



## Pattern of cervical lymph node metastasis in tonsil cancer: Predictive factor analysis of contralateral and retropharyngeal lymph node metastasis

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### SUMMARY

The purpose of this study was to determine the pattern of cervical lymph node metastasis in tonsil cancer including the retropharyngeal (RPLN) nodal metastasis. Seventy-six tonsillar squamous cell carcinoma patients who underwent surgery-based treatment were retrospectively analyzed. Most patients had advanced stage (stages III and IV: 81.6%) tonsil cancer. Sixteen patients were treated with surgery only. Postoperative radiotherapy was performed to 38 patients, and chemoradiation to 22 patients. Seventy-one therapeutic neck dissections and 27 elective neck dissections were performed. Thirty-four patients underwent RPLN dissection based on the preoperative inclusion criteria. There was a statistically significant metastasis in level I or V nodes, when the ipsilateral multilevel, or contralateral nodes were positive. The rate of contralateral occult cases was 28.6%. T3–4 stages, primary lesions close to the midline, or ipsilateral multilevel involvement were significantly associated with contralateral metastasis. Ipsilateral multilevel involvement was the independent factor with multivariate analysis. RPLN metastasis was confirmed in 9 of the 34 (26.5%) subjects. Disease-specific survival rate was significantly different according to RPLN status (82.1% vs. 55.6%;  $p = 0.021$ ). Positive pre-operative image, posