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The management of glottic and supraglottic cancers of the larynx in relation to neck metastasis

Glottik ve supraglottik larenks kanserlerinde tedavinin boyun metastazı açısından değerlendirilmesi

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Objectives: We evaluated the management of glottic and supraglottic laryngeal cancers in relation to neck metastasis.

Patients and Methods: Fifty-two patients (51 males, 1 female; mean age 59.2 years; range 27 to 82 years) underwent surgery for primary laryngeal cancers. Preoperative and postoperative TNM classification and staging were made according to the AJCC 1997 criteria. The mean follow-up period was 39.4 months (range 6 to 74 months).

Results: The tumors were glottic in 31 patients and supraglottic in 21 patients. Laryngectomies were partial in 34 patients and total in 18 patients. All the patients with supraglottic tumors and those with glottic T₂₋₄ tumors underwent neck dissection, as well. Radiotherapy was administered to 22 patients with established N₂ or N₃ tumors. Clinical assessment was in agreement with the pathological result in 63.5%; 13.5% and 23.1% of cases were underdiagnosed and overdiagnosed, respectively. The rates of neck metastasis were 0% in T₁, 25% in T₂, 75% in T₃, and 66.7% in T₄ supraglottic tumors. The corresponding rates for glottic cancers were 0%, 16.7%, 28.6%, and 60%, respectively. The overall rate of N₊ tumors was 28.9%. Four patients (7.7%) developed local, two patients (3.9%) developed regional recurrences. Mortality occurred in eight patients (15.4%) due to following causes: laryngeal recurrence (T₄N₂, T₄N₂, T₃N₁), regional recurrence (T₄N₂), a second primary malignancy in one patient, and other causes in three patients. Five- and two-year disease-specific survival rates (Kaplan-Meier analysis) were 90.7%, and overall survival rates were 73.7% and 87.3%, respectively.

Conclusion: Neck metastasis and advanced stage of the tumor were the most effective prognostic factors.

Key Words: Carcinoma, squamous cell/surgery; laryngeal neoplasms/diagnosis/surgery; lymph nodes/pathology; lymphatic metastasis; neck; neck dissection; neoplasm staging; survival rate.

Amaç: Glottik ve supraglottik larenks kanserlerinde tedavinin boyun metastazı ile ilgili boyutları değerlendirildi.

Hastalar ve Yöntemler: Çalışmaya primer larenks kanseri nedeniyle cerrahi tedavi uygulanan 52 hasta (51 erkek, 1 kadın; ort. yaş 59.2; dağılım 27-82) alındı. Ameliyat öncesi ve sonrası TNM sınıflandırması ve evreleme AJCC 1997 ölçütlerine göre yapıldı. Ortalama izlem süresi 39.4 ay (dağılım 6-74 ay) idi.

Bulgular: Otuz bir hastada glottik, 21 hastada supraglottik kanser saptandı. Otuz dört hastada parsiyel, 18 hastada total larenjektomi uygulandı. Supraglottik ve T₂₋₄ glottik kanserlerin hepsine aynı seansta boyun diseksiyonu da uygulandı. Patolojik incelemede N₂ veya pN₃ bulunan 22 hastaya ameliyat sonrasında radyoterapi uygulandı. Klinik değerlendirmenin patolojik sonuçla uyumu %63.5 bulundu; olguların %13.5'inde ve %23.1'inde değerlendirme eksik veya fazla yapılmıştı. Boyun metastazı oranı supraglottik kanserlerde T₁'de %0, T₂'de %25, T₃'te %75, T₄'te %66.7 bulundu. Glottik kanserlerde bu oranlar sırasıyla %0, %16.7, %28.6 ve T₄'te %60 olarak belirlendi. N₊ tümörlerin genel oranı %28.9 idi. Dört hastada (%7.7) lokal, iki hastada (%3.9) rejyonel nüks görüldü. İzlem süresi içinde sekiz hasta şu nedenlerle yaşamını yitirdi: Larenjeal nüks (T₄N₂, T₄N₂, T₃N₁), rejyonel nüks (T₄N₂), ikinci primer tümör (1 hasta), kanser dışı nedenler (3 hasta). Beş ve iki yıllık hastalığa özgü sağkalım oranı %90.7; toplam sağkalım sırasıyla %73.7 ve %87.3 bulundu (Kaplan-Meier analizi).

Sonuç: Boyun metastazı ve ileri tümör evresi larenks kanserinde en etkin prognostik faktörlerdir.

Anahtar Sözcükler: Karsinom, yassı epitel hücreli/cerrahi; larenjeal neoplaziler/tanı/cerrahi; lenf nodu/patoloji; lenfatik metastaz; boyun; boyun diseksiyonu; neoplazi evrelemesi; sağkalım oranı.

