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RESULTS OF RADIATION THERAPY IN CARICINOMA OF THE LARYNX

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Abstract

Between 1973 and 1977, 254 patients with previously untreated squamous cell carcinoma of the larynx received ^{60}Co external beam therapy; 161 patients (63.4%) survived without evidence of malignancy for five years after the radiation therapy alone, and 21 patients survived after salvage surgery. The overall crude survival rate was 182/254, i.e. 71.7 per cent at five years. Five-year survival rates without evidence of malignancy were 81.6 per cent in stage I, 73.4 per cent in stage II, and 40.8 per cent in stage III.

In the Cracow region, carcinoma of the larynx accounts for about 5 per cent of all cancers in men. It is the fifth most frequent malignancy in men after cancer of the bronchus, stomach, skin and urinary bladder (12).

Radiation therapy and surgery, used alone or in combination, are effective treatment methods for laryngeal carcinoma, but the choice between these modalities is still controversial.

The aim of this paper is to present experiences gained from 254 patients treated at this Institute by irradiation, with surgery in reserve.

Material and Methods

All patients with carcinoma of the larynx were referred to this Institute by the local laryngologists. They were all examined by a radiation oncologist and a head and neck surgeon, who jointly decided on the policy of treatment. As a rule, all patients with primary tumour confined to the anatomic limits of the larynx, without considerable loss of mobility or complete fixation of the cord, invasion of the cartilage, severe obstruction of the larynx, or massive involvement of the cervical nodes, were qualified for radical radiation therapy. All the remaining patients with more advanced disease, and patients with subglottic carcinoma, were qualified either for surgery or for combined therapy. Some patients with highly advanced malignancy were irradiated with palliative intention.

From January 1973 to December 1977, 254 patients (238 men, 16 women, ratio = 14.9:1; mean age 55 years, range 29 to 83 years) with previously untreated, microscopically confirmed, squamous cell carcinoma of the larynx were irradiated with radical intention. The mean duration of the symptoms was 7.5 months with a range from 1 to 48 months.

The site of the primary tumour and the stage distribution (20) are presented in Table 1. There was a striking prevalence of patients with carcinoma of the supraglottis, which is the most common site of laryngeal cancer in Poland (14).

The site of the primary tumour and the status of the regional lymph nodes appear in Table 2. Clinically positive neck nodes were found in 23.5 per cent of the patients with supraglottic tumours and in 4.3 per cent of those with glottic tumours. This difference was highly significant (χ^2 test, $p<0.001$).

Treatment. All patients were treated with ^{60}Co teletherapy. In 176 patients with primary tumour stages T1N0 and T2N0, two antero-lateral, oblique,

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wedged fields were irradiated. The field sizes varied from 5 cm × 5 cm to 6 cm × 7 cm. The target volume included only the larynx in patients with early glottic tumour, and the larynx along with the midjugular nodes in most patients with early supraglottic malignancy. The tumour dose was 60 Gy in 24 fractions over 5 weeks, given with 5 fractions per week.

In patients with more advanced disease and in some patients with supraglottic tumour, stage T2N0, two parallel opposing fields—one wedged and one plane—were irradiated. The field sizes varied from 6 cm × 8 cm in patients with T2N0 supraglottic carcinoma, up to 10 cm × 12 cm in patients with more advanced lesions. Seventy-eight patients were irradiated in this way. The standard tumour dose was 60 Gy in 30 fractions over 6 weeks, but in some patients with extensive lesions an additional dose of 4 Gy to 8 Gy in 3 to 4 fractions was given through a reduced portal.

Reaction and complications. In all patients a mucosal reaction of various degrees occurred, appearing usually within 2 to 3 weeks from the beginning of the treatment. In 241 patients (94.9%) the reaction did not cause any interruption of therapy. In 10 patients an interruption of the treatment for several days was necessary, and in another 3 patients the planned dose was not delivered because of severe radiation mucositis.

Severe late complications occurred in 6 patients (2.4%). Four patients developed laryngeal oedema necessitating tracheostomy for a short period, 2 patients developed perichondritis of the thyroid cartilage, which healed after conservative treatment.

No deaths due to complications occurred.

Results

One hundred and sixty-one patients, i.e. 63.4 per cent of those irradiated, survived without evidence of malignancy for five years after radiation therapy alone. In addition, 21 patients survived for five years without evidence of malignancy after salvage surgery for a recurrent tumour. Thus, the overall crude survival rate was 182/254, i.e. 71.7 per cent at five years.

