Original Article / Çalışma - Araştırma

Paratracheal lymph node dissection, in which patients should it be performed?

Paratrakeal lenf nodu diseksiyonu hangi hastalarda uygulanmalıdır?

Şenol Çomoğlu, MD.,[1] Ece Çomoğlu, MD.,[2] Necati Enver, MD.,[1] Eren Yılmaz, MD.,[1] Mehmet Çelik, MD.,[1] Beldan Polat, MD.,[1] Murat Ulusan, MD.,[1] İsmet Aslan, MD.,[1] Kemal Değer, MD.[1]

[1]Department of Otolaryngology, Medicine Faculty of İstanbul University, İstanbul, Turkey
[2]Department of Otolaryngology, Kağıthane State Hospital, İstanbul, Turkey

ABSTRACT

Objectives: This study aims to evaluate the effect of paratracheal lymph node (PTLN) metastasis on survival in patients with advanced laryngeal and hypopharyngeal cancer.

Patients and Methods: Medical records of advanced laryngeal and hypopharyngeal cancers who underwent surgery between May 1995 and June 2008 were assessed and 78 of the patients (63 males, 15 females; mean age 55±11.3 years; range 25 to 76 years) who has PTLN metastasis were included in this study. The mean follow-up period was 23 months. Fifty-three patients had primary laryngeal cancer, and the remaining 25 patients had primary hypopharyngeal cancer.

Results: Paratracheal lymph node metastasis was detected in eight (15%) of 53 patients with laryngeal carcinoma, six (42%) of 14 patients with postcricoid carcinoma, and one (14%) of seven patients with posterior pharyngeal wall carcinoma. Paratracheal lymph node metastasis was not detected in patients with pyriform sinus carcinoma (n=4). Paratracheal lymph node metastasis was detected in a total of 15 patients, of whom 11 had extranodal spread (ENS). Multivariate analysis showed that the presence of ENS was the most effective prognostic factor on the overall survival (p<0.0005).

Conclusion: The presence of PTLN metastasis with ENS is an important prognostic indicator on overall survival. We recommend PTLN dissection particularly in patients with advanced laryngeal or hypopharyngeal cancer for histopathological analysis and prognostication because ENS can only be precisely detected by pathological evaluation.

Keywords: Head and neck cancer; hypopharynx; larynx; paratracheal lymph node metastasis; prognosis; total laryngectomy.

ÖZ

Amaç: Bu çalışmada paratrakeal lenf nodu (PTLN) metastazının ileri evre larengeal ve hipofarenks kanseri hastalarında sağkalıma etkisi değerlendirildi.

Hastalar ve Yöntemler: Mayıs 1995 - Haziran 2008 tarihleri arasında ameliyat olan ileri evre larengeal ve hipofarengeal kanserli hastaların tıbbi kayıtları değerlendirildi ve PTLN metastazı olan hastaların 78'i (63 erkek, 15 kadın; ort. yaş 55±11.3 yıl; dağılım 25-76 yıl) çalışmaya dahil edildi. Ortalama izlem süresi 23 aydı. Elli üç hasta primer larenks kanseri ve kalan 25 hasta primer hipofarengeal kanseri idi.

Bulgular: Paratrakeal lenf nodu metastazı 53 hastanın sekizinde (%15) larenks kanseri ile, 14 hastanın altısında (%42) postkrikoid kanseri ile, ve yedi hastanın birinde (%14) ise yutak arka duvar kanseri ile tespit edildi. Paratrakeal lenf nodu metastazı, hipofarenksin piriform sinüsünden gelişen kanserli hastalarda tespit edilmedi (n=4). Paratrakeal lenf nodu metastazı 11'inde ekstranodal yayılması (ENS) olan toplam 15 hastada saptandı. Çoklu analizler ENS varlığının genel sağkalım üzerinde en etkili prognostik faktör olduğunu gösterdi (p<0.0005).

Sonuç: Ekstranodal yayılması ile PTLN metastazı varlığı genel sağkalım üzerinde önemli bir prognostik göstergedir. Paratrakeal lenf nodu diseksiyonu özellikle ileri evre larengeal veya hipofarengeal kanserli hastalarda histopatolojik analiz ve prognoz için tavsiye edilmektedir çünkü ENS sadece patolojik değerlendirme ile kesin olarak tespit edilebilir.

Anahtar Sözcükler: Baş ve boyun kanseri; hipofarenks; larenks; paratrakeal lenf nodu metastazı; prognoz; total larenjektomi.

