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HEAD AND NECK

Lymph node yield and lymph node density for elective level II–IV neck dissections in laryngeal squamous cell carcinoma patients

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Abstract

Purpose To determine the minimum lymph node yield (LNY) in patients with laryngeal squamous cell carcinoma (LSCCs).

Methods This retrospective study was performed in a tertiary care hospital setting and included 42 LSCC patients aged 39–81 years (females, $n=2$; males, $n=40$) who underwent a total or partial laryngectomy and elective bilateral level II–IV neck dissections (unilateral neck dissections: $n=84$).

Results The average LNY in the unilateral level II–IV lymph node dissections was 25.9 ± 10, and the average metastatic LNY was 0.9 ± 1.9. The unilateral neck dissections were grouped according to the number of lymph nodes. There was no significant difference between the groups in terms of the metastatic LNY ($p=0.5$). The metastatic lymph node density (LND) (metastatic lymph node yield/LNY) was 0.043 for unilateral neck level II–IV neck dissections. A Cox regression analysis revealed no significant relationship between survival and the LNY and LND in bilateral neck dissections ($p=0.4$ and $p=0.8$, respectively).

Conclusions The results revealed no minimum number of lymph nodes that could reliably detect metastatic lymph nodes in LSCC patients.

Keywords Lymph node yield · Laryngeal squamous cell carcinoma · Neck dissection · Metastatic lymph node yield

Introduction

Laryngeal squamous cell carcinomas (LSCCs) are the second most common cancer of the respiratory tract after lung cancer [1]. Worldwide, LSCCs constitute 0.8% of all diagnosed cancers and 0.6% of all cancer-related mortalities [2]. The survival rate in LSCC cases remains poor, despite recent developments in therapeutic modalities and organ-preserving treatment methods [3, 4]. In this context, several studies have examined prognostic factors related to survival in LSCC patients. Determination of prognostic factors can play an important role in the development of new therapeutic strategies. Lymph node metastasis is one of the most important prognostic factors, [5, 6], decreasing the survival rate up to 50% [7]. In LSCC patients who are clinically lymph node negative (cN0), elective lymph node dissection is performed at levels II–IV [8].

Recent studies reported that lymph node density (LND) was an independent risk factor in many types of cancer, including squamous cell carcinoma of the bladder, oesophageal cancer, oropharyngeal cancer, and hypopharyngeal cancer [9–13]. Some studies found that the LND was useful for the prediction of survival in LSCC cases [14, 15].

Lymph node dissection is the mainstay of oncological treatment for LSCCs. The previous research on the number of lymph nodes that should be removed and evaluated by a pathologist suggested the following minimum lymph node yields (LNYs): 10 lymph nodes during axillary dissection in breast cancer [16, 17], 12 lymph nodes during mesocolonic and mesorectal excisions in colorectal cancer [18], and 15 lymph nodes (DI and DII lymph nodes) in

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stomach cancer [19]. These threshold values for the LNY have gained widespread acceptance in the literature. However, according to a recent study, the removal of more 18 lymph nodes had a positive effect on survival in oral cavity squamous cancers [20]. Therefore, in patients, where the LNY does not exceed a particular threshold value, lymph node dissection may be insufficient, and the resulting treatment may not be optimum.

Therefore, the objective of the present study was to determine the minimum LNY that could reliably aid the detection of metastatic lymph nodes in LSCC patients who were cN0 and underwent a total or partial laryngectomy and bilateral lymph node dissection at levels II–IV.

Patients and methods

This retrospective analysis consisted of 42 patients followed up between 2010 and 2019 at Ankara Numune Training and Research Hospital, a tertiary care hospital. All the patients had been diagnosed with LSCCs and undergone a total or partial laryngectomy and elective bilateral neck dissection as initial treatment. Patients with clinical lymph node metastasis at the time of diagnosis and those who had undergone radiotherapy or chemoradiotherapy for laryngeal cancer before the laryngectomy and neck dissection were excluded.

The number of lymph nodes extracted and counted by pathologist from the neck dissection material was called LNY, whereas the number of lymph nodes with metastasis was called metastatic LNY. Data on the LNY and metastatic LNY were obtained from the hospital's registry system. The metastatic LND was calculated as follows: (metastatic LNY/LNY).

All investigations were performed in accordance with the Declaration of Helsinki on biomedical studies involving human subjects, and informed consent was obtained from all the patients. The study was approved by the local institutional review board.

