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Original Article / *Özgün Makale*

Long-term analysis of bilateral versus unilateral neck dissection in the treatment of early-stage supraglottic laryngeal cancer

Supraglottik larenks kanser tedavisinde iki taraflı ve tek taraflı boyun diseksiyonu uzun dönem sonuçlarının karşılaştırılması

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ABSTRACT

Objectives: This study aimed to investigate the effect of routine bilateral neck dissection on the survival outcomes of supraglottic laryngeal cancer patients with lateralized tumors and clinically negative necks.

Patients and Methods: The data of 234 patients surgically treated for supraglottic squamous cell carcinoma between January 2000 and September 2014 were retrospectively collected. Patients treated previously for head and neck cancer, patients who could not be contacted, and those with missing data were excluded. Of the remaining 187 patients, 124 patients with early-stage primaries (T1-T2) (116 males, 8 females; mean age: 55.5±9.5 years; range, 33 to 82 years) were included. Age and sex of the patients, site of the primary tumor, TNM stage, type of the neck dissection, length of follow-up, and survival rates were evaluated. The tumors were classified into three groups according to their relationship with the median line of the larynx, and the neck dissections were recorded as unilateral or bilateral. Recurrences and survival outcomes were evaluated.

Results: There was no statistically significant difference in the recurrences according to tumor site groups (p=0.39). Similarly, there was no statistically significant difference in 10-year overall survival rates in patient groups according to the tumor site (p=0.072). We found no statistically significant difference in 10-year overall survival rates between the patients who underwent unilateral and bilateral neck dissection (p=0.580).

Conclusion: Long-term survival analysis of 124 patients with supraglottic carcinoma did not show a survival benefit of elective contralateral neck dissection in lateralized supraglottic cancer with contralateral clinically negative neck.

Keywords: Laryngeal cancer, neck dissection, supraglottis.

ÖZ

Amaç: Bu çalışmada lateralize tümörlü supraglottik larenks kanseri hastalarında, klinik olarak negatif boyun varlığında rutin iki taraflı boyun diseksiyonunun sağkalım sonuçlarına etkisi araştırıldı.

Hastalar ve Yöntemler: Skuamöz hücreli supraglottik larenks karsinomu nedeniyle Ocak 2000 - Eylül 2014 tarihleri arasında cerrahi olarak tedavi edilen 234 hastanın verileri retrospektif olarak toplandı. Daha önce baş ve boyun kanseri nedeniyle tedavi gören hastalar ile ulaşılamayan veya verileri eksik olan hastalar çalışma dışı bırakıldı. Geriye kalan 187 hastadan, erken evreli primerleri (T1-T2) olan 124 hasta (116 erkek, 8 kadın; ort. yaş: 55.5±9.5 yıl; dağılım, 33-82 yıl) çalışmaya dahil edildi. Hastaların yaş ve cinsiyeti, primer tümörün yerleşim yeri, TNM evresi, boyun diseksiyonu tipi, takip süresi ve sağkalım oranları değerlendirildi. Tümörler larenks orta hat ile ilişkilerine göre üç gruba ayrıldı, boyun diseksiyonları da tek taraflı veya iki taraflı olarak kaydedildi. Rekürrensler ve sağkalım sonuçları değerlendirildi.

Bulgular: Tümör yerleşim yerine göre oluşturulan gruplarda, rekürrens oranları arasında istatistiksel olarak anlamlı bir fark bulunmadı (p=0.39). Benzer şekilde, tümör yerleşim yerine göre 10 yıllık sağkalım oranlarında da istatistiksel olarak anlamlı bir fark yoktu (p=0.072). Tek taraflı ve iki taraflı boyun diseksiyonu yapılan hastalar arasında da 10 yıllık genel sağkalım oranları açısından istatistiksel olarak anlamlı bir fark saptanmadı (p=0.580).

