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Is Bilateral Neck Dissection Necessary in N0 Necks in Laryngeal Cancer? In the Same Session, or Staged Surgery?

Larenks Kanserinde N0 Boyunda Bilateral Boyun Diseksiyonu Gerekli midir? Aynı Seans mı, Farklı Seans mı?

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ABSTRACT Objective: In this study, we aimed to determine ipsilateral and contralateral occult neck metastasis rate in patients who underwent bilateral neck dissection due to T1-T4 N0 laryngeal carcinoma, and put forward the need for bilateral neck dissection. **Material and Methods:** This study included 60 patients who underwent bilateral neck dissections due to T1-T4 N0 laryngeal carcinoma between 1998 and 2015. The patients were divided into three groups according to the localization of the tumor (supraglottic, glottic, and transglottic). Each group was divided into 3 subgroups as unilateral lesion, midline lesion, and unilateral lesion passing across the midline. The neck metastases were classified as ipsilateral, contralateral, or bilateral. **Results:** The tumor was supraglottic in 14, glottic in 13, and transglottic in 33 patients. There was neck metastasis in 9 of 60 patients (3 patients had N1, 3 patients had N2b, and 3 patients had N2c necks). Contralateral neck metastasis was not seen in any of the patients with unilateral tumors. Contralateral neck metastasis was not evident when there was not an ipsilateral neck metastasis. The rate of contralateral neck metastasis in presence of ipsilateral neck metastasis was 33% in supraglottic, 50% in glottic T4a, and 25% in transglottic tumors. **Conclusion:** The results of this study indicated that unilateral neck dissection was sufficient in all groups in case of unilateral tumors, and unilateral tumors passing across the midline when there is no ipsilateral neck metastasis, but bilateral neck dissection is needed in midline tumors.

Keywords: Laryngeal cancer; neck dissection; metastasis

ÖZET Amaç: Bu çalısmada amacımız, T1-T4 N0 larinks kanseri nedeniyle bilateral boyun diseksiyonu yapılan hastalarda, lezyon tarafı ve kontralateral occult metastaz oranlarını saptayarak, bilateral boyun diseksiyonu gerekliliğini belirlemektir. **Gereç ve Yöntemler:** Bu çalışmada 1998-2015 yılları arasında, T1-T4 N0 larinks kanseri nedeniyle bilateral boyun diseksiyonu uygulanan 60 hasta değerlendirilmiştir. Hastalar tümör lokalizasyonuna göre 3 grupta incelenmiştir (supraglottik, glottik, transglottik). Her grup kendi içinde tek taraflı lezyon, orta hat ve orta hattı geçmiş tek taraflı lezyon seklinde 3 gruba ayrıldı.Tüm grupların metastaz oranları unilateral, kontralateral ve bilateral olarak sınıflandırıldı. **Bulgular:** Tümör, 14 hastada supraglottik, 13 hastada glottik, 33 hastada transglottik idi. Altmış hastanın 9'unda boyun metastazı saptandı (3 N1, 3 N2b,3 N2c). Tek taraflı lezyonların hiçbirinde karşı tarafta metastaz tespit edilmedi. Lezyon tarafında metastaz saptanmayan olguların hepsinde karsı tarafta da metastaz saptanmadı. Lezyon tarafında metastaz saptanan olgularda karsı tarafta metastaz saptanma oranı supraglottik lezyonlarda %33, glottik T4a lezyonlarda %50, transglottik lezyonlarda %25 olarak saptandı. **Sonuç:** Bu bulgular tum lezyon gruplarında tek taraflı ve orta hattı geçen tek taraflı tümörlerde lezyon tarafında metastaz saptanmaması durumunda unilateral boyun diseksiyonunun yeterli olduğu, orta hat lezyonlarında ise bilateral boyun diseksiyonu yapılmasının uygun olacağı sonucunu ortaya koymaktadır.

Anahtar Kelimeler: Larinks kanseri; boyun diseksiyonu; metastaz

Metastatic nodal disease is the most important prognostic factor in laryngeal cancer as in the other head and neck cancers.[1] Histologically identified regional metastasis is correlated with an increased risk for recurrence, and approximately 50% decrease in survival.[2] Although the incidence of occult neck metastasis varies in relation with localization, stage, and differentiation of the laryngeal cancer, occult neck metastasis was reported as 30% in supraglottic laryngeal cancer, and 20% in T3-T4 glottic laryngeal

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cancer.[3-5] The most important cause of treatment failure and decreased survival is recurrence in the neck in laryngeal carcinoma. The most important factor for neck recurrence is the presence of occult metastasis that could not be determined by physical examination and radiological imaging.[6] However, both need for elective neck dissection, and the surgical procedure have been debated in N0 necks in patients with laryngeal carcinoma. Various studies indicated that N0 neck could be treated with surgery alone, or radiotherapy alone.[7,8] Only neck dissection may elucidate the presence of occult metastasis, and it has the advantage of determining clinical stage and the need for adjuvant treatment.

