Treatment Result in Advanced T3 and T4 Glottic Carcinoma; YUMC Experience

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Between January 1980 and September 1988, 68 patients with advanced T3 & T4 glottic carcinoma were treated with RT and surgery/RT in the Department of Radiation Oncology, Yonsei Cancer Center and ENT, Yonsei University College of Medicine.

The mean age was 60 years old (range 33 to 79 years old). The 34 patients were treated with irradiation alone, and the remaining 34 patients with surgery and irradiation. Initial nodal presentation was 37% (25/68); 31% (11/34) in RT alone group and 41% (14/34) in combined treatment group. The minimum follow-up was 2 years.

The local control rate after treatment was 47% in RT alone group and 65% in combined treatment group; 57% for node negative and 27% for node positive patients treated with RT alone; 65% for node negative and 64% for node positive patients treated with combined treatment. The treatment failure was observed in 30 patients; 14 patients for primary local failure, 6 patients for regional nodal failure, 6 patients for local and regional failure,26 patients for primary failure and/or distant metastasis, and 2 patient for regional failure and/or distant metastasis. The overall 5-year survival rate was 57%; 37% in RT alone group and 76% in combined treatment group; 55% for node negative and 20% for node positive patients treated with RT alone; 73% for node negative and 77% for node positive patients treated with combined treatment.

In conclusion, the combined treatment groups in the treatment of advanced T3 and T4 glottic cancer showed the better results in local control rates and 5-year actuarial survival rates than RT alone group. We suggest that total laryngectomy and postoperative RT in the most patients of advanced glottic cancer were performed. However, in cases of node negative patints, RT alone is prefer as a treatment modality over combined surgery and RT since the treatment results were comparable and furthermore functional preservation could be achieved.

Key Words: Advanced glottic cancer, Radiation therapy

INTRODUCTION

Most patients with T3 & T4 lesions of the glottic cancer have been treated by total laryngectomy, either alone or in combination with irradiation[1,2,5]. Controversy exists in the literature over the best management policy for advanced T3 & T4 glottic cancer between the advocates for primary radiation therapy reserving surgery for salvage of persistent or recurrent disease and those who advocate primary surgery with or without pre or postoperative radiation therapy[2,4,5,6,7,10,11,13].

Especially in T3 glottic cancer, encouraging results have also been reported using radiation therapy alone with local control rates of approximately 50% and 5 year cure rates similar to those observed with surgery[1~8]. The purpose of this paper is to report the results of treatment with RT alone and surgery/RT at the Yonsei University College of Medicine and to assess the role of primary RT for functional voice preservation as a treatment of advanced T3 & T4 glottic cancer.

METHODS AND MATERIALS

This is the retrospective analysis of 68 patients with advanced T3 & T4 glottic cancer treated with RT alone and surgery/RT at the Yonsei University College of Medicine and Yonsei Cancer Center from January 1980 to December 1988.

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The patients were clinically staged according to the recommendations of the American Joint Committee (AJC). The minimum follow-up was 2 years with a range of 2 to 8 years. 54 (79%) of 68 patients were able to follow-up. The patients were contained to this study only when it did not exist in distant metastasis at the initial admission.

Histologic diagnoses were carried out by laryngeal microsurgery (LMS) with biopsy of primary lesion, and all 68 cases were confirmed as epidermoid carcinoma of the larynx including 1 case of epidermoid spindle cell type.

Age, sex, pathology of 68 patients are listed in Table 1. Initially, neck node positive patients were 37% (25/68); RT alone group was 32% (11/34) and surgery/RT group was 41% (14/34) (Table 2).

All patients were treated with RT alone or surgery/RT (Table 3). Thirty-one patients were treated with single or multiple regimen chemotherapy using bleomycin, cis-platin, vincristin (vinblastin) and 5-FU as a induction or salvage treatment modalities.

All patients were treated with the Co-60 teletherapy unit cr 4-MV linear accelerator. Radiation treatment techniques have evolved from opposed lateral portals using opened field to opposed lateral portals using wedged filter technique.

