glottic cancer, emphasized on preserving of the larynx and natural voice.

Key Words: Glottic cancer, Radiotherapy, Voice preservation.

INTRODUCTION

Radiation therapy is a highly effective method as the primary treatment in early glottic cancer.

Patients with glottic cancer tend to be found at early stage because of hoarseness. Because of its anatomical location it is easy to do the biopsy and observe the response to treatment. Furthermore, the true vocal cord has no capillary lymphatics. So, the incidence of the regional and distant metastasis is very low.

Patients who failed in the radiation therapy are frequently salvaged by surgery. However, there is a controversy about the management of T₃ glottic cancer.

This paper presents the results of glottic cancer treated at the Department of Therapeutic Radiology, Seoul National University Hospital from March, 1979 to September, 1982.

METHODS AND MATERIALS

35 patients with the carcinoma of the vocal cord were seen at the Department of Therapeutic Radiology, Seoul National University Hospital from

March 1979 to September. Of the patients, 4 patients were referred for postoperative radiotherapy after partial or total laryngectomy, and 2 patients who were treated incompletely were excluded from this analysis.

The minimum follow up was 3 years with a range of 3 to 6.5 years and no patients were lost during the follow up.

The patients were staged according to the AJC TNM system (Table 1). Table 2 shows their distribution as regards age, sex, histologic type, and stage.

All patients were treated with a Co⁶⁰ unit. The treatment was given by lateral opposed open and wedge fields measuring 5×5 or 6×6cm².

A tumor dose of 6000-7000 rad was delivered in six to seven weeks at a rate of 1000 rad divided into five fractions per week with NSD of 1670-2050 ret.

Survival is calculated from the first day of the radiation treatment. Kaplan-Meier method was used to calculate the survival rate. Some direct comparisons of pairs of survival data were done using logrank test.

RESULTS

Of the 9 patients with T₁ lesion, 78% (7/9) were NED following radiation therapy at three years. One patient was successfully salvaged by surgery. Therefore, an overall NED rate of 89% was achieved.

Of the 15 patients with T₂ lesion, 9 or 60% were NED following radiation therapy at three years. Three patients were successfully salvaged by surgery. Therefore an overall NED rate of 80% was achieved. There was no statistically significant difference in the survival rate between T₁N₀ and T₂N₀ lesion.

The 4 patients with T₃N₀ lesion had a 50% three year recurrence free survival. (Table 3. Fig. 1.)

Table 1. Glottic Cancer (AJCC)

TIS	Carcinoma in situ
T1	Confined to vocal cord(s), normal mobility, includes involvement of anterior or posterior commissures
T2	Supraglottic and/or subglottic extension, normal or impaired cord mobility
T3	Confined to larynx with cord fixation
T4	Massive, with thyroid cartilage destruction and/or extension beyond the larynx

Table 2. Patient Characteristics

Sex			
	F	1	(3%)
	M	28	(97%)
Age			
	Median		56.0 year
	Minimum		35.0 year
	Maximum		74.0 year
Histologic type			29
	Squamous		29
	W/D		14
	M/D		11
	P/D		2
	Not specified		2
Stage			
	T1 N0 M0		9
	T2 N0 M0		15
	T3 N0 M0		4
	T4 N1 M0		1

Of the 11 patients who failed to respond to radiation therapy, 4 refused operation, and 4 were successfully salvaged by surgery.

Of the 22 patients who survived without evidence of disease, 16 or 73% retained larynx or normal voice.

The median time to recurrence in T₁, T₂ and T₃ lesions were 17.3, 17.8 and 3.2 months respectively.

Table 4 gives the distribution by the stage and pathological grade.