There is no consensus on the surgical procedure to treat neck, or need for ipsilateral or bilateral neck dissection. Some studies recommend only ipsilateral neck dissection, while some others claim that bilateral neck dissection is needed.[9-14]

The need for tracheotomy after surgery decreased with widespread use of laser and robotic surgery in surgical treatment of laryngeal cancer. However, studies have recommended neck dissection 3 weeks after primary surgery since concomitant neck dissection increased the need for tracheotomy due to edema.[15] The limiting factors of bilateral neck dissection are possible complications of neck dissection, and edema causing difficulty of decanulation in case of partial laryngectomy.

In this study, we aimed to determine ipsilateral and contralateral occult neck metastasis rate in patients who underwent bilateral neck dissection due to T1-T4 N0 laryngeal carcinoma, and put forward the need for bilateral neck dissection.

MATERIAL AND METHODS

This study included 60 patients who underwent bilateral neck dissections due to T1-T4 N0 laryngeal carcinoma in Otorhinolaryngology Clinic between 1998 and 2015. The data of the patients were retrospectively analyzed after approval of the study protocol by Ethics Committee for Clinical Research (June 20, 2015; decree no: 24/26).

The primary treatment modalities of the patients included total laryngectomy, open partial laryngectomy techniques chosen in relation with the localization and stage of the tumor, and laser- assisted partial laryngectomy. The patients with previous surgery, radiotherapy, chemotherapy, and extralaryngeal involvement were excluded. The patients were staged in accordance with 1992 AJCC criteria.[16] The tumor was supraglottic in 14, glottic in 13, and transglottic in 33 patients. The patients were divided into three groups according to the localization of the tumor (supraglottic, glottic, and transglottic). Each group was divided into 3 subgroups as unilateral lesion, midline lesion, and unilateral lesion passing across the midline. The metastasis rate was analyzed in each group. The metastases were classified as ipsilateral (at the side of the laryngeal tumor), contralateral (at the opposite side of the laryngeal tumor), or bilateral.

Patient characteristics including age, gender, use of alcohol, and smoking, and tumor characteristics such as localization, stage, and histopathological differentiation were noted. The type of the neck dissection performed, and the histopathological report of the specimen were also recorded.

The primary tumor was evaluated with direct laryngoscopy, computed tomography (CT), and macroscopic examination of the surgical specimen. Neck metastasis was assessed with palpation of the neck, ultrasonography, and CT. The patients with the signs of neck metastasis in the preoperative period were not included in the study. Fifty patients had lateral neck dissection, 6 patients had level 1-2-3-4 dissection, 2 patients had level 1-2-3-4-5 dissection, 1 patient had level 2-3-4-5 dissection, and 1 patient had level 2-3-4-5-6-7 dissection.

STATISTICAL ANALYSIS

Data analysis was performed by using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, United States). While, continuous data were shown as mean±SD (standard deviation), number of cases and percent (%) were used for categorical variables. The mean differences in age between patients with neck metastasis and without neck metastasis were compared by Student's t-test. Categorical data were analyzed by Fisher's exact or Likelihood Ratio test, where appropriate. A p value less than 0.05 was considered statistically significant.

RESULTS

The mean age of 60 patients with clinically N0 necks was 61.0±8.7 (44-85) years, and all patients were males. In supraglottic group, 10 patients had T2, and 4 patients had T3 tumors. In glottic group, 8 patients had T2, 3 patients had T3, 2 patients had T4a tumors while in transglottic group 1 patient had T2, 24 patients had T3, and 8 patients had T4a tumors. Table 1 shows descriptive statistics of demographic and clinical characteristics of 60 patients.

The mean age (p=0.847), and history of alcohol consumption (p=0.422) were similar in patients with and without neck metastasis.

The distribution of the lesion types did not show any significant differences between the patients with and without neck metastasis (p=0.727). The sides of the lesions were similar when all patients included in the study were taken into consideration (p=0.224). The T stage showed a significant difference between the patients with neck metastasis and without neck metastasis, and the rate of T4a tumors was higher in patients with neck metastasis (p=0.034). The differentiations of the tumors were similar when patients with and without neck metastasis were taken into consideration (p=0.669) (Table 2).

