Nodal Yield: Is it a Prognostic Factor for Head and Neck Squamous Cell Carcinoma?

Zhien Feng, MD, PhD, * *Li Zheng Qin, MD, PhD,* † *Xin Huang, MD, PhD,* ‡ *Jin Zhong Li, MD, PhD,* § *Ming Su, MD, PhD,* ‖ *and Zhengxue Han, MD, PhD* ¶

Purpose: The prognostic value of lymph node yield (LNY) in head and neck squamous cell carcinoma (HNSCC) remains controversial. The aim of this study was to explore whether LNY influences locoregional recurrence risk and prognosis in patients with HNSCC.

Patients and Methods: This retrospective cohort study reviewed the records of 1,546 eligible patients with HNSCC who were treated at Beijing Stomatological Hospital, Capital Medical University, from July 1989 to October 2012. The predictor variable was LNY. The main outcome assessment parameters were 2-year neck recurrence rate (NRR) and 5-year disease-specific survival (DSS). All statistical analyses were performed using SPSS 19.0 for Windows.

Results: The mean and median LNY per neck dissection were 25.1 and 23.0, respectively. There was no significant association between LNY quartile and 2-year NRR in the pN0 ($P = .397$) or pN^+ ($P = .335$) group. Univariate analysis of the pN0 group showed no significant association between LNY and 5-year DSS ($P = .676$). The analysis of patients with pN^+ who underwent only selective neck dissection showed a significantly higher prognostic risk with an increased LNY (LNY <19 vs ≥34, 79.2% vs 59.4%; $P = .014$). Interestingly, in the comprehensive neck dissection subgroup, there was an obvious tendency for patients with a high LNY to have a better 5-year DSS than those with a low LNY (LNY <19 vs ≥34, 55.6% vs 76.4%; $P = .021$). Multivariate analysis showed that LNY was not an independent predictive factor for 2-year NRR or 5-year DSS.

Conclusions: LNY is statistically associated with the risk of lymph node metastasis, but does not predict neck recurrence. The exact prognostic value of LNY for patients with pN^+ remains unknown, and further study is needed to validate the present findings.

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Worldwide, approximately 635,000 new cases of head and neck cancer are diagnosed annually; more than 12% of these cases are in China. Unfortunately, 75% of Chinese patients already have advanced-stage disease at the time of diagnosis, and more than 76,000 patients die each year.[1] It is well known that lymph node metastases are the most important prognostic factor in head and neck cancer.[2-5] Recently, it was reported that lymph node yield (LNY) was likely an independent prognostic factor in patients undergoing neck dissection for head and neck squamous cell carcinoma (HNSCC). Some investigators believe that a nodal yield higher than 20, in addition to increased age, male gender, and primary site, correspond to an increased likelihood of cervical metastases in early-stage HNSCC.[6] However, some investigators have

Received from the Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University, Beijing, China.

*Attending Doctor.

†Associate Senior Doctor.

‡Senior Doctor.

§Attending Doctor.

‖Resident Doctor.

¶Department Head.

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Address correspondence and reprint requests to Dr Han: Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University, No 4 Tian Tan Xi Li, Dongcheng District, Beijing 100050, People's Republic of China; e-mail: hanf1989@hotmail.com

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proposed that a high LNY is a positive independent prognostic factor in patients with cN0 HNSCC and that an adequate elective lymphadenectomy should include at least 18 nodes.[7,8] Nonetheless, other investigators believe that LNY is not an important prognostic factor.[9] Currently, the prognostic value of LNY in the Chinese HNSCC population still lacks a clear conclusion from a large clinical study.

In the authors' department, simultaneous neck dissection is the primary treatment for HNSCC. The purpose of this study was to determine whether the LNY is obviously different in patients with pN0 versus pN^+ and to evaluate whether the LNY is an independent prognostic factor for HNSCC. The authors hypothesized that LNY also would be affected by the patients' lymph node status (pN0 or pN^+) and the surgical approach to neck dissection. The specific aim was to determine whether LNY is associated with locoregional recurrence risk and survival in patients with pN0 and pN^+ who undergo neck dissection.

Patients and Methods

STUDY DESIGN AND SAMPLE

This research was conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (2002 version), and was approved by the institutional review board at the Beijing Stomatological Hospital of Capital Medical University (Beijing, China). To answer the research questions, the authors designed and conducted a retrospective cohort study. Owing to the retrospective nature of this study, it was granted a written exemption by the institutional review board. The study population included all patients who had been pathologically diagnosed with HNSCC and were evaluated and managed by the Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University, from July 1989 to October 2012.

The following inclusion criteria were used for the study sample: *1)* patients who underwent neck dissections; *2)* patients with a primary tumor without evidence of distant metastasis; and *3)* patients with a tumor located in the tongue, lower gingiva, upper gingiva, buccal mucosa, floor of the mouth, oropharynx, or hard palate. The exclusion criteria included preoperative chemotherapy or radiotherapy, perioperative mortality, an LNY less than 10, and lack of adequate information to determine the LNY.

STUDY VARIABLES

The predictor variable was LNY. The main outcome assessment parameters were 2-year neck recurrence rate (NRR) and 5-year disease-specific survival (DSS). NRR was defined as the percentage of patients for whom neck recurrence was not associated with local recurrence. DSS was calculated from the time of the first operation to the time of death or last follow-up; patients who died of causes other than HNSCC were censored at the time of death. Other variables included demographic (age and gender), anatomic (T stage, growth pattern, and sites), habit (tobacco and alcohol use), and pathologic (pN status, grade, extracapsular spread [ECS], perineural invasion, vascular emboli, and diffuse infiltration) characteristics.

DATA COLLECTION METHODS OF NECK DISSECTION

Neck dissection specimens were resected en bloc, and each node level was indicated. Surgical specimens were carefully palpated and dissected out by the second assistant. Before being embedded in paraffin, residual neck specimens were sent to pathologists for rechecking in case of omission. Then, all identified lymph nodes were sectioned at 2- to 3-mm intervals, and standard hematoxylin and eosin staining was performed. The LNY data were obtained from original pathology reports. In patients in whom a bilateral neck dissection was performed, the average LNY of the 2 sides was used.

DATA ANALYSES

The cutoff date for all surviving patients was October 1, 2014. Descriptive statistics are summarized using frequencies, percentages, and means $\pm$ standard deviations. All baseline variables (gender, site, etc) related to the LNY were statistically analyzed using the χ^2 test. The Kaplan-Meier method was used to provide estimates of the 2-year NRR and 5-year DSS. Statistical significance was determined using the log-rank test. A Cox proportional hazards model was used to adjust for the effect of other potential confounders. All tests were 2-sided, and P values less than .05 were considered statistically significant. All statistical analyses were performed using SPSS 19.0 for Windows (SPSS, Inc, Chicago, IL).

Results

PATIENTS

From July 1989 to October 2012, 2,640 consecutive patients with primary oral SCC were scheduled for radical surgery in the authors' hospital. A total of 1,094 patients were excluded owing to never having undergone neck dissection or not having available data on lymph node numbers. A total of 1,546 patients, including 938 (60.7%) men and 608 (39.3%) women, were eligible for the final analysis. The median age was 58 years (range, 16 to 89 years). The primary sites