Available online at
www.kbbihtisas.org
doi: 10.5606/kbbihtisas.2016.22129
QR (Quick Response) Code

Received / *Geliş tarihi:* August 28, 2015 Accepted / *Kabul tarihi:* March 30, 2016

Correspondence / İletişim adresi: Şenol Çomoğlu, MD. İstanbul Üniversitesi İstanbul Tıp Fakültesi Kulak Burun Boğaz Hastalıkları Anabilim Dalı, 34093 Fatih, Çapa, İstanbul, Turkey.

Tel: +90 530 - 746 02 34 e-mail *(e-posta):* drcomoglu@gmail.com

Metastatic nodal disease is an important prognostic factor in head and neck cancer.[1] Neck dissection is the gold standard for treatment of neck metastasis. In clinically N_0 necks, selective neck dissection is performed for regions at risk by taking the stage and location of the tumor into account.[2] In laryngeal and hypopharyngeal cancers, the paratracheal region is among the regions at high risk for metastatic nodal disease.[3] However, it is not clear yet when it is necessary to include the paratracheal region while performing elective neck dissection. The present study aimed to evaluate the incidence of paratracheal nodal metastatic disease in patients with advanced laryngeal and hypopharyngeal cancer, its relationship with the stage and location of the tumor, and the prognostic significance of paratracheal lymph node (PTLN) metastasis in patients who underwent laryngectomy alone or with pharyngectomy.

PATIENTS AND METHODS

The records of 78 patients (63 males and 15 females; mean age 55±11.3 years; range, 25 to 76 years), who underwent paratracheal dissection with the diagnosis of primary laryngeal or hypopharyngeal carcinoma at the Ear-Nose-Throat Department of Istanbul Medical Faculty, Istanbul University between May 1995 and June 2008, were retrospectively reviewed. Fifty-three patients had primary laryngeal cancer, and the remaining 25 patients had primary hypopharyngeal cancer. The study protocol was approved by the Istanbul University Faculty of Medicine Ethics Committee. Written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Tumors were staged according to the Union for International Cancer Control (UICC) tumor-node-metastasis (TNM) classification.[4] All patients were those with laryngeal or hypopharyngeal squamous cell carcinoma confirmed by biopsy in whom primary surgery was planned. Only patients with advanced stage tumors (T_3 and T_4) requiring total laryngectomy were included in the study. Radical or modified radical neck dissection was performed on patients with clinical or radiological evidence of neck metastases, whereas lateral neck dissection was performed on other patients. Paratracheal dissection was performed by extending the dissection field downwards on the side in which the neck dissection was performed. If the neck dissection was performed bilaterally, the paratracheal dissection was also performed bilaterally. The limits for the PTLN dissection included the trachea medially, the carotid laterally, and the region providing a safe resection inferiorly. The mean follow-up period after surgery was 23 months (range, 1-55 months).

Statistical analysis

Kaplan-Meier survival analysis was performed to estimate survival probability, and the differences between the groups were determined using the log-rank chi-square test. Multivariate analysis was used to assess effects of prognostic factors on survival. Association between PTLN metastasis and the stage of the neck disease was showed using Pearson chi-square test. The statistical analysis was performed using WinStat Statistical Package, (Version 2009.1, Fitch Software, Cambridge, MA, USA).

RESULTS

For the treatment of the primary tumor site, total laryngectomy was performed on 53 patients with laryngeal cancer, whereas 25 patients with hypopharyngeal tumors underwent total laryngectomy and partial/total pharyngectomy and/or total esophagectomy. Distribution of the patients who died due to recurrence according to the primary tumor site is presented in Table 1.

Table 1. Distribution of patients who died due to recurrence according to primary tumor site

Primary tumor site	Number of patients	Death due to recurrence
Larynx	53	12
Postcricoid area	14	6
Sinus pyriformis	4	1
Posterior pharyngeal wall	7	5