There was neck metastasis in 9 of 60 patients. The metastasis was at level 2a in 4, at levels 2a and 3 in 4, and at levels 3 and 4 in 1 patient. None of the patients had metastasis at level 2b. Level 4 metastasis was seen in a patient with T4a glottic cancer (Table 3).

When the neck metastases were analyzed according to the side of the tumor, it was seen that contralateral neck metastasis was not seen in patients without ipsilateral neck metastasis. Analysis of the neck metastases according to the localizations of the tumors revealed that neck metastasis was evident in 2 patients with T2, and in 1 patient with T3 tumors among 14 patients with supraglottic tumors. The rate of metastasis was determined as 30% in supraglottic T2 tumors, and as 25% in supraglottic T3 tumors. Only ipsilateral neck metastasis was seen in unilateral laryngeal tumors, however there was bilateral metastasis in case of midline lesions. Ipsilateral neck metastases were seen in unilateral tumors passing across the midline (Table 4).

There was neck metastasis in 2 of 13 patients with glottic tumors. There were no neck metastases in T2 or T3 tumors, however all patients with T4a tumors had neck metastasis. Two patients with metastasis had T4a tumors. In case of unilateral tumors

TABLE 1: Demographic and clinical characteristics of the patients.

Variables	n=60
Age (years)	61.0±8.7
Age range (years)	44-85
Alcohol consumption	16 (26.7%)
Localization of the tumor	
Supraglottic	14 (23.3%)
Glottic	13 (21.7%)
Transglottic	33 (55.0%)
Side of the tumor	
Unilateral	33 (55.0%)
Midline	4 (6.7%)
Unilateral passing across the midline	23 (38.3%)
T stage	
T2	19 (31.7%)
T3	31 (51.7%)
T4a	10 (16.7%)
Neck metastasis	9 (15.0%)
Localization of neck metastasis	
Ipsilateral	6 (66.7%)
Bilateral	3 (33.3%)
Postoperative N stage	
N0	51 (85.0%)
N1	3 (5.0%)
N2	6 (10.0%)
N2b	3 (5.0%)
N2c	3 (5.0%)
Tumor differentiation	
Well differentiated	17 (28.3%)
Moderately differentiated	30 (50.0%)
Poorly differentiated	13 (21.7%)
Type of neck dissection	
Level 2-3-4	50 (83.3%)
Level 1-2-3-4	6 (10.0%)
Level 1-2-3-4-5	2 (3.3%)
Level 2-3-4-5	1 (1.7%)
Level 2-3-4-5-6-7	1 (1.7%)

TABLE 2: Demographic and clinical characteristics of the patients included in the study (n=60) in relation with the presence of neck metastasis.

Variables	Metastasis negative (n=51)	Metastasis positive (n=9)	p
Age	61.1±8.9	60.4±7.6	0.847†
Alcohol consumption	15 (29.4%)	1 (11.1%)	0.422‡
Tumor			0.727¶
Supraglottic	11 (21.6%)	3 (33.3%)	
Glottic	11 (21.6%)	2 (22.2%)	
Transglottic	29 (56.9%)	4 (%44.4)	
Side of the tumor			0.224¶
Unilateral	29 (56.9%)	4 (44.4%)	
Midline	2 (3.9%)	2 (22.2%)	
Unilateral passing across the midline	20 (39.2%)	3 (33.3%)	
T stage			
T2	17 (33.3%)	2 (22.2%)	0.705‡
T3	28 (54.9%)	3 (33.3%)	0.292‡
T4a	6 (11.8%)	4 (44.4%)	0.034‡
Tumor differentiation			0.669¶
Well differentiated	15 (29.4%)	2 (22.2%)	
Moderately differentiated	26 (51.0%)	4 (44.4%)	
Poorly differentiated	10 (19.6%)	3 (33.3%)	

† Student's t test, ‡ Fisher's exact test, ¶ Likelihood Ratio test.

passing across the midline, only one patient had ipsilateral, and one patient had ipsilateral and contralateral neck metastases (Table 5).

There was neck metastasis in 4 of 33 patients with transglottic tumors. Two of 24 (8.3%) patients with T3 tumors, and 2 of 8 (25%) patients with T4a tumors had lymph node metastasis. All 3 patients with unilateral tumors had ipsilateral neck metastasis, however midline lesions showed bilateral neck metastases (Table 6).

When 9 patients with neck metastasis were taken into consideration, the tumor was unilateral in 4, in the midline in 2, and unilateral passing across the midline in 3 patients. Contralateral neck metastasis was not determined in any of the unilateral tumors. All midline tumors made metastasis to contralateral neck. One third (33.3%) of the unilateral tumors passing across the midline showed metastasis in the contralateral neck. In case of ipsilateral neck metastasis,

TABLE 3: Distribution of patients with postoperative neck metastasis, according to the regions with metastasis (n=9).

