

Evaluation of the treatment results of laryngeal carcinoma: our experience over 10 years

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Aim: To retrospectively analyze the treatment results for laryngeal carcinoma and to find the impact of the clinical parameters on the survival of the patients.

Materials and methods: The medical records of 150 consecutive patients, operated on for laryngeal squamous cell carcinoma between 1991 and 2009, were reviewed. Tumor localization, TNM stages, treatment modalities, radiotherapy, second primary tumors, and tumor recurrence were recorded, and the survival data were obtained.

Results: Neck metastasis was rare (3.6%) in T1 and T2 glottic tumors, while there was a significant increase in the rate of N+ neck (35%) in T3 and T4 glottic tumors ($P < 0.05$). N+ neck was encountered in 28% of the early and 33% of the late-stage supraglottic cancers ($P > 0.05$). There was a significant relation between survival and tumor recurrence ($P < 0.05$), whereas the other clinical parameters were not associated with survival ($P > 0.05$). The risk for death of the disease increased by 63.3% when tumor recurrence occurred (odds ratio = 6.3573).

Conclusion: Aggressive treatment of the primary tumor and neck may eliminate the impact of advanced tumor stage on survival. Local and regional recurrence and second primary diagnosis are the most important factors involved in survival in laryngeal carcinoma.

Key words: Laryngeal carcinoma, treatment, prognosis, recurrence, survival

Introduction

Laryngeal carcinoma is one of the most frequently encountered cancers in the practice of otolaryngology. Although its treatment has been established, an improvement in the survival rates is warranted. The main therapeutic dilemma occurs when a patient presents with an N0 neck that may potentially harbor an occult metastatic disease (1). Management of N0 neck is advocated when the possibility of occult neck metastasis is greater than 20% (2), although this issue is debated.

In our practice, the treatment is mainly surgical and is combined with postoperative radiotherapy when indicated. We do not perform induction

chemotherapy. We usually perform total laryngectomy in advanced tumors (T3 and T4) and partial surgery in early-stage tumors. The management of N0 neck is performed as follows: watchful waiting in early-stage glottic cancer, ipsilateral neck dissection and watchful waiting for the contralateral neck in advanced glottic cancer, and bilateral neck dissection in supraglottic tumors. Neck dissection is elective, selective, or modified radical, depending upon the clinical judgment. N+ neck is treated with radical or modified radical type I dissection. We recommend postoperative radiotherapy when there is metastasis in at least one of the cervical lymph nodes, or thyroid cartilage or neurovascular invasion.

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In this study, we aimed to retrospectively analyze the treatment results of laryngeal carcinoma as well as to find the impact of the clinical parameters of the patients on survival.

Materials and methods

The medical records of 150 consecutive patients who were operated on for laryngeal squamous cell carcinoma between 1991 and 2009 were reviewed. All of the patients were treated and followed up with at the Department of Otolaryngology and Head and Neck Surgery of a university hospital. Only 2 of the patients were women. The ages of the patients ranged from 30 to 87 years (mean: 58.1 years). The minimum follow-up time was 1 year, and the mean follow-up time was 4.8 years.

The clinical parameters of the patients (tumor localization, T and N stages, treatment modalities, radiotherapy, metastasis, second primary diagnosis, and tumor recurrence) were recorded. Tumor staging was made according to clinical examination with palpation, laryngoscopy, and computed tomography, unless the patient was operated on. Otherwise, staging was based on the postoperative histopathological evaluation. The data regarding the survival of the patients were obtained according to follow-up results noted in the patient files, as well as from telephone interviews with the family members of the patients (Table 1).

Statistics: SPSS 11.0 for Windows was used to perform the statistical analyses. The parameters of the surviving and deceased patients were compared using one-way ANOVA. The impact of the clinical parameters on survival was evaluated using Cox regression analysis. The survival curves were calculated using the Kaplan–Meier method.

Results

Of the 150 patients, 138 were treated surgically, while 12 patients who had T1 tumors were treated with radiotherapy. Surgical treatment included partial and total laryngectomy. Radical, modified radical (types I, II, or III), or selective neck dissection was performed accordingly.

All of the patients who underwent total laryngectomy had either T3 or T4 tumors. Most

of the patients with T2 and T3 supraglottic tumors underwent supraglottic laryngectomy, while total laryngectomy was performed in T4 supraglottic cancers. None of the patients had been irradiated before surgery, while 22 patients had postoperative radiotherapy (Table 2).