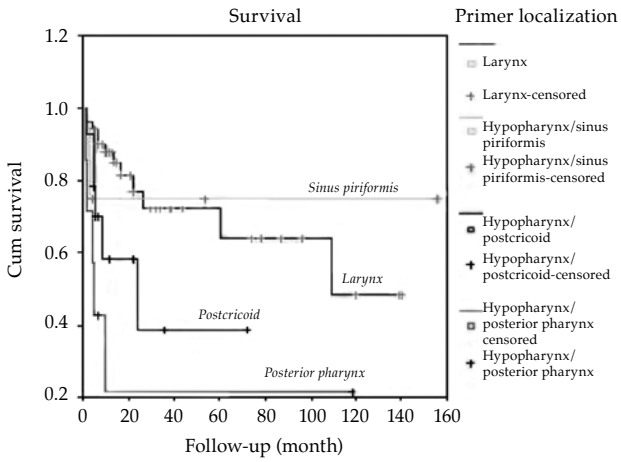

Figure 1. *Mean survival of patients grouped according to primary tumor site.*

The survival of patients in whom the primary tumor site was the larynx was observed to be slightly better than those in whom the primary tumor site was the hypopharynx. Patients with cancer of the posterior pharyngeal wall had the worst prognosis. Significant differences were found between patients grouped according to primary tumor site in terms of mean survival ($p<0.05$, log-rank chi-square test; Figure 1).

The rates of PTLN metastasis according to primary tumor site in 78 patients who underwent total laryngectomy and PTLN dissection are presented in Table 2. In the present study, the rate of PTLN metastasis was 19%. The incidence of PTLN metastasis was assessed according to primary tumor site and extension of tumor. Paratracheal lymph node metastasis was present in eight (15%) of 53 patients with laryngeal tumor, and seven (28%) of 25 patients with hypopharyngeal tumor. Sites of hypopharyngeal tumor in patients with PTLN metastasis were postcricoid in six and posterior pharyngeal wall in one respectively. Non of the patients with pyriform sinus site had PTLN metastasis. Paratracheal lymph node metastasis was also observed in five (12%) of 39 laryngeal tumor patients with subglottic extension and three (21%) of 14 laryngeal tumor patients without subglottic extension. Although not statistically significant, the overall survival of the patients with PTLN metastasis was lower than that of those without PTLN metastasis ($p<0.1060$; Figure 2).

In the present study, the relationship between PTLN metastasis and the stage of neck disease was also assessed. While no PTLN metastasis was observed in any of the patients with N_0 neck disease, it was noted in one of the patients with N_1 and N_{2a} neck disease, in four of the patients with N_{2b} neck disease, and in nine of the patients with N_{2c} neck disease. There was a significant positive association between the rate of PTLN metastasis and the stage of neck disease (Pearson chi-square test, $p<0.001$; Figure 3). Multivariate analysis showed that the presence of ENS was the most effective prognostic factor on the overall survival ($p<0.0005$).

When the rates of PTLN were analyzed according to the stage of the primary tumor, two (9%) of the patients with stage T_3 tumor and 13 (%23.2) of the patients with stage T_4 tumor were determined to have PTLN metastasis. There was a positive, but not significant, association between the rate of PTLN metastasis and the stage of the primary tumor ($p=0.210$; Figure 4).

Extracapsular spread (extranodal spread; ENS) was present in 66% of patients with paratracheal neck metastasis. The mean survival of the patients with PTLN metastasis and extracapsular spread (P+, ENS+) was significantly lower than that of the patients with PTLN metastasis without extracapsular spread (P+, ENS-; $p<0.03$, log-rank chi-square test). There was no statistically significant difference

Table 2. Rates of paratracheal lymph node metastasis according to primary tumor site

Primary tumor site	Number of patients	PTLN metastasis	
		n	%
Larynx	53	8	15
Postcricoid area	14	6	42
Sinus pyriformis	4	0	0
Posterior pharyngeal wall	7	1	14

PTLN: Paratracheal lymph node.

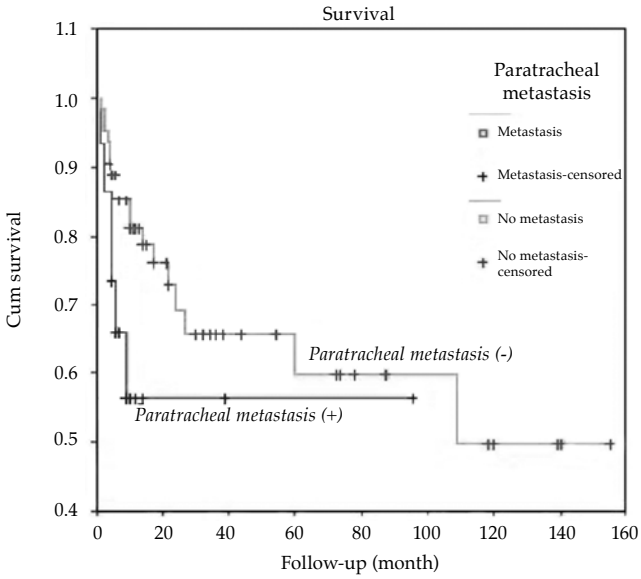

Figure 2. *Mean survival of patients with and without paratracheal lymph node metastasis.*