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Squamous cell carcinoma of the larynx is a highly curable malignancy of the upper aerodigestive tract. The detection and treatment of cervical lymph node metastases are of relevant issues for prognosis in the management of laryngeal cancers.^[1,2] The general consensus is that the neck has to be included into the treatment, even if it is N₀, with the exception of early glottic cancers. The choice of treatment of the neck between surgery and radiotherapy generally depends on the treatment modality of the primary tumor.^[3]

In this study, we evaluated lymph node metastasis and prognosis in patients who underwent surgery for primary laryngeal cancers.

PATIENTS AND METHODS

The study included 52 patients (51 males, 1 female; mean age 59.2 years; range 27 to 82 years) who underwent laryngectomy for primary laryngeal cancers in the Department of Otorhinolaryngology, Head and Neck Surgery, at Medicine Faculty of Celal Bayar University, between 1996 and 2002. Only the patients who had a follow-up of at least six months were involved; those who lost to follow-up were excluded.

The location of the tumor, surgical technique for the primary tumor and cervical lymph nodes, preoperative and postoperative TNM classification and staging (AJCC 1997),^[4] follow-up period, and the use of postoperative radiotherapy were evaluated. The findings from the indirect and direct laryngoscopy examinations, imaging methods, and postoperative pathology reports were re-assessed for TNM classification of the primary tumor. Preoperative status of the lymph nodes was evaluated in the light of clinical assessment (palpation), ultrasonography, com-

	pN ₀	pN ₁	pN _{2a}	pN _{2b}	pN _{2c}	pN ₃
cN ₀	25	1			1	
cN ₁	4	1	2	2		
cN _{2a}	2		2			
cN _{2b}	2			2		
cN _{2c}	4				3	1
cN ₃						

Agreement rate 63.5%, underdiagnosis 13.5%, overdiagnosis 23.1%.

puted tomography (CT), and magnetic resonance imaging (MRI) findings. Histopathologic findings of the surgical specimens were used for postoperative TNM classification. Survival was estimated using the Kaplan-Meier survival analysis on the SPSS statistical software.

The mean follow-up period was 39.4 months (range 6 to 74 months).

RESULTS

The laryngeal tumors were glottic in 31 patients (59.6%) and supraglottic in 21 patients (40.4%). Laryngectomies were partial in 34 patients (65.4%) and total in 18 patients (34.6%). Two patients with positive surgical margins underwent extended laryngectomy within 10 days postoperatively. Partial laryngectomy resulted in successful decannulation and a satisfactory swallowing pattern and voice quality in all the patients.

A comparison of the clinical (cTNM) and pathological (pTNM) results is presented in Table I and II. For all the laryngeal cancers, clinical assessment was

TABLE II
CLINICAL (cN) AND PATHOLOGICAL (pN) ASSESSMENTS FOR SUPRAGLOTTIC AND GLOTTIC CANCERS

	Supraglottic						Glottic					
	pN ₀	pN ₁	pN _{2a}	pN _{2b}	pN _{2c}	pN ₃	pN ₀	pN ₁	pN _{2a}	pN _{2b}	pN _{2c}	pN ₃
cN ₀	7	1	–	–	1	–	18	–	–	–	–	–
cN ₁	2	–	1	1	–	–	2	1	1	1	–	–
cN _{2a}	1	–	–	–	–	–	1	–	2	–	–	–
cN _{2b}	–	–	–	2	–	–	2	–	–	–	–	–
cN _{2c}	2	–	–	–	3	–	2	–	–	–	–	1
cN ₃	–	–	–	–	–	–	–	–	–	–	–	–

For supraglottic cancers: Agreement rate 57.1%, underdiagnosis 19%, overdiagnosis 23.8%;

For glottic cancers: Agreement rate 67.7%, underdiagnosis 10%, overdiagnosis 22.6%.

in agreement with the pathological assessment in 63.5%; however, 13.5% and 23.1% of cases were underdiagnosed and overdiagnosed, respectively.

Radical or modified radical neck dissections were performed. All the patients with supraglottic tumors and those with glottic T₂, T₃, T₄ tumors underwent neck dissection at the same session with laryngectomy. A bilateral neck dissection was performed in supraglottic cancers and in glottic cancers grossly involving the supraglottis or subglottis. Patients with T₂N₀ glottic cancer underwent an ipsilateral neck dissection. Adjuvant radiotherapy was administered to 22 patients whose tumors were established to be pN₂ or pN₃. Postoperative radiotherapy was not used in two patients with pN₁.