Thirty-four patients were treated with radiation therapy alone. 30 of 34 patients were delivered in a daliy fraction of 200 cGy with a treatment of 5 days per week to a total dose of more than 6000 rad using a continuous course technique. 2 of 34 patients were treated with twice-a-day fractionation receiving 150 cGy/fraction to a total dose of 6600 cGy and 7500 cGy using continuos-sourse technique. Treatment field size was 10×10 to 11×11 cm for primary tumors and cervical nodes, and through a single anterior portal including lower neck nodes in a daily fraction size 200 cGy , treating 5 days per week, up to 4400~5000 cGy, this was followed by a reduced field to a primary site and upper neck nodal area in order to exclude the spinal cord,

Table 1. Patients Characteristics

		RT alone	Surgery/RT
No. of patients		34	34
Age	Mean	61	58
	Range	(41–79)	(33–73)
Sex	(M : F)	33 : 1	33:1
Pathology grade			
WD epidermoid		11	15
MD epidermoid		6	12
PD epidermoid		2	3
Unknown		15	3*
Chemotherapy			
No		17	20
Yes		17	14
Tracheostomy		5	4

* included 1 case of epidermoid spindle cell type.

Table 2. Nodal Presentation at Diagnosis

	RT alone		Surgery/RT	
	No	N+ (%)	No	N+ (%)
T3	14	6 (30)	9	9 (50)
T4	9	5 (36)	11	5 (31)
Total	23	11 (32)	20	14 (41)

Table 3. Treatment Modality

	RT alone	Surgery/RT
Chemotherapy		
Single	3	1
Combination	14	13
RT field size (cm^2)	112.4 ± 24	121.1 ± 86
RT dosage (Gy)		
Less than 60	4	14
More than 60	30	20
Surgery		
TL*	0	19
TL + RND#	0	15

* TL ; total laryngectomy
\# RND ; radical neck dissection

Table 4. Local Control Rates

	RT alone (%)	Surgery/RT (%)	P value
T3/4 N0	13/18 (72)	13/17 (76)	> 0.05
T3/4 N+	3/ 8 (38)	9/11 (81)	< 0.05
Total	16/26 (61)	22/28 (79)	> 0.05

delivered with the additional dose of 1500~2000 cGy.

Thirty-four patients were treated with total laryngectomy and/or one or both radical neck dissection followed by postoperative irradiation. Two of 14 patients with positive neck node were treated with total laryngectomy alone following postoperative irradiation ot total dose of 6000 rad. All patients were treated with continuous-course technique, up to 5000~6500 cGy.

The local control of the primary lesion and the cervical node metastasis following radiation therapy were assessed at a 1 year follow-up after the completion of treatment in 54 patients capable to follow-up. This study was finished at the time of local recurrence or death. Survival is calculated from the day of the first radiation treatment or from the day of surgery if surgery was performed.

All survival data were calculated using the acturial method, because patients were followed for varying lengths of time and this method is the most accurate way to utilize all information on every patients.

RESULT

Initial node presentation at the diagnosis in advanced T3 and T4 glottic cancer is shown in Table 2. In previously reports, it reported that the cervical node metastasis was about 10%, and our results were 37%, this was higher than others.

Control of disease at the primary site and the neck is shown in Table 4. The local control rates of T3/4 NO patients treated with RT alone were 72% (13/18) and it was comparable to 76% (13/17) of T3/4 NO patients treated with surgery/RT ($p>0.05$). Also the local control rates of T3/4 N+ patients treated with RT alone and surgery/RT were 38% (3/8) and 81% (9/11), respectively ($p>0.05$). Overall response rates were 61% in RT alone group and 79% in surgery/RT group, and so the slight higher response rate was seen in surgery/RT group ($p>0.05$).

Analysis of treatment failure pattern between two groups is shown in Fig. 1. Fig. 1 shows the most patients treated with RT alone and/or surgery/RT were locoregional failure. Two of patients treated

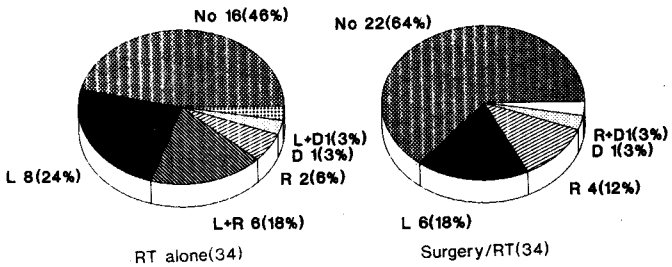

Fig. 1. Treatment failure patterns.