Sonuç: Supraglottik karsinomlu 124 hastanın uzun dönem sağkalım analizine göre, klinik olarak karşı taraf boynu negatif lateralize supraglottik kanserde, elektif karşı taraf boyun diseksiyonunun sağkalım üzerine avantajı gözlenmedi.

Anahtar sözcükler: Larenks kanseri, boyun diseksiyonu, supraglottis.

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In head and neck cancers, the most important parameter in terms of survival is the stage of metastatic disease in the neck.[1] Supraglottic carcinoma of the larynx has a strong predilection for cervical metastases since it has rich lymphatic drainage compared to other laryngeal sites.[2,3] Nodal status is the main prognostic factor in the curability and survival of those patients.[4-7] Since the incidence of occult neck metastasis has been reported to reach up to 30%, the elective treatment of the N0 neck is routinely performed.[8] The primary therapy chosen for the treatment of the primary lesion is generally the accepted treatment also for the N0 neck,[4] and thus selective neck dissection is performed correspondingly in case of surgical treatment of the primary lesion.

Supraglottic cancers have a higher risk of contralateral or bilateral neck metastases. However, it is reported that lateralized primary tumors are rarely metastatic to the contralateral neck at the time of diagnosis.[9] Longer operative time, increased postoperative complications and morbidity are the potential risks of bilateral neck dissections.[10] When to perform bilateral neck dissection in a lateralized primary with a clinically negative neck is still a matter of debate.

The current trend in the treatment of laryngeal cancer shows that radiotherapy or chemoradiotherapy protocols are frequently preferred. If surgery is chosen as the primary treatment modality, it should be targeted to reduce morbidity and improve the long-term quality of life without impairing the patient's life expectancy. Consequently, surgery of the contralateral neck in lateralized laryngeal cancer is a controversial issue regarding the patient's perioperative and postoperative morbidity. This study aimed to investigate whether routine bilateral neck dissection in clinically negative necks improves treatment outcomes of the supraglottic cancer patients with lateralized tumors by retrospectively analyzing the clinical, pathological, and follow-up data.

PATIENTS AND METHODS

In this study, retrospective data of 234 patients surgically treated for supraglottic squamous cell carcinoma by supraglottic laryngectomy and its modifications were collected from January 2000 and September 2014. The data was collected from three different tertiary referral centers. Patients treated previously for head and neck cancer with surgery or radiotherapy and patients who could not be contacted or those with missing data were excluded from the study. Of the remaining 187 patients, 124 patients (116 males, 8 females; mean age: 55.5±9.5 years; range, 33 to 82 years) with early-stage primaries [T-stage 1 and 2 according to the 8th edition of American Joint Committee on Cancer (AJCC) staging manual] were included in the study; T3 and T4 tumors and N-positive patients (n=53) were excluded. Age and sex of the patients, site of the primary tumor, TNM stage, type of the neck dissection, length of follow-up after surgery, and the survival rates were evaluated.

The tumors were classified according to their relationship with the median line of the larynx as following: well-lateralized tumors not involving the midline (Group 1), lateralized tumors extending up to the midline (Group 2), and centrally located tumors involving both sides equally (Group 3).

Inclusion criteria to define the N0 neck in laryngeal cancer patients were based upon characteristics of detectable lymph nodes in contrast-enhanced computed tomography or magnetic resonance imaging. The neck dissections were performed either as unilateral or

Table 1
Tumor site, neck dissection, and evaluation of recurrence according to neck dissection and tumor site (n=28)

			Recurrence				
	n	%	Local	Regional	Systemic	*Total* p=0.39‡	*p*
Tumor site							
Lateralized	16	12.9	2	-	2	4	0.494†
Extending to midline	75	60.5	1	6	7	14	0.590†
Central	33	26.6	3	5	2	10	1.000†
Neck dissection							
Unilateral	69	55.6	-	5	-	-	0.177‡
Bilateral	55	44.1	-	6	-	-	

† Yates Continuity Correction test; ‡ Pearson chi-square test.