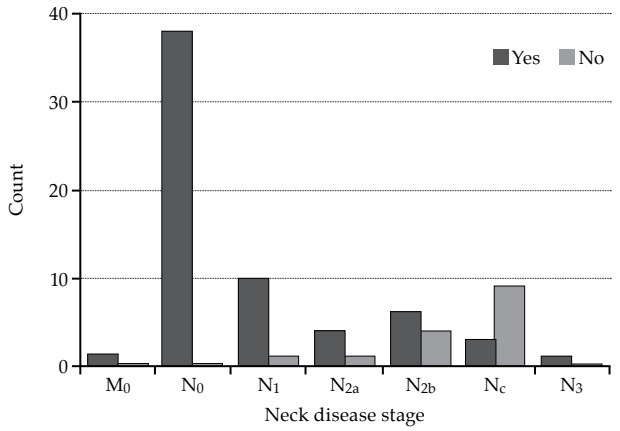

Figure 3. *Association between stage of neck disease and paratracheal metastasis.*

in survival rates between the patients with PTLN metastasis without extracapsular spread (P+, ENS-) and those without PTLN metastasis and extracapsular spread (P-, ENS-; Figure 5).

DISCUSSION

The effect of neck metastasis on the prognosis and treatment of advanced laryngeal and hypopharyngeal cancers is well known.[1] The lymphatic network of the head and neck region and the pattern of lymphatic spread in head and neck cancers are also well known. However, knowledge regarding the onset and pattern of tumor spread to the upper mediastinum and the paratracheal region, as well as the impact of this spread is limited. Because this region forms the border of the neck with the thorax, there is a need for an algorithmic approach for the surgical planning. In the present study, we aimed to understand the importance of metastases to this region.

The incidence of paratracheal metastasis in the present study was found to be 19%, which was comparable to the findings of the retrospective studies of Weber et al.[3] and Timon et al.[5] (21% and 26%, respectively). In the present study, the incidence of paratracheal metastasis was also assessed according to the primary tumor site and extension of the tumor. Paratracheal lymph

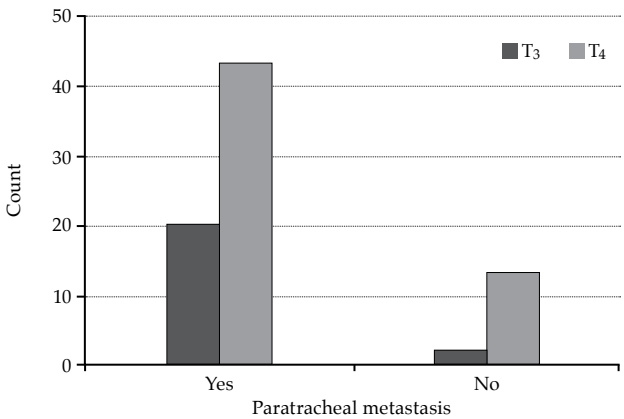

Figure 4. *Association between tumor stage (T) and paratracheal metastasis.*

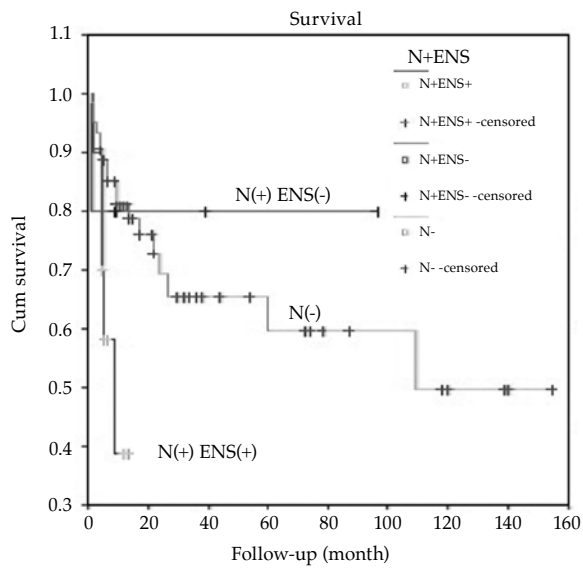

Figure 5. *Mean survival of patients according to stage of neck disease (N) and extranodal spread (ENS).*