Neck dissection procedure

All the patients were diagnosed with cN0 LSCCs according to a physical and radiological examination, and all the patients underwent bilateral neck dissections at levels II, III, and IV. All the adipose tissues at levels II, III, and IV were completely removed, preserving the sternocleidomastoid muscle, internal jugular vein, and spinal accessory in all cases [21, 22]. The pathological specimens were immediately divided according to the neck levels in the operating theatre. A "Berry picking" approach was not applied in the neck dissections.

Statistical analysis

Statistical analysis was performed using SPSS software, version 16 (IBM SPSS Statistics, Chicago, IL, USA), with statistical significance set at 0.05. Survival was calculated from the date of surgery to the date of death. Pearson's correlation analysis was performed to investigate the relationship between the LNY and LND. An analysis of variance was conducted to determine the difference in the LND among the lymph node groups. Cox regression analysis was performed to investigate the possible effect of the LNY and LND on survival.

Results

This study included 42 LSCC patients (females, $n=2$; males, $n=40$) aged 39–81 years who underwent a total ($n=34$) or partial ($n=8$) laryngectomy and elective bilateral neck dissection. The mean age of the patients was 58.7 ± 9.6 years. In the partial laryngectomies, supracricoid laryngectomy was performed in five cases, and supraglottic laryngectomy was performed in the other three cases. In all the patients, the bilateral neck dissections included levels II–IV.

The follow-up period of the patients was 60 ± 31 months (8–102 months). During this follow-up period, 8 (19%) patients died. The lymph node metastasis rate was 31% in the study group, and the rate of bilateral metastasis was 14.3%.

The clinical characteristics of the patients are shown in Table 1.

The LNY in the bilateral level II–IV lymph node dissections was 57 ± 22, and the metastatic LNY was 1.5 ± 2.8. The LND in the bilateral neck level II–IV neck dissections was 0.036.

The LNY and metastatic LNY for each neck dissection side and for each sublevel of the neck are shown in Tables 2 and 3.

The right and left neck dissections were evaluated separately ($n=84$ in total). The LNY for unilateral level II–IV lymph node dissections was 25.9 ± 10, and the metastatic LNY was 0.9 ± 1.9. The LND for unilateral neck level II–IV neck dissections was 0.043.

The unilateral neck dissections were grouped according to the LNY (Table 4). However, we did not find any significant difference between the groups in terms of metastatic LNY ($p=0.5$). Pearson's correlation analysis also revealed no significant correlation between the LNY and metastatic LND ($p=0.6$). Cox regression analysis showed no significant relationship between survival and the LNY and LND in bilateral neck dissections ($p=0.4$ and $p=0.8$, respectively).

Table 1 Characteristics of the study population

Parameter	N (%)
Number of patients	42 (100)
Gender	
Male	40 (95.2)
Female	2 (4.8)
Tumor stage	
cT2N0	8 (19)
cT3N0	6 (14.3)
cT4N0	28 (66.7)
Surgical treatment for larynx	
Total laryngectomy	34 (81)
Supracricoid laryngectomy	5 (12)
Supraglottic laryngectomy	3 (7)
Surgical treatment for neck	
Bilateral neck dissection including levels II, III, IV	42 (100)
Pathologic nodal disease	
pN = 0	29 (69)
pN+	13 (31)
Postoperatif radiotherapy/chemoradiotherapy	
Yes	28 (67)
No	14 (33)

Table 2 Lymph node yield for each sub-levels of both for the right and the left neck dissections

	Right neck ($n=42$)	Left neck ($n=42$)
Level 2A lymph node yield	7.5 ± 5.6 (0–24)	7.4 ± 4.5 (0–18)
Level 2B lymph node yield	4.1 ± 5.6 (0–24)	2.7 ± 3.1 (0–10)
Level 3 lymph node yield	8 ± 5.3 (0–20)	8.2 ± 5.4 (0–20)
Level 4 lymph node yield	6.3 ± 5.8 (0–25)	7.5 ± 5 (0–19)
Total lymph node yield	26 ± 11 (3–51)	25.2 ± 10.2 (10–50)

Table 3 Metastatic lymph yield for each sub-levels of both for the right and the left neck dissections