Neck metastasis was rare (3.6%) in T1 and T2 glottic tumors, while there was a significant increase in the rate of N+ necks (35%) in T3 and T4 glottic tumors ($P = 0.006$). N+ neck was encountered in 28% of the early and 33% of the late-stage supraglottic cancers ($P > 0.05$). Metastasis to the cervical lymph nodes was also high in T3 and T4 transglottic tumors (Table 3).

Of the 150 patients, 18 (12%) died in the postoperative follow-up period. Local, regional, and peristomal tumor recurrences were observed in 1 (0.7%), 2 (1.3%), and 4 (2.7%) of the 150 patients, respectively. A second primary tumor was encountered in 2 (1.3%) patients; 1 was in the esophagus and 1 was in the lung. These were metachronous second primaries.

Upon variance analysis, there was no significant difference between the clinical parameters of the patients who died and those who survived, except for tumor recurrence. Cox regression analysis revealed that there was a significant relation between survival and tumor recurrence ($r = 0.183$, $df = 1$, $P = 0.008$), whereas the other clinical parameters were not associated with survival ($P > 0.05$). Recurrence was an independent prognostic factor. The risk for death from the disease increased by 63.3% when tumor recurrence occurred (odds ratio = 6.3573) (Figure).

Discussion

Appropriate management of N0 neck in supraglottic laryngeal cancer is controversial in head and neck surgery. The procedure of choice used to be complete functional neck dissection, removing levels I through V, with an associated risk of spinal nerve, deep cervical plexus, and thoracic canal damage (3). However, aggressive surgical management (bilateral dissection of levels I through V) can be made in the clinical N0 neck because of the high incidence of occult regional disease, even in early-stage supraglottic cancer (4). In a study performed on 41 consecutive patients who

Table 1. Clinical parameters of the patients with laryngeal carcinoma.

Parameter	Status	
	Survival n (%)	Death n (%)
Localization		
Glottic	42 (31.8)	6 (33.3)
Supraglottic	54 (40.9)	6 (33.3)
Transglottic	32 (24.2)	5 (27.8)
Subglottic	4 (3)	1 (5.6)
T stage		
T1	19 (14.4)	2 (11.1)
T2	35 (26.5)	5 (27.8)
T3	58 (43.9)	5 (27.8)
T4	20 (15.2)	6 (33.3)
N stage		
N0	100 (75.8)	11 (61.1)
N1	13 (9.8)	3 (16.7)
N2	19 (14.4)	4 (22.2)
Treatment		
Radiotherapy	12 (9.1)	-
Total laryngectomy	84 (63.6)	12 (66.7)
Partial laryngectomy	36 (27.3)	6 (33.3)
Tumor recurrence		
Present	3 (2.3)	4 (22.2)
Absent	129 (97.7)	14 (77.8)

underwent supraglottic laryngectomy, the overall tumor-free survival, with a 2-year minimum follow-up period, was 90%. In the same study, the favorable results were attributed to frozen section control of surgical margins, surgical or radiation therapy, and treatment of cervical lymph nodes at risk for metastatic disease (5). In our series, N+ neck was encountered in 28% of the early and 33% of the late-stage supraglottic cancers. These patients underwent bilateral neck dissection. The surgical treatment was supraglottic laryngectomy in most of the T2 and T3 tumors, and total laryngectomy in the T4 tumors.

Early-stage glottic tumors can be treated with radiation therapy or partial laryngectomy. In our series, the neck metastasis rate was 3.6% in T1 and T2 glottic tumors. In general, neck dissection is

not necessary in early-stage glottic cancers unless there is a clinically detectable cervical metastasis. However, treatment of the neck in T3N0 and T4N0 glottic tumors is controversial because of the low risk of neck metastasis in these cancers, which ranges from 3% to 30% (6–8). Although the treatment of N0 neck T3 and T4 glottic cancers is debated, most otolaryngologists perform neck dissections in these tumors (6). In T3N0 cancer, regional control is 69% if the neck nodes are not treated electively, compared with 98% for the planned combined (surgery and radiotherapy) treatment group, which necessitates elective treatment of the neck nodes (9). As suggested in a study by Kada et al., we also perform neck dissection in advanced glottic cancers (10). In our series, 35% of the patients with T3 and T4 glottic

Table 2. Treatment of the patients with laryngeal carcinoma.