The 5-year survival rates according to sex, age, clinical stage, site and local extension of the primary tumour, and state of the cervical lymph nodes appear in Table 3. Women had a significantly better chance of survival than men (χ^2 test, $p<0.01$). The relation between the age of the patients and their survival was more complicated. The survival rate was lowest in patients under 40, but in comparison with the other groups the difference was not statistically significant. This was probably due to the small number of patients in the youngest age group. Better results were obtained in the patients between 40 and 60 in comparison with the patients over 60. The difference was statistically significant (χ^2 test, $p<0.05$).

A statistically significant correlation also existed between survival and stage of the disease, local extension of the primary tumour, and clinical state of the cervical lymph nodes. No statistically significant relationship was found between the results obtained in patients with supraglottic and glottic tumours. To analyse the latter relation, the results obtained in patients with supraglottic and glottic tumours according to the clinical stage were compared (Table 4). The differences between the survival rates obtained in patients with stage I and II lesions were statistically not significant in the groups compared. The prognosis was much poorer in patients with stage III carcinoma of the larynx,

Table 1

Site of the primary tumour and clinical stage (20) in 254 patients

Stage	Site				Total	
	Supraglottis		Glottis		No. of cases	Per cent
	No. of cases	Per cent	No. of cases	Per cent		
I	75	29.5	66	26.0	141	55.5
II	44	17.3	20	7.9	64	25.2
III	43	16.9	6	2.4	49	19.3
Total	162	63.7	92	36.3	254	100.0

Table 2

Site of the primary tumour and status of regional lymph nodes

Site of the primary tumour	No. of cases	Regional nodes considered to contain growth	
		No. of cases	Per cent
Supraglottis	162	38	23.5
Glottis	92	4	4.3
Total	254	42	16.5

Table 3

Five-year symptom-free survival in 254 patients with carcinoma of the larynx

Clinical features	No. of cases	5-year survival without evidence of malignancy			
		Irradiation only		Irradiation plus surgery for recurrence	
		No. of cases	Per cent	No. of cases	Per cent
Sex					
Male	238	146	61.3	167	70.2
Female	16	15	93.8	15	93.8
Age					
Under 40	13	7	53.8	9	69.2
40–60	149	103	69.1	113	75.8
Over 60	92	51	55.4	60	65.2
Site of primary tumour					
Supraglottis	162	97	59.9	113	69.8
Glottis	92	64	69.6	69	75.0
Stage of disease					
I	141	107	75.9	115	81.6
II	64	41	64.1	47	73.4
III	49	13	26.5	20	40.8
Local extension of primary tumour					
T1	165	116	70.3	130	78.8
T2	80	44	55.0	50	62.5
T3	9	1	11.1	2	22.2
Status of regional lymph nodes					
Clinically negative	212	149	70.3	164	77.4
Clinically positive	42	12	28.6	18	42.9
Total	254	161	63.4	182	71.7

Table 4

Five-year symptom-free survival in relation to site of the primary tumour and clinical stage

Stage	Supraglottis					Glottis				
	No. of cases	5-year survival				No. of cases	5-year survival			
		Irradiation only		Irradiation plus surgery for recurrence			Irradiation only		Irradiation plus surgery for recurrence	
		No. of cases	Per cent	No. of cases	Per cent		No. of cases	Per cent	No. of cases	Per cent
I	75	53	70.7	58	77.3	66	54	81.8	57	86.4
II	44	31	70.5	35	79.5	20	10	50.0	12	60.0
III	43	13	30.2	20	46.5	6	0	0	0	0
Total	162	97	59.9	113	69.8	92	64	69.6	69	75.0

regardless of the site of the primary lesion, but the small number of patients in this group made the comparison between supraglottic and glottic tumours doubtful.

The causes of death according to the clinical stage are given in Table 5. Definite loco-regional failure as a major cause of death was observed in 15.7 per cent of the patients. A significant correlation existed be-