The evaluation of metastatic lymph nodes in relation to tumor stage and localization is presented in Table III. In supraglottic larynx cancers, the rates of lymph node metastasis were found 0% in T₁, 25% in T₂, 75% in T₃, and 66.7% in T₄ tumors. The corresponding rates for glottic cancers were 0%, 16.7%, 28.6%, and 60%, respectively. The overall rates of neck metastasis in relation to tumor stage were 0% in T₁, 21.4% in T₂, 45.5% in T₃, 63.6% in T₄ tumors. The overall rate of N₊ tumors was 28.9% (15/52).

Of a mean follow-up period of 39.4 months, the length of the follow-up period exceeded two years in 31 patients (59.6%). Mortality occurred in eight patients (15.4%) due to following causes: three patients from laryngeal recurrence (T₄N₂, T₄N₂, T₃N₁), one patient from regional recurrence (T₄N₂), one patient from a second primary malignancy (pulmonary), and three patients from other causes (suicide, cerebrovascular accident, and acute gastroenteritis, respectively).

All recurrences were determined between eight and 29 months postoperatively, all of which were seen in stage IV patients. Four patients (7.7%) developed local, two patients (3.9%) developed regional recurrences. Local recurrences were dealt with by total laryngectomy and/or radiotherapy, and regional recurrences by radiotherapy. Extracapsular invasion of lymphatic metastasis had been reported in two patients (pN_{2c}), one of whom had cervical recurrence. Three patients with local recurrences and one patient with regional recurrence died.

Five- and two-year disease-specific survival rates were 90.7%, and overall (actuarial) survival rates were 73.7% and 87.3%, respectively (Fig. 1). Mortality was not encountered in patients with stage I, II, and III tumors.

TABLE III
THE NUMBER OF CERVICAL METASTASES IN RELATION TO TUMOR STAGE AND LOCALIZATION

	n	pN ₀		pN ₁		pN _{2a}		pN _{2b}		pN _{2c}		pN ₃		Total (pN ₊)	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
pT ₁ (n=16)		16	100	–	–	–	–	–	–	–	–	–	–	–	–
Supraglottic	3	3		–	–	–	–	–	–	–	–	–	–	–	–
Glottic	13	13		–	–	–	–	–	–	–	–	–	–	–	–
pT ₂ (n=14)		11	79	1	7	–	–	–	–	1	7	1	7	3	21.4
Supraglottic	8	6		1		–	–	–	–	1		–	–	2	25.0
Glottic	6	5		–	–	–	–	–	–	–		1		1	16.7
pT ₃ (n=11)		6	55	1	9	2	18	1	9	1	9	–	–	5	45.5
Supraglottic	4	1		–	–	1		1		1		–	–	3	75.0
Glottic	7	5		1		1		–	–	–		–	–	2	28.6
pT ₄ (n=11)		4	36	–	–	2	18	3	27	2	18	–	–	7	63.6
Supraglottic	6	2		–	–	–	–	2		2		–	–	4	66.7
Glottic	5	2		–	–	2		1		–		–	–	3	60.0
Total															
Supraglottic	21	12	57.1	1	4.8	1	4.8	3	14.3	4	19.1	–	–	9	42.9
Glottic	31	25	80.7	1	3.2	3	9.7	1	3.2	–	–	1	3.2	6	19.4

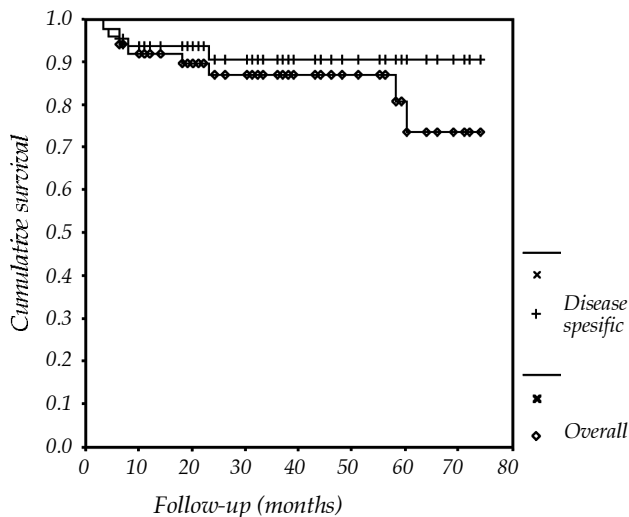


Fig. 1 - Disease-specific and overall survival functions.