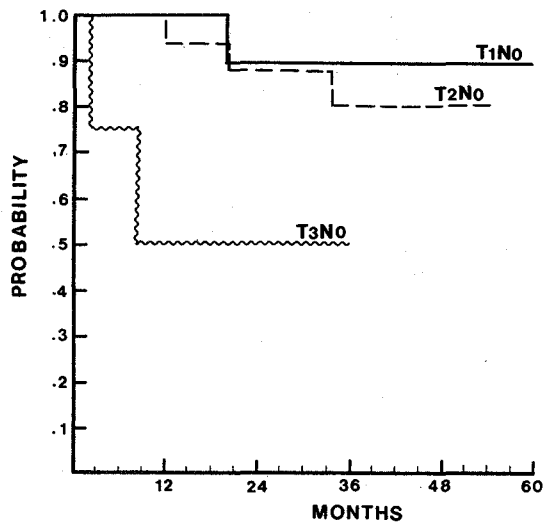


Fig. 1. Glottic Cancer: 3 Year NED Survival by Stage

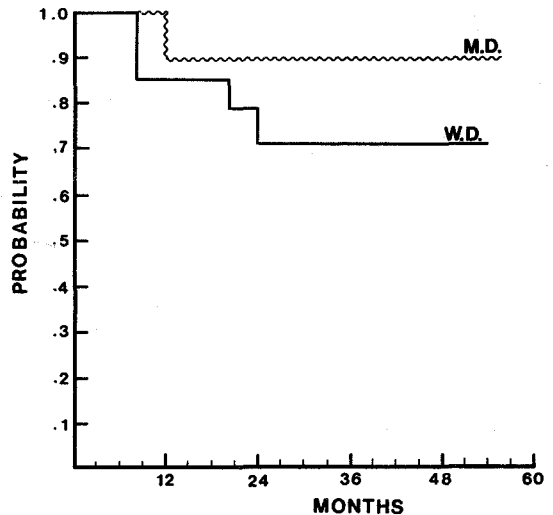


Fig. 2. Glottic Cancer: 3 Year NED Survival by Histologic Grade

Table 3. Three-Year NED Rates Following Radiation Therapy for Glottic Cancer

	Number of Cases	NED After RT	Surgical Salvage #NED/#Attempted	Overall NED	NED patients with Retained Larynx
T ₁ N ₀ M ₀	9	7/ 9 (78%)	1/2 (50%)	8/ 9 (89%)	7/ 8 (88%)
T ₂ N ₀ M ₀	15	9/15 (60%)	3/5 (60%)	12/15 (80%)	9/12 (75%)
T ₃ N ₀ M ₀	4	2/ 4 (50%)	0	2/ 4 (50%)	1/2 (50%)
T ₃ N ₁ M ₀	1	0/ 1	0	0	0
Total	29	18/29 (62%)	4/7 (57%)	22/29 (76%)	17/22 (77%)

3 year NED survival rates for well differentiated and moderately well differentiated groups were 71 % and 90 % respectively (Fig. 2). 3 year NED survival rates for patients over the age of 60 years and for those below the age of 60 years were 77 % and 84 % respectively (Fig. 3).

DISCUSSION

Heredity, voice abuse, alcohol, tobacco, asbestos, and poor hygiene are recognized as important causal factors for laryngeal cancer.¹⁾

Carcinoma arising from the true vocal cords produces hoarseness at a very early stage. Pain or sore throat is a symptom of advanced lesions. Airway obstruction producing respiratory distress is a feature of advanced lesions and is rarely seen even with bulky early stage lesions.

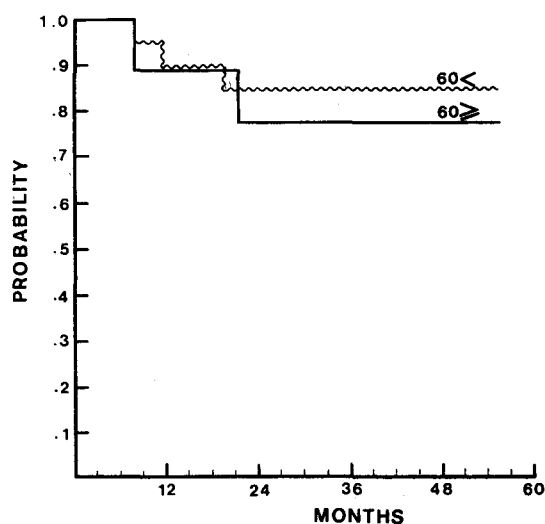
The laryngeal surfaces of the epiglottis and vocal cords are lined with stratified squamous epithelium and the remainder of the larynx is lined with pseudostratified ciliated columnar epithelium. Majority of glottic cancers arise from the free margin, superior surface, and inferomedial surface of the vocal cords. Therefore squamous cell carcinoma is common.²⁾ Most carcinoma of the vocal cord are either well differentiated or moderately well differentiated.³⁾

When carcinomas of the vocal cord are diagnosed, about two thirds are confined to one cord. The anterior portion of the cord is the most common site. While the growth of cancer arising in the true vocal cord is initially limited by the thyroid cartilage anteriorly, cancer can easily grow into the pyriform sinus and cricoarytenoid region posteriorly as there is no effective barrier. It is for this reason that cancers arising in the anterior half of the larynx have much better prognosis than those arising in the posterior half of the larynx. The conus elasticus acts initially as a barrier to subglottic extension.²⁾

Table 4. Stage and Histologic Grade

	W/D	M/D	P/D	Not Specified
T ₁ N ₀ M ₀	2 (1)	5 (1)		2 (0)
T ₂ N ₀ M ₀	9 (3)	4 (2)	2 (1)	
T ₃ N ₀ M ₀	2 (1)	2 (1)		
T ₃ N ₁ M ₀	1 (1)			

* Numbers in parenthesis are number of recurrence.