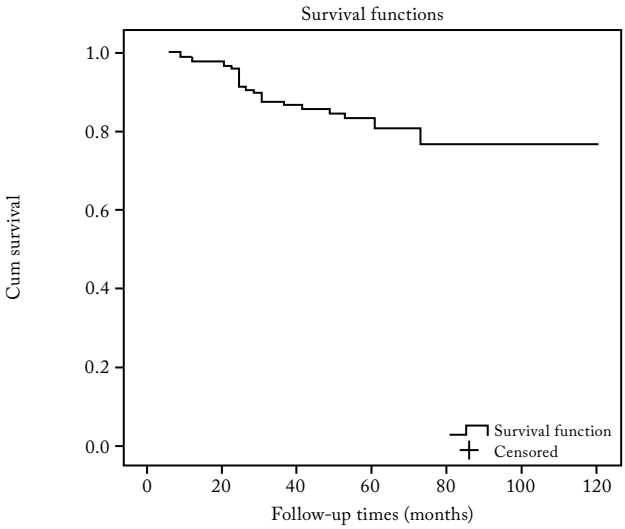


Figure 1. Overall survival curve.

bilateral considering the laterality of the primary tumor, meaning that unilateral neck dissection was chosen for well-lateralized tumors, and bilateral neck dissection was performed for midline tumors and those crossing the midline.

Statistical analysis

Statistical analyses was performed using the IBM SPSS version 21.0 software (IBM Corp.; Armonk, NY, USA). In addition to standard descriptive statistical calculations (median, standard deviation, frequency, and ratio), One-way analysis of variance (ANOVA), Pearson chi-square test, Yates' continuity correction, and Fisher's exact test were used in the assessment of parameters. The overall survival and disease-specific survival rates were calculated with the Kaplan-Meier method and log-rank test. The statistical significance level was determined as $p<0.05$.

RESULTS

The median follow-up time was 68.6±42.2 (range, 60 to 120) months.

Evaluation of tumor site

Group 1 consisted of 16 (12.9%) patients with well-lateralized tumors, Group 2 consisted of 75 (60.5%) patients with lateralized tumors extending up to the midline, and Group 3 consisted of 33 (26.6%) patients with centrally located tumors (Table 1).

TNM staging

The tumors were classified as T1 in 16 (12.9%) patients and T2 in 108 (87.1%) patients. All patients were staged N0 preoperatively. Final pathological examination demonstrated N0 in 101 (81.5%) patients and N1 in 23 (18.5%) patients. Thus, the neck status of 23 patients was upstaged in the postoperative pathological staging, and the unilateral metastatic lymph node was located ipsilaterally in all patients. No contralateral metastasis was observed.

Neck dissection

Bilateral neck dissections were performed in 55 (44.4%) patients, and unilateral neck dissection was performed in 69 (55.6%) patients (Table 1). All patients in Group 3 and 22 patients in Group 2 with primary tumor stage T2 underwent bilateral neck dissection.

Recurrences

Recurrences were classified as local, regional, and systemic, which was observed in 28 (22.6%) patients, and the details were given in Table 1. The median time to relapse was 43.9±49.1 months. There was no statistically significant difference in recurrences according to the tumor site and the type of neck dissection ($p>0.05$).

Table 2
Survival analysis according to neck dissection types and tumor site

	Overall survival		Disease specific survival		Disease specific mean survival time	95% CI
	n	%	n	%	Mean±SD	Lower-Upper
Neck dissection						
Unilateral (n=69)	55	79.7	60	86.9	102.9±3.5	96.155-109.702
Bilateral (n=55)	42	76.4	46	83.6	99.5±5.2	89.285-109.795
Tumor site						
Lateralized (n=16)	14	87.5	14	87.5	99.5±5.1	89.589-109.405
Extending to midline (n=75)	58	77.3	65	86.7	109.1±3.6	108.074-116.203
Central (n=33)	25	75.8	27	81.8	92.5±6.9	78.862-106.088

SD: Standard deviation; CI: Confidence interval; Kaplan-Meier Analysis.