	Right neck	Left neck
Level 2A metastatic lymph node yield	0.4 ± 1.1 (0–5)	0.35 ± 0.9 (0–3)
Level 2B metastatic lymph node yield	0.04 ± 0.3 (0–2)	0
Level 3 metastatic lymph node yield	0.35 ± 1 (0–5)	0.21 ± 0.75 (0–4)
Level 4 metastatic lymph node yield	0.21 ± 0.7 (0–3)	0.14 ± 0.15 (0–2)
Total metastatic lymph node yield	1.02 ± 2.1 (0–8)	0.7 ± 1.6 (0–6)

Discussion

The present study provided two important results: (I) a threshold value for the LNY could not be determined from specimens obtained with lymph node dissection. (II) There was no correlation between the LND and survival in LSCC patients who underwent surgery.

The previous studies on head and neck squamous cell cancers demonstrated that the LND was a useful prognostic indicator [12, 13, 23, 24]. Two previous studies demonstrated that the LND was an important predictive factor for survival [14, 15]. However, another study provided conflicting evidence and concluded that the effect of LND on survival was limited [25]. However, other research found that a high LND was a predictive factor for locoregional recurrence in oral cavity cancers and LSCCs. The same study recommended adjuvant chemotherapy in patients with a high LND [26].

In the present study, we found no significant relationship between the LND and survival. Several factors may explain the discord between the findings of the present study and those in the literature. First, several parameters affect the LND, which is a mathematically calculated value. Second, there is a lack of established guidelines on the number of lymph nodes that should be selected and evaluated in LSCCs. Third, lymph node metastasis detected macroscopically by the pathologist, but deemed not worthy of inclusion in a microscopic examination was excluded. Fourth, various features, such as the presence of a high tumour load and extracapsular spread, were detected in positive lymph nodes. Fifth, micro-metastasis may have been present in sections stained with normal haematoxylin–eosin and been overlooked during the examination. Finally, different pathologists were responsible for the selection of the lymph nodes and preparation of the specimens, and they used different procedures in specimen preparation.

In lymph node dissections, all lymphatic pathways that drain the related cancer region should be included in the specimen during the surgical procedure. The extent of lymph node dissection remains a matter of debate. Guided by the LNY, experts have attempted to standardize the extent of the dissection area to each specific cancer type. Threshold LNY values have been determined for colorectal [27], breast [28], bladder [29], penile [30], stomach [31], and oesophageal cancers [32]. These threshold values were selected based on a significant correlation of the LNY with survival rates. Although threshold LNY values have not yet been established in otolaryngology, some previous studies proposed a threshold LNY value of 20 for head and neck squamous cell carcinomas [33]. In one study, in patients with oral cavity squamous cell

Table 4 Metastatic lymph node density according to the lymph node yield groups

Lymph node yield groups	< 18	18–24	25–35	> 35	*p* value*
Metastatic lymph node	0.9 ± 1.7 (0–5)	1.03 ± 2 (0–7)	0.8 ± 2 (0–8)	0.7 ± 1.6 (0–5)	0.5

*ANOVA

carcinomas, an LNY of < 18 was related to poor disease-free survival rates in patients [20] and directly related to overall survival in another study [34].

In the present study, the results did not reveal a threshold value for the LNY that was correlated with survival in LSCC patients who underwent lymph node dissections at levels II–IV. The present study also revealed no minimum LNY value that could enable a more reliable determination of metastasis among cN0 patients who underwent a partial or total laryngectomy. The neck dissections were performed according to well established surgical principles and all adipose tissues at described neck levels were removed during these surgical interventions [8, 21, 22]. According to the previous research on patients with cN0 laryngeal cancer, neck dissections not only provided information on the need for radiotherapy, but also on the prognosis [8].

In common with similar studies in the literature, the present study had a retrospective design and relied upon evaluations of the patients' pathology reports. The limited sample size and retrospective design were the main limitations of our study. Other limitations were that different surgeons performed the interventions and that different pathologists evaluated the LNY.

Conclusions

The present study revealed no correlation between the LND and survival in patients who underwent a partial or total laryngectomy and bilateral lymph node dissections at levels II–IV due to LSCCs. The results also did not reveal a minimum number of lymph nodes that should be selected during bilateral lymph node dissections at neck levels II–IV for evaluation by a pathologist. We conclude that prospective randomized studies with larger sample sizes are needed to shed light on the minimum LNY and LND in patients with LSCCs.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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