**Fig. 3.** Glottic Cancer: 3 Year NED Survival by Age

As glottic cancer enlarges, it extends into the ventricle, false cord, vocal process of the arythenoid, and subglottic region. Infiltrative lesion invades the cricoarytenoid joint, thyroarytenoid muscle, and laryngeal nerve, eventually reaches the thyroid cartilage.³⁾

The incidence of clinically positive nodes at diagnosis approaches zero for T₁ lesions and 2% to 5% for T₂ lesions. The incidence of neck metastasis increases to 20% to 30% for T₃ and T₄

lesions. Supraglottic spread is associated with metastasis to the jugulodigastric nodes. Invasion into the anterior commissure and subglottis is associated with midjugular, lower jugular, and midline pretracheal node involvement.

Cancer of the larynx is mainly a disease of the middle aged men. Only about 10 percent of the patient are women. The mean age is 61 years old. Survival rate for the men over 60 years is significantly higher than that for the men under 60 years.^{4,5)} Although the survival rate of well differentiated groups is lower than that of moderately well differentiated ones and the survival rate of patients over the age over 60 years was lower than the survival rate of patients below the age of 60 years, these results may be due to the small sample size in our study. Women with glottic cancer respond better than men to radiation treatment. Even though the sample size was small, the present study showed a high incidence of laryngeal cancer in the sixth decade (38%) and male predominance (97%). The failure rates by the degree of differentiation were 24% in the well-differentiated, 41% in the moderately well differentiated, and 67% in the poorly differentiated group.⁶⁾

As 20% of poorly differentiated tumors developed regional metastatic lymph nodes, the use of prophylactic neck irradiation is indicated for poorly differentiated tumors.⁶⁾

External beam irradiation and surgery are the primary modes of treatment available. The radiation therapy group had better ratings than the surgery group, in terms of preservation of volume, pitch, ability to communicate, quality, rate of speech, and flow of speech.⁷⁾ Radiation therapy is the initial choice of treatment for early lesions, with operation reserved for salvage of irradiation failures. The mainstay of treatment for advanced lesion is total laryngectomy with or without preoperative or postoperative irradiation.

For T₁ lesion, the field size was 5 × 5cm and a total dose of 6000-7000 rad was given in 30-35 fractions, 180-200 rad/fraction, 2 fields a day, 5 days a week (1670-2050 ret). Patients with T₁N₀ glottic lesion had 90% three year disease free survival and 97% after salvage surgery.⁸⁾ The lesions arising from the anterior two thirds of the cord(s) and/or anterior commissure had a better results than the lesions arising from the posterior cord with 3 year NED rates of 92 and 85% respectively. Surgical salvage rates were 81% and 72% respectively. The net overall NED rate were 98% and 93%.⁸⁾

There are many possible explanations for the failure of radiation therapy to control approximately 10% of T₁ glottic cancer. Inadequate evaluation of the extent of the lesion, low dose for the volume of cancer, and specific location of the tumor unfavorable to radiation therapy can be considered. However, there is considerable evidence to suggest that in animals and men one of the major causes for local failure is hypoxia of tumor cells. In order to improve the results of treatment in this disease, innovative prospective studies using radiosensitizers or neutrons need to be designed.^{4,9)}

For T₂ lesions, the field size was 6 × 6cm and a total dose of 6000-7000 rad was given in 30-35 fractions, 180-200 rad/fraction, 2 fields a day, 5 days a week (1670-2050 ret). Patients with T₂N₀ glottic lesion had 65-75% three year disease free survival and 85% after salvage surgery.^{5,8,10)}

According to the AJCC classification, extension of the tumor outside the true cord is the main criteria for T₂ staging, and impairment of vocal cord mobility does not result in a subdivision within this group.¹¹⁾ Several authors have emphasized the importance of this distinction and some have proposed to subdivide T₂ into T₂A (extension) and T₂B (impaired mobility),^{12,13,14)} where T₂A lesions would have a prognosis close to T₁ lesions and T₂B lesions would have an outcome close to T₃ lesions.¹²⁾

The adverse prognostic influence of impaired mobility has been largely eliminated by surgically treating the patients with containing impaired mobility after initial radiotherapy.¹³⁾

Subglottic extension was once regarded as a contraindication for irradiation in some centers.^{15,16)} As tumor spreads to the long distance submucosally once it extends into the subglottic space, it is essential that large radiation fields are used. Now presence or absence of subglottic extension has no influence on prognosis.^{10,12,13)}

The choice of treatment modalities in T₃ glottic cancer is controversial at present, even though radical laryngectomy is the mainstay of the management. Some authors advocate surgery as the primary treatment while others advocate radiation therapy with rescue surgery for patients with local failure or insufficient regression of the lesion after radiotherapy.