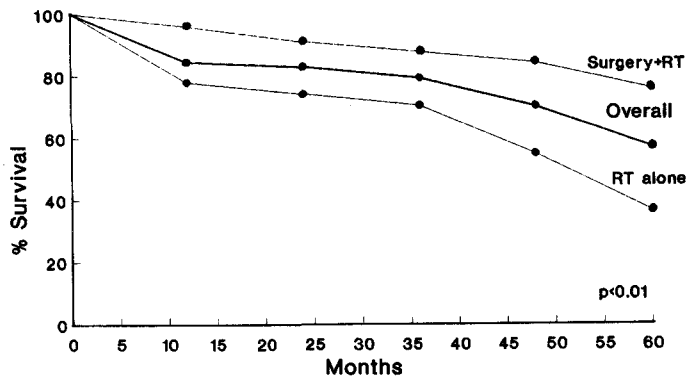

Fig. 2. 5-Year survival rates.

with RT alone and/or were stomal site recurrence and all six patienst with local failure were surgical margin failure. There were 4 distant metastases. Overall distant failure rates were 6% (4/68). Two were distant metastasis only, and also it was lung and bone. Treatment failure patterns between two groups were no difference. This failure patients were treated with salvage surgery, chemotherapy and re-irradiation, but the analysis according to salvage treatment were not performed.

The overall 5-year actuarial survival rates were 57%; surgery/RT group was 76% and RT alone group was 37% in Fig. 2. There was difference significantly ($p<0.01$). Fig. 2 shows surgery/RT in T3 and T4 glottic cancer were superior results than RT alone group. Therefore we could be known that surgery and postoperative RT in advanced glottic cancer was good treatment modality. But for the purpose of functional voice preservation, we were analyzed about the role of primary radiation therapy in the advanced T3 and T4 glottic cancer, especially node negative patients (Fig. 3 and 4).

Fig. 3 shows 5-year actuarial survival rates in node negative patients, and there was no difference significantly (surgery/RT vs. RT alone=73% vs. 55%, $p>0.05$). But Fig. 4 shows 5-year actuarial survival rates in node positive patients, and there was difference significantly (surgery/RT vs. RT alone=77% vs. 20%, $p<0.01$).

Table 5 is shown about 5-year survival rates following chemotherapy and tracheostomy, and it is not affected to survival although it was impossible to assess the precise results. Moreover, it was no evidence to reduce the local control and 5-year survival rates by chemotherapy.

Therefore, we are recommanded the radiation therapy as the primary treatment modality in node negative patients of advanced T3 and T4 glottic cancer respectively.

DISCUSSION

The purposes of this study was to analyze the results treated with RT alone and surgery/RT in the

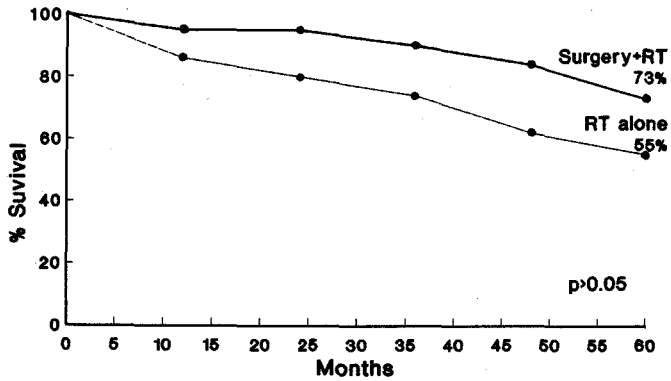

Fig. 3. 5-Year survival rates in NO patients.