Laryngeal surgery	Ipsilateral neck	Contralateral neck	Postoperative radiation therapy
Total laryngectomy (n = 96)	RND (n = 91)	RND (n = 27) MRND (n = 42)	16
Supraglottic laryngectomy (n = 27)	RND (n = 27)	RND (n = 18) MRND (n = 9)	6
Vertical laryngectomy (n = 6)	-	-	-
Corpectomy (n = 9)	-	-	-
Total (n = 138)	RND (n = 118)	RND (n = 45) MRND (n = 51)	12

RND: Radical neck dissection, MRND: modified radical neck dissection.

tumors had N+ neck. Therefore, we recommend neck dissection in these tumors.

It was suggested that administration of postoperative radiotherapy in patients with surgically treated laryngeal cancer with histologically proven positive neck nodes does not change the survival or local recurrence rates (11). This contention is in parallel with our results because in our series, we also irradiated 22 patients who had histopathologically proven positive neck lymph nodes after surgery, and the survival and recurrence rates of these patients were similar with the others.

Transglottic tumors were proposed to have a poor prognosis regarding survival when compared to supraglottic tumors (12). It was suggested that in T3N0 and T3N1 glottic and transglottic carcinoma, recurrences in the neck were seen in 16.4% of the patients who underwent surgery and in 10.5% of those who had radiotherapy. It was suggested that the 5-year overall survival rate was 56.3% in a surgically treated group and 35.2% in a radiotherapy group

(13). According to our results, there was no relation between tumor localization and survival.

There are numerous factors suggested to impact survival, such as tumor localization, advanced tumor stage, lymph node metastasis, distant metastasis, peristomal recurrence, cartilage invasion, local or regional recurrence, surgical margins, and the site of metastasis (8,14,15). However, locoregional recurrence appears to be particularly important in laryngeal cancer. It can be seen in up to 21% of the patients (16) and was 4.7% in our study. Recurrence can be seen in different local and regional sites. The peristomal recurrence rate ranges from 1.8% to 8.7% (16–18) and was 2.7% in our series. In glottic cancer, survival with no evidence of disease was chiefly determined by the development of regional recurrence, distant metastasis, and a new primary cancer (19). The overall survival rate was 88% in our series. In supraglottic tumors, the overall 3-year survival was 83.6%, and there was a significant difference in the recurrence rate between patients

Table 3. Status of the cervical lymph nodes in laryngeal carcinoma.

Tumor	Glottic		Supraglottic		Transglottic		Subglottic	
	N0 n (%)	N+ n (%)	N0 n (%)	N+ n (%)	N0 n (%)	N+ n (%)	N0 n (%)	N+ n (%)
T1-2	27 (96.4)	1 (3.6)	21 (72)	8 (28)	1 (100)	-	1 (33.3)	2 (66.6)
T3-4	13 (65)	7 (35)	21 (67)	10 (33)	25 (69.4)	11 (29.6)	2 (100)	-

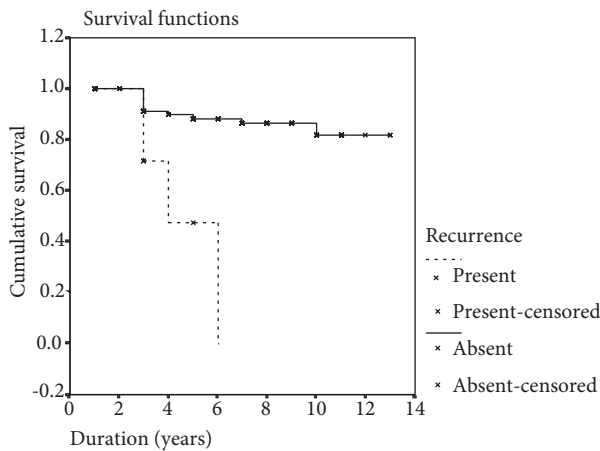


Figure. Kaplan-Meier survival graphic in the patients with recurrence.

with N0 and N+ necks (20). We did not find a significant correlation between N stage and survival. In our series, tumor recurrence was the single most

important factor associated with survival. The risk of mortality of the disease increased by 63.3% when tumor recurrence occurred. Locoregional failure is prognostic with a significant decrease in overall survival (12,21). In a study by Bilici et al., it was reported that age, lymph node involvement, clinical stage, and the extent of surgical margin are prognostic factors associated with survival time in gastric cancer (22). Strongin et al. showed in their study that the primary tumor volume is an important prognostic factor of local and regional control and overall survival among patients with squamous cell carcinoma of the head and neck, which is in parallel with our findings (23).

In conclusion, aggressive treatment of the primary tumor and neck may eliminate the impact of advanced tumor stage on survival. Local and regional recurrence and second primary diagnosis are the most important factors associated with survival in laryngeal carcinoma.

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