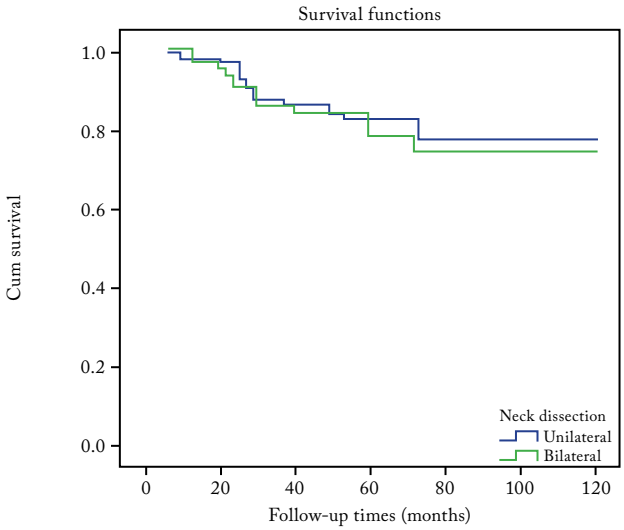


Figure 2. Survival curves according to the neck dissection performed.

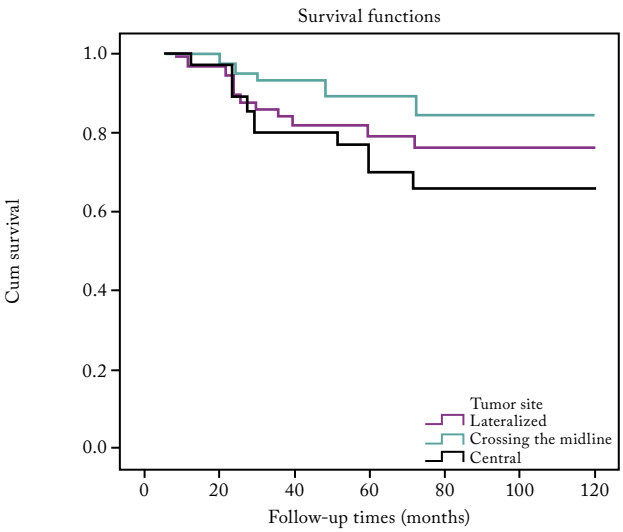


Figure 3. Survival curves according to the tumor site.

Survival analysis

Of all 124 patients, 97 (78.2%) survived, and 27 died. Of the 27 patients, 18 died due to recurrence or metastasis of the laryngeal cancer, and the disease-specific survival rate was 87.1%. The mean survival time was 101.8±2.9 months (Figure 1). Among the patients (n=69) who underwent unilateral neck dissection, 55 (79.7%) patients survived. Of the 55 patients who underwent the bilateral neck dissection, 42 (76.4%) survived. There was no statistically significant difference in 10-year overall survival rates between the patients who underwent unilateral or bilateral neck dissection by the log-rank test (p=0.580; p>0.05)

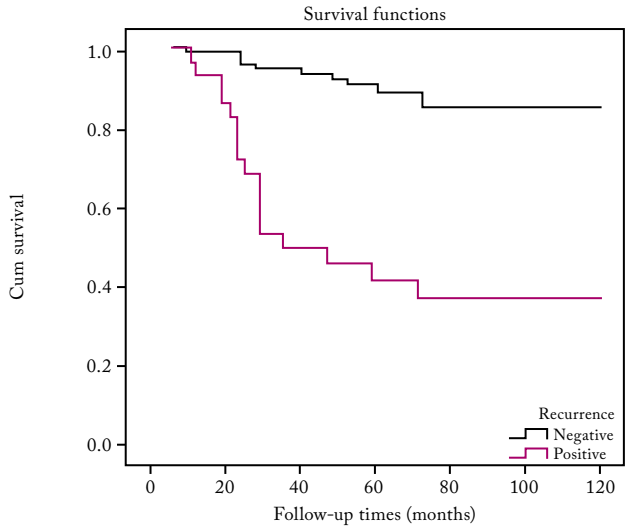


Figure 4. Survival curves according to the status of recurrence.