Localization	n	%
Only level 2A	4	44.44
Levels 2A and 3	4	44.44
Levels 3 and 4	1	11.11

TABLE 4: Distributions of the tumors in relation with the T stages, and the localizations of the neck metastasis in supraglottic tumors (n=14).

	No metastasis	Unilateral	Bilateral
T2 (n=10)			
Unilateral	4 (40.0%)	1 (10.0%)	-
Unilateral passing across the midline	4 (40.0%)	1 (10.0%)	-
T3 (n=4)			
Unilateral	2 (50.0%)	-	-
Midline	1 (25.0%)	-	1 (25.0%)

TABLE 5: Distribution of localizations of the metastasis in glottic tumors (n=13).

	No metastasis	Unilateral	Bilateral
T2 (n=8)			
Unilateral	5 (62.5%)	-	-
Unilateral passing across the midline	3 (37.5%)	-	-
T3 (n=3)			
Unilateral	1 (33.3%)	-	-
Unilateral passing across the midline	2 (66.7%)	-	-
T4a (n=2)			
Unilateral passing across the midline	-	1 (50.0%)	1 (50.0)

TABLE 6: Distributions of the tumors and localizations of the metastases in relation with the T and N stages in transglottic tumors (n=33).

	No metastasis	Unilateral	Bilateral
T2 (n=1)			
Unilateral	1 (100.0%)	-	-
T3 (n=24)			
Unilateral	15 (62.5%)	2 (8.3%)	-
Unilateral passing across the midline	7 (29.2%)	-	-
T4a (n=8)			
Unilateral	1 (12.5%)	1 (12.5%)	-
Midline	1 (12.5%)	-	1 (12.5%)
Unilateral passing across the midline	4 (50.0%)	-	-

the rate of contralateral neck metastasis was 33% in supraglottic, 50% in glottic T4a, and 25% in transglottic tumors.

DISCUSSION

Treatment of neck is an important part of surgical treatment in laryngeal cancer since lymph node metastasis is the most important prognostic factor.[1,11,17,18] Studies showed that treatment of N0 neck after appearance of overt neck metastasis caused smaller survival rates when compared to the group that had neck dissection at the time of the primary surgery.[14,19-21] Therefore, the type, timing, and side of neck dissection are important in treatment of laryngeal cancer due to their significant effect on survival, and still debated.

The need for elective neck dissection, and the type of the surgical procedure are still debated in N0 necks of the patients with laryngeal cancer. In case of N0 neck, surgical protocol to be employed, and the need for ipsilateral or bilateral neck dissection are still not clear. Some studies suggest neck dissection only for the ipsilateral neck, however some others claim that bilateral neck dissection is necessary.[9-14,22]

Although current minimally invasive surgical techniques and hemostatic equipment, and low complication rates of anesthesia are in favor of selective neck dissection, the neck dissection procedures still have variable complication rates.[23-25] In case of N0 necks, Basheeth et al. reported that the patients that had bilateral neck dissections and salvage laryngectomy had higher complication rates when compared to the ones that had unilateral neck dissections.[25] Today, widespread use of laser and robotic surgery particularly in early-stage larynx cancer made the degree of edema very important at the site of surgery for the need of tracheotomy after surgery. Weinstein et al. claimed that neck dissection performed at the same session with the primary surgery increased the need for tracheotomy due to edema in the surgical field, and therefore neck dissection should be staged and performed 3 weeks after the primary surgery.[15]

Possible complications, and edema causing difficulty of decanulation in case of partial laryngeal surgery are the limitations of bilateral neck dissection.