Table 5

Status of 254 patients at five years after treatment

Status of patients	Clinical stage						Total	
	I		II		III		No. of cases	Per cent
	No. of cases	Per cent	No. of cases	Per cent	No. of cases	Per cent		
Alive without cancer after irradiation only	107	75.9	41	64.1	13	26.5	161	63.4
Alive without cancer after surgery for recurrences	8	5.7	6	9.3	7	14.3	21	8.3
Dead from distant metastases without loco-regional recurrence	2	1.4	1	1.6	5	10.2	8	3.1
Dead from other malignancy without evidence of laryngeal cancer	6	4.3	0	0	4	8.2	10	3.9
Dead from other causes without evidence of laryngeal cancer	6	4.3	1	1.6	2	4.1	9	3.6
Cause of death unknown	1	0.7	2	3.1	2	4.1	5	2.0
Dead because of loco-regional failure								
Local recurrence	4	2.8	9	14.1	14	28.6	27	10.6
Local recurrence and regional lymph node metastases	2	1.4	2	3.1	1	2.0	5	2.0
Regional lymph node metastases	5	3.5	2	3.1	1	2.0	8	3.1
Total	141	100.0	64	100.0	49	100.0	254	100.0

tween the clinical stage and loco-regional control of the malignancy.

In 10 patients (3.9%) a second lesion was diagnosed within the five-year period of observation. Carcinoma of the lung occurred in 8 patients, of the stomach in one patient, and of the oral cavity in one patient. In 3 additional patients with recurrent carcinoma of the larynx a second malignancy was diagnosed: in the pharynx in 2, and in the lip in one patient. Thus, there were 13 patients (5.1%) with a second malignancy.

Distant metastases occurred in 3 of 205 patients (1.5%) with stage I and II and in 5 of 49 patients (10.2%) with stage III carcinoma of the larynx. This difference is statistically significant (χ^2 test, $p<0.01$). In all cases the lungs were affected.

The causes of failure of the salvage procedure in the group of 40 patients who died because of loco-regional recurrence are shown in Table 6. Twenty-two of 40 patients (55%) died because of failure of the salvage operation or poor general health precluding surgery, and in 18 patients (45%) failure of the therapy was related to their poor compliance.

Table 6

Causes of failure of the salvage procedure in 40 patients who died with loco-regional recurrence

Cause of failure of the salvage procedure	No. of cases	Per cent
Second loco-regional recurrence after salvage surgery	11	27.5
Patients not suitable for salvage surgery		
Medical reasons	11	27.5
Refused operation	8	20.0
Presented too late for follow-up examination with inoperable lesion	10	25.0
Total	40	100.0

Discussion

The present results substantiate the view that megavoltage irradiation is a highly effective method of treatment for patients with stage I and II supraglottic and glottic carcinoma of the larynx. The thera-

peutic results with irradiation are good and there is still a considerable possibility for surgical salvage of recurrences. This corresponds with a previous report (17), and with the opinion of some other authors (2, 4, 5, 6, 7, 9, 11, 18, 19, 21), although some head and neck surgeons still advocate primary laryngectomies (1, 3, 13). The surgical results, however, are not better than those obtained by primarily employed radiation therapy with surgery in reserve. Therefore, in view of the fact that surgery is more mutilating than irradiation, we consider that primary radiation therapy is the method of choice for patients with early supraglottic and glottic tumours.

The analysis of the therapy failures showed, paradoxically, a higher rate of nodal relapse in patients with early laryngeal malignancy (Table 5). Six of 8 patients who died because of the nodal recurrence had supraglottic tumours. The patients with early supraglottic carcinoma were irradiated with small portals, covering the larynx and midjugular nodes only. Based on this observation, it is considered that in patients with early supraglottic malignancy the irradiated area should include not only the middle but also the upper cervical nodes (4, 5, 7, 15).

The results of radiation therapy were poorer in patients with stage III carcinoma. The main cause of failure was local recurrence. Some authors suggest a possibility of improvement by using a higher tumour dose (4, 8, 10, 21). The other problem was poor compliance on the part of these patients (Table 6). The patients, particularly those with advanced malignancy, very often have severe emotional problems and a history of chronic alcoholism and nicotinism. They are frequently uncooperative and need not only medical but also psychologic assistance. Without good cooperation from the patient, the policy of primary radiation therapy with surgery in reserve, based on careful observation of the patient after irradiation, becomes unreliable.

The results with primary irradiation of advanced laryngeal malignancy were unsatisfactory. Therefore, at present, most of these patients are referred for laryngectomy combined with postoperative irradiation. Primary radiation therapy is reserved for patients with advanced laryngeal carcinoma who are unfit for radical surgery for medical reasons, or who refuse the proposed laryngectomy. The tumour dose delivered in these cases is higher, i.e. 65 Gy to 70 Gy in 35 fractions over 7 weeks. Some patients with advanced laryngeal malignancy are also being irradiated with fast neutrons (16).

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