DISCUSSION

Male preponderance was strikingly high (50 to 1) in our study compared with previous studies which reported 5 to 1 and 20 to 1.^[3,5,6] Although the mean age for laryngeal cancer falls between the sixth and seventh decades,^[3,7] our patients were younger, possibly because of the smoking habits (heavy smokers, younger smoking age, etc.) of the Turkish population.

The tumors were of glottic and supraglottic origin in 59.6% and 40.4% of the study patients, respectively. In one study, these rates were reported as 34% for glottic and 66% for supraglottic cancers.^[7] As far as T₃ and T₄ tumors were concerned, the frequencies of glottic and supraglottic cancers were found as 54% and 46%, respectively.^[8]

Considering better prognostic results reported with postoperative radiotherapy in T₄ tumors and N₊ patients,^[1,3,9,10] we administered adjuvant radiotherapy to all N₊ patients except for two who were found to have N₁ disease.

Metastatic lymph nodes were determined in 42.9% of supraglottic and 19.4% of glottic larynx cancers. Pathological findings showed that metastasis to lymph nodes had been correctly estimated in 63.5%, with 23.1% and 13.5% of cases being overdiagnosed and underdiagnosed, respectively (Table I).

The rate of occult metastasis was found as 15.3% in our cases. Occult metastasis has been reported as 21% in laryngeal cancers,^[2] 27% in supraglottic laryn-

geal cancers,^[11] 23% in T₁-T₂ supraglottic cancers,^[12] and 30% in T₃-T₄ laryngeal cancers.^[13]

A ratio of the longitudinal/transverse diameters lower than 2, narrowing or absence of the hilum, eccentric widening of the cortex, and an increase in the size of neck lymph nodes have been accepted as malignancy criteria.^[14,15] However, these criteria, especially increases in the size of lymph nodes may not have sufficient reliability, in that, as is the case in our study, determining N₊ patients depending on the size of the lymph nodes measured larger than 1.5 cm may have a decreasing effect on occult metastasis rates on one hand, and an increasing effect on overdiagnosis rates, on the other.

The rate of overdiagnosis in the evaluation of cervical lymph nodes was found as 3% with CT, and 7% with MRI, agreement rates being 82% and 58%, respectively.^[16] It was pointed out that agreement rates could be more than 90% if palpation and CT were used together.^[14,15] The agreement rates found with the use of several techniques were reported as 70% with palpation, 73% with ultrasonography, 85% with CT, 85% with MRI, 89% with ultrasonography-guided fine-needle aspiration biopsy, and 90% with positron-emission tomography.^[17] In our study, each patient was examined both by palpation and ultrasonography, and we employed CT and/or MRI in most of the cases. These yielded an agreement rate of 63.5% and an overdiagnosis rate of 23.1%.

The rates of neck metastasis associated with supraglottic larynx cancers were 0% for T₁, 25% for T₂, 75% for T₃, and 66.7% for T₄ tumors (Table III). Esposito et al.^[11] reported these rates as 27%, 26%, 59%, and 86%, respectively. The rate of occult metastasis in early supraglottic larynx cancers (T₁ and T₂) were reported as 23%.^[12]

Neck metastasis was detected in 0% of T₁, 21.4% of T₂, 45.5% of T₃, and 63.6% of T₄ tumors (Table III). When all laryngeal cancers were included, the overall rate of neck metastasis was 28.9%. In a study by Nguyen-Tan et al.^[8] the rate of cervical metastasis was found as 40.8% for T₃-T₄ larynx cancers (13% N₁, 20.2% N₂, and 7.6% N₃).

Concerning the side of the neck, cervical metastasis was detected in 90% of ipsilateral cN₊ necks, and in 37% of contralateral necks in laryngeal cancers; in cN₀ patients nodal metastases were found in 36% and 27% of ipsilateral and contralateral necks, respectively.^[9]

Several studies reported occult metastasis in 27%,^[11] 30%,^[14] and 36%^[9] of supraglottic cancers. Contralateral neck metastasis ranged from 27% to 40% in ipsilateral pN₊ laryngeal cancers.^[9,18]

Neck dissection or radiotherapy has been advocated in supraglottic cancers for better prognosis.^[9,11] In our study, neck dissection was performed in all the patients with supraglottic cancer. In addition, we preferred to perform neck dissection in glottic cancers except for T₁N₀ cases because of the risk of occult metastasis due to the involvement of the subglottis or supraglottis.

Our disease-specific survival rate was found as 90.7% for two years and five years. The overall survival rate was 87.3% for two years, and 73.7% for five years, with disease-related deaths occurring in patients with advanced tumors (T₃ and T₄) and neck metastasis. None of the patients with stage I, II, and III disease died. We concluded that neck metastasis and advanced stage were the most effective prognostic factors.

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