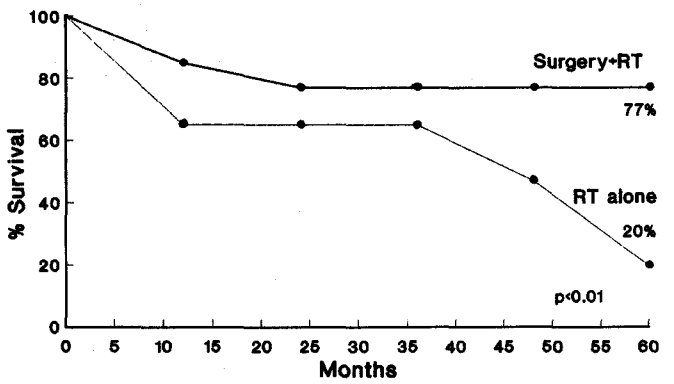

Fig. 4. 5-Year survival rates in N+ patients.

Table 5. 5-Years Survival Rates Following Chemotherapy & Tracheostomy

	RT alone (%)		Surgery/RT (%)	
Chemotherapy				
No	41.4		70.7	
Yes	28.2		83.4	
		p>0.05		p>0.05
Tracheostomy				
No	43.1		78.0	
Yes	26.0		67.0	
		p>0.05		p>0.05

patients of advanced T3 and T4 glottic cancer, retrospectively, and to determine what it is the role of initial radiation therapy in advanced glottic cancer. Recently, the radiation treatment in early and late glottic cancer was prefer to surgery as initial treatment modalities for the preservation of functional voice[2,4,7,10,11,13]. Especially, radiation therapy was a highly effective method as the primary treatment of the early glottic cancer, emphasized on preserving of the larynx and natural voice[16]. Therefore we were selected the cases of comparable results of survival and local control when the primary radiation treatment in the advanced glottic cancer was performed.

Most patients with advanced glottic cancer were treated by total laryngectomy, either alone or in combination with irradiation[1,2,5]. Skolnik et al reported that surgery is the treatment of choice for advanced glottic cancer. The 5-year survival end results are 49% for surgery and 30% for radiation therapy. Lymph node metastasis affects the end results significantly. In patients without lymph node involvement, the overall 5-year survival rate is 70%. When nodal metastasis is present, the survival rate drops to 30%[6]. Other report was performed to hemilaryngecomy as a surgical treatment. Lee et al[12] reported the results of 30 patients treated with laryngeal radiation after hemilaryngectomy. Ultimate local control rates including 3 patients treated with salvaged total laryngectomy were 77%. Lesinski et al[9] was reported the results of the 18 patients treated with hemilaryngectomy. The ultimate 5-year survival rates were 85%. True vocal cord fixation in the advanced glottic cancer is generally caused by invasion of the vocalis muscle and thus may be well encompasssed by a hemilaryngectomy.

Especially, encouraging results in T3 glottic cancer had been reported using radiation therapy with local control rates of approximately 50% and 5-year cure rates similar to those observed with surgery[1~8]. In T3 glottic cancer, there is a singificant reduction in local recurrence in those patients who were treated to greater than 1700 ret as compared to less than 1650 ret. No advantage is apparent when the dose is increased beyond 1750 ret[11]. And the patients of T4 glottic cancer showed the results treated with irradiation alone were worse than surgery alone or postoperative adjuvant irradiation[1,2] and our results were similar. Local control rates were 37% and 76%. Therefore, total laryngectomy and postoperative irradiation as a treatment modalities of advanced T3 and T4 glottic cancer although it was recommanded to the primary radiation treatment in a selected cases, i.e. node negative patients or T3NO without hypopharyngeal involvement, was superior results than irradiation alone.

But Harwood et al reported radical radiotherapy with surgery for salvage was a good method of treatment for T4 glottic cancer, particularly those patients who do not have hypopharyngeal involvement and control by irradiation is poorer in patients with hypopharyngeal as compared to thyroid cartilage involvement[13]. The results of the radical radiation treatment according to the status of the mobility of the involved cord and the extent of the mucosal surface spread are presented[4]; the absolute and determinate 5-year survival rates were 69% and 78% respectively. Also 5-year NED rates for lesions with normal, impaired and fixed cord mobility were 90%, 65% and 25% respectively. And 70% of radiation failure were cured by subsequent surgery without postoperative complication. But this report were not evaluated the local control and survival rates according to the cord mobility and hypopharyngeal involvement because of inaccurate records.