Many patients with T₃ glottic cancer were treated with radiotherapy because of patients' fear of surgery or preexisting contraindication to surgery. This negative patient selection might have adversely influenced the results of radiation therapy compared

to those of surgery.¹⁷⁾ Local control significantly improved when a tumor dose of greater than 1700 ret as compared to less than 1650 ret was given. The complication of radiation and the morbidity from salvage operation in patients treated with doses of 1700-1750 ret were acceptably low.^{10,18)} The general public's fear of laryngectomy and its effect on the quality of life is well-illustrated in a article by McNeil et al. Volunteers with T₃ glottic cancer were given two treatment options primary laryngectomy with loss of laryngeal speech producing a 60% 3 year survival rate, versus primary radiation therapy with preservation of the larynx in the majority producing lower survival rate of 30-40%. Despite the lower survival rate, 20% of the volunteers chose radiation with preservation of laryngeal function.¹⁹⁾ Most of the recurrences were within 3 years. Therefore close follow up is necessary to detect the early recurrence within 3 years. Early diagnosis of recurrence is likely to improve the results of surgical salvage. Results of initial radiation therapy with surgical salvage improved with adequate treatment ports, adequate dose, and close follow up, yielding equivalent survival rate to that of primary surgery.^{5,20)} At present, increasing number of patients with T₃ glottic cancer are treated by radiotherapy followed by surgical salvage.

The criteria of T₃N₀ laryngeal cancers most suitable for radiation therapy have yet to be defined. The bulky glottic lesion with vocal cord fixation caused by mechanical impedance rather than deep infiltration, the exophytic supraglottic lesion with minimal hypopharyngeal extension and without vocal cord fixation, old age, and female sexuality are some of the criteria in favor of radiation therapy.^{4,5)}

The whole neck including the upper, middle and lower deep cervical lymph nodes were treated for T₃ glottic cancer; The superior border of the field included the whole epiglottis, the inferior border was a minimum of 3cm below the known extent of the tumor, the posterior border was anterior to the spinal cord, and the anterior border was in front of the skin of the neck. The minimum dose for T₃ glottic cancer was 1700 ret (5500 rad in 24 fractions in five weeks). The optimal dose for T₃ glottic cancer was 2130 ret (7500 rad in 33 fractions in 6½ weeks). 3 year NED rate was 45-55% after radiation therapy. Overall 3 year NED rate was 70-80% after salvage operation.^{5,20)}

The mainstay of treatment of T₄ glottic cancer is radical laryngectomy and postoperative irradiation.

Primary site failure is the most common type of

failure. So more radical local treatment modalities are needed. There are both acute and chronic complication of radiation. Acute ones are increased hoarseness, mucositis, edema, and desquamation. Chronic ones are persistent laryngeal edema, and perichondritis. But the larynx tolerates well upto 2040 ret.²¹⁾ Secondary cancer is reported frequently but its mechanism is not known yet.

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== 국문초록 ==

성문암의 방사선치료

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조 문 준 · 김 일 한 · 박 찬 일

성문암은 술, 담배가 주 원인적 인자로 밝혀져 있다. 성문암은 원목소리 등으로 조기발견이 용이하며 대부분 분화도가 좋은 편평상피암이고 해부학적 위치상 조직생검 및 치료경과 관찰이 용이하며, 성문에는 임파절이 없으므로 전이가 적다. 국소 치료인 방사선치료와 수술이 치료의 주종을 이루며 방사선치료는 음성보전 측면에서 효과적이므로 초기병변에는 방사선치료를 진행된 병변의 경우 수술 혹은 수술 및 방사선 복합요법을 사용하고 있다.

저자들은 1979년 3월부터 1982년 9월까지 서울대학교병원 치료방사선과에서 성문암으로 치료받은 환자들을 추적 조사하여 다음과 같은 결과를 얻었다.

1. 방사선치료후 3년 무병생존율이 T_1N_0 : 78% T_2N_0 : 60% T_3N_0 : 50%
2. 구제적 수술후 3년 무병생존율이 T_1N_0 : 89% T_2N_0 : 80% T_3N_0 : 50%
3. 재발은 대개 3년이내에 하였다.