The pattern of metastasis varies in relation with the localization of the laryngeal tumor. Supraglottic larynx develops as a distinct subunit in the embryo, and this fact has constituted the basis for suggesting bilateral neck dissection in case of supraglottic tumors.[12-14] Chiu et al. reported that bilateral neck dissection prolonged survival in supraglottic laryngeal cancer, and proposed routine bilateral neck dissection since it decreased recurrence in the neck.[13] Similarly, Scola et al. recommended routine bilateral neck dissection in supraglottic tumors due to the high rate of lymphatic metastasis.[12] However, Werner et al. performed lymphatic mapping by injecting intraoperative peritumoral radioisotope in supraglottic cancer arising from the epiglottis, and did not report any involvement in the contralateral neck.[26] Rodrigo et al. compared unilateral and bilateral neck dissection in patients with supraglottic larynx cancer, and did not find any difference between the groups for survival.[9] They determined the rate of lymph node metastasis as 32% in patients with T1-T2 tumors. Cağli et al. analyzed 72 patients that had bilateral neck dissection due to suproglottic laryngeal cancer, and reported that there was no contralateral metastasis in absence of ipsilateral metastasis, and recommended unilateral neck dissection in patients with unilateral tumors.[22] The authors found occult metastasis rates as 8.3% in T2 tumors, as 22.7% in T3 tumors, and as 31.2% in T4 tumors. Our results are in accordance with the results of the aforementioned studies. In our study, we did not find any contralateral lymph node metastasis in absence of ipsilateral lymph node metastasis. In supraglottic tumors, the metastasis rate was found as 20% in T2 tumors, and 25% in T3 tumors. Ipsilateral neck metastasis was seen in case of unilateral tumors, however bilateral neck metastasis was evident in midline tumors. In case of unilateral tumors passing across the midline, only ipsilateral metastasis was present.

The rate of neck metastasis was relatively smaller in glottic tumors when compared to supraglottic tumors, however occult metastasis rate was reported as 20% in T3 and T4 tumors.[4,5] In our study, neck metastasis was not seen in T2 and T3 tumors, however all patients with T4a tumors had neck metastasis. In case of unilateral tumors passing across the midline, one patient had ipsilateral neck metastasis, and one patient had ipsilateral and contralateral neck metastasis.

Kowalski et al. reported the rate of neck metastasis as 41% in transglottic tumors.[6] We determined neck metastasis rate as 8.3% in T3 transglottic tumors, and 25% in T4a tumors. Ipsilateral neck metastasis was seen in all of 3 patients with unilateral tumors, however bilateral neck metastasis was evident in midline tumors. The low metastasis rate in transglottic tumors in the present study may be related to the fact that most of those patients had T3 tumors.

In the light of those findings, one might conclude that unilateral elective neck dissection could be sufficient in case of unilateral tumors, and unilateral tumors passing across the midline irrespective of the localization of the tumor in larynx, however bilateral neck dissection might be more suitable in case of midline tumors. Performing unilateral neck dissection during surgery for the primary tumor, and deciding for the contralateral neck dissection in relation with the ipsilateral neck metastasis is important to prevent overtreatment. This conclusion has been supported by the other similar studies.[9,22] Presence of contralateral metastasis in case of ipsilateral neck metastasis is 33% in supraglottic tumors, 50% in glottic T4a tumors, and 25% in transglottic tumors. This result indicates the necessity of treating contralateral neck when histopathological ipsilateral neck metastasis is proven. In case of histopathological neck metastasis, contralateral neck dissection performed in another session, or elective radiotherapy of contralateral neck are the treatment options. The contralateral neck dissection may be decided in the same session with the primary surgery if metastasis is reported in frozen section of macroscopically suspicious lymph nodes. In this way, overtreatment may be prevented in laryngeal cancers that have a low rate of neck metastasis, and the complications related to neck dissection and a longer duration of anesthesia may be prevented. This procedure is particularly important to decrease edema in the surgical field, and

hence the need for tracheotomy in partial laryngectomies.

The neck levels to be included in the neck dissection has been debated as well as the side of the neck dissection in N0 necks in laryngeal cancer. A number of studies showed that lateral neck dissection was sufficient in N0 necks.[27-29] Our results support this opinion. In 4 patients with metastasis, the metastasis was in level 2a, there were metastases in levels 2a and 3 in 4 patients, and there were metastases in levels 3 and 4 in 1 patient. None of the patients had metastasis in level 2b. Metastasis to level 4 was seen in 1 patient with T4a glottic cancer.

Studies reported that the presence of occult metastasis was related to localization, T stage, and histopathological differentiation of the tumor.[3] Although the patients with and without neck metastasis showed a significant difference for T stage in our study (p=0.034), there were no differences for tumor differentiation or localization. However, those factors should be studied in a larger patient population.

CONCLUSION

The results of our study indicate that ipsilateral neck dissection is sufficient in unilateral tumors and unilateral tumors passing across the midline irrespective of the localization of the tumor in the larynx, however bilateral neck dissection is needed in case of midline tumors. Unilateral neck dissection at the same session with the surgical treatment of the primary tumor, and deciding contralateral neck dissection in relation with the metastasis in the ipsilateral neck is important to prevent overtreatment. In this way, the complications related to neck dissection and a longer duration of anesthesia may be reduced, as well as the edema in the surgical field and the need for tracheotomy.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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