In patients with moderately advanced tumors (T3NOMO), 3 different plans of therapy may be offered; a. planned preoperative radiation therapy followed by total laryngectomy and radical neck dissection; b. initial radiotherapy followed by total laryngectomy and elective neck dissection in selective cases only, i.e. in patients where there is evidence of residual tumor in the larynx; c. initial total laryngectomy and elective radical neck dissection with or without postoperative radiation. As the tumor extends to other regions with fixation or outside the larynx (T4NOMO), or metastasizes to cervical nodes (N1-3), total laryngectomy with radical neck dissection may give the best chance for

long time survival. Radiotherapy is an important adjuvant and is probably most effective when given preoperatively[2]. Our results are similar, and local control rates and 5-year survival rates of the patients treated with RT alone in T3/4NOMO glottic cancer were 57% and 55% respectively.

Other treatment in advanced glottic cancer, i.e. induction or adjuvant chemotherapy was introduced in previous reports. Previously, the theoretical reasons of induction chemotherapy were suggested; reduction in tumor size might facilitate subsequent surgery and radiation therapy; finally, systemic chemotherapy might reduce the number of distant failure, which may be as high as 30% of stage IV head and neck cancer patients who fail local therapy. As has been described in many pilot studies of induction chemotherapy of head and neck cancer, chemotherapy responders had a more favorable disease-free survival than chemotherapy nonresponders in the total group of patients receiving adjuvant chemotherapy. Taylor et al[14] reported the results of a randomized trial of adjuvant chemotherapy. Although several positive results with induction chemotherapy had recently appeared[15], most reported results and our results were no survival benefit; were not prevented from distant failure.

Because this study was performed retrospectively and determination of eligibility in each treatment groups was difficult, it was difficult to determine the role of initial radiation therapy in advanced glottic cancer although the 5-year survival rates of node negative patients treated with RT alone was comparable to surgery/RT group. But at least, we are recommanded to treat with initial radiation therapy in node negative T3 and T4 glottic cancer patients for the purpose of functional voice preservation and if failed, it will be considered to treat with salvage surgery as a modality of further treatment. And so, because most cases of advanced glottic cancer showed the loco-regional failure, we suggest it will be achieved studies about the better modality of local treatment.

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= 국문초록 =

T3, T4병기 성문암의 치료성적

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1980년 1월부터 1988년 9월사이에 연세대학병원, 연세암센터 치료방사선과 및 이비인후과에서 치료받았던 68예의 T3, T4병기의 성문암 환자를 대상으로 후향적분석을 하였다. 이 중 34명은 방사선치료 단독으로 치료하였고 34명은 성문절제술후 방사선치료를 하였으며 이들 환자의 최소 추적기간은 2년이었고 54명(79%)에서 5년 추적조사가 가능하였다.

치료후 국소관해율은 방사선치료 단독군에서는 61%, 수술 및 수술후 방사선치료군에서는 79%이었고 임파절 음성군에서는 72%, 76%였으며 임파절 양성군에서는 31%, 81%이었다. 이들의 치료실패요인은 대부분 국소 국한적이었고 30명(44%)에서 관찰되었다.

치료에 따른 5년 생존율은 방사선치료 단독군에서는 37%, 수술 및 수술후 방사선치료군에서는 76%로서 T3, T5병기의 성문암환자에 있어서 수술시행후 방사선치료를 병용하는 복합요법이 더 좋은 치료결과를 얻을 수 있음을 알았다. 그러나 임파절 음성군에서는 방사선치료 단독군과 수술 및 수술후 방사선치료군을 비교해 본 결과 5년 생존율이 55%와 73%로 통계학적으로 유의한 차이를 보이지는 않았다.

따라서 본 저자들은 T3, T4병기의 성문암치료시 수술 및 방사선치료 병용요법이 더 좋은 치료결과를 얻을 수 있지만 임파절 음성군에서는 기능적인 보존측면에서 방사선치료가 일차적 차료방법으로서 효과적이리라 사료된다.