(Table 2, Figure 2). There was no statistically significant difference in 10-year overall survival rates between patient groups according to tumor site (p=0.072; p>0.05) (Table 2, Figure 3). The overall survival rate was lower in patients with recurrences (p<0.01) (Figure 4).

DISCUSSION

The presence of neck metastases invariably affects the survival of patients with laryngeal cancer.[8] Despite advances in diagnostic tools, occult metastases may not be identified accurately. Carcinomas originating from the supraglottic region have a strong predilection for neck metastases due to the rich lymphatic network and the increased likelihood of early occult lymphatic metastases. Therefore, in most centers, routine elective neck dissection of both sides of the neck is performed in clinically and radiologically N0 patients with supraglottic carcinoma.[11] Simultaneous neck dissection of the opposite side may have some side effects, such as prolonged operation time, risk of ansa cervicalis injury in both sides, and increased laryngeal edema, which delays decannulation and swallowing rehabilitation. Thus, a contralateral neck dissection without oncological benefits will cause a delay in the patient's postoperative rehabilitation process.

It is unclear how and when to treat the clinically negative neck. The lymphatic drainage pattern is imperative in estimating the pattern of metastases. There is no contralateral lymphatic flow in the neck. Additionally, there are numerous valves, which favors descending unidirectional flow within the lymphatic vessels. Therefore, lateralized supraglottic carcinoma

follows the ipsilateral lymphatic vessels draining to levels II and III.[12] The pattern of lymphatic distribution can change after surgical procedures for negative pathologies.[13] Elective neck dissection removes a barrier to the spread of disease and may disturb the mechanisms of recognition and elimination of neoplastic emboli.

When ipsilateral neck metastases are clinically evident, the contralateral neck is treated either by neck dissection or postoperative irradiation.[13] Contralateral metastases in lateralized lesions are infrequent in the absence of ipsilateral metastases.[14] Two authors reported a prevalence of less than 10% of contralateral metastases in lateral supraglottic neoplasms.[15,16] A higher prevalence was observed only when central and lateral neoplasms were concurrent.[3] In our study, 18% of the patients were upstaged from N0 to N1; however, the unilateral metastatic lymph node was located ipsilaterally in all patients.

Unnecessary neck dissections may be correlated with higher morbidity due to the increased operation time, longer hospital stay, and delayed wound healing.[17] Routine use of bilateral neck dissection in clinically and radiologically N0 patients results in more than 50% negative neck specimens.[18] Bilateral elective neck dissection is advised in centrally located lesions since centrally located supraglottic tumors have a high risk of bilateral metastases.[6,14]

Gallo et al.[9] reported that bilateral neck involvement is more frequent in the group of patients with midline supraglottic tumors than those extending up to the midline, whereas well-lateralized tumors has the lowest metastasis rate. This finding is consistent with our study. Similarly, our results do not support contralateral elective neck dissection for the clinically negative neck since unnecessary bilateral procedures do not contribute to survival. Bilateral neck dissections may be reserved for the cases with a clinically positive ipsilateral neck. However, it should be noted that the cohort of this study comprised exclusively early T-stage tumors (T1, T2); T3-T4 tumors were excluded from this study.

In conclusion, long-term survival of 124 patients with early-stage supraglottic carcinoma did not show a statistical benefit of elective contralateral neck dissection in patients with lateralized supraglottic cancer and a contralateral clinically negative neck. In lateralized supraglottic tumors, bilateral neck dissections may be reserved for cases with a clinically positive ipsilateral neck to lessen the surgical complications and morbidity.

Declaration of conflicting interests

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