node metastasis was detected in 15% of patients with laryngeal cancer and in 28% of patients with hypopharyngeal cancer. Weber et al.[3] reported the rates of PTLN metastasis to be 18% for laryngeal tumors, 8% for hypopharyngeal tumors, and 71% for tumors of the cervical esophagus. Timon et al.[5] determined the rates of paratracheal nodal metastasis to be 20% for laryngeal tumors and 43% for tumors of the cervical esophagus (including the postcricoid region). In the study by Plaat et al.,[6] the rates of the PTLN metastasis were reported to be 20% for laryngeal tumors and 35% for hypopharyngeal and cervical esophageal tumors. In that particular study, paratracheal metastasis was not observed in hypopharyngeal tumors (excluding postcricoid region). In the present study, the incidence of PTLN metastasis was higher in hypopharyngeal tumors than in laryngeal tumors. When the tumors of the postcricoid region were excluded, PTLN metastasis was present only in one tumor of the posterior hypopharyngeal wall. No metastasis was observed in any tumors of the pyriform sinus. The reason underlying the discrepancy between the rates of the paratracheal metastasis reported in the literature is the lack of a clear definition of the selection criteria for patients in whom paratracheal dissection will be performed. Thus, a comparison of the findings of these studies is difficult.

In the present study, the survival of the patients with PTLN metastasis was lower than that of the patients without metastasis; however, this result was not statistically significant (log rank chi-square test, $p<0.1060$). The mean survival of the patients with PTLN metastasis and extracapsular spread (P+, ENS+) was poorer than that of the patients with PTLN metastasis without extracapsular spread (P+, ENS-; $p<0.05$). The survival of the patients without PTLN metastasis and extracapsular spread (P-, ENS-) was not better than that of the patients with paratracheal metastasis without extracapsular spread (P+, ENS-). The presence of PTLN metastasis with extracapsular spread appears to be an important prognostic factor on the survival in patients with laryngeal and hypopharyngeal tumors. This result was similar to that reported in the study by Plaat et al.[6] However, these results were not consistent with other studies in which the paratracheal metastasis alone was reported to be the only prognostic factor.[7,8]

Subglottic extension of the tumor is considered a possible cause for the PTLN metastasis. In the present study, in patients with laryngeal tumors, PTLN metastasis was present in 12% of the patients with subglottic extension and in 21% of the patients without subglottic extension. The rate of PTLN metastasis was higher in patients with laryngeal tumor without subglottic extension. In the present study, significant outcomes were obtained by considering the stages of the tumor and neck disease in addition to the presence of the subglottic extension during the decision-making of paratracheal dissection in patients with laryngeal tumors.

In conclusion, extranodal spread to the paratracheal lymph nodes in patients with advanced laryngeal or hypopharyngeal cancers appears to be an important prognostic factor. We performed PTLN dissection according to the tumor site and the extension of the tumor. Currently, there is no clear information regarding the conditions under which PTLN dissection should be performed. To clarify this issue, well-planned prospective studies are required. In advanced stage cancers, particularly in advanced stage neck disease, performing PTLN dissection during neck dissection may be recommended, as it does not increase the morbidity and the length of the surgery. Because, preoperative detection of the extranodal spread is considerably difficult, even impossible, the use of adjuvant therapy in the presence of metastasis or extranodal spread in patients undergoing PTLN dissection can be helpful to decrease the risk of recurrence.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Shah JP. Patterns of cervical lymph node metastasis from squamous carcinomas of the upper aerodigestive tract. Am J Surg 1990;160:405-9.
2. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage N0 neck. Arch Otolaryngol Head Neck Surg 1994;120:699-702.

3. Weber RS, Marvel J, Smith P, Hankins P, Wolf P, Goepfert H. Paratracheal lymph node dissection for carcinoma of the larynx, hypopharynx, and cervical esophagus. Otolaryngol Head Neck Surg 1993;108:11-7.
4. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC cancer staging manual. 7th ed. New York: Springer; 2010.
5. Timon CV, Toner M, Conlon BJ. Paratracheal lymph node involvement in advanced cancer of the larynx, hypopharynx, and cervical esophagus. Laryngoscope 2003;113:1595-9.
6. Plaat RE, de Bree R, Kuik DJ, van den Brekel MW, van Hattum AH, Snow GB, et al. Prognostic importance of paratracheal lymph node metastases. Laryngoscope 2005;115:894-8.
7. Rockley TJ, Powell J, Robin PE, Reid AP. Post-laryngectomy stomal recurrence: tumour implantation or paratracheal lymphatic metastasis? Clin Otolaryngol Allied Sci 1991;16:43-7.
8. Petrovic Z, Djordjevic V. Stomal recurrence after primary total laryngectomy. Clin Otolaryngol Allied Sci 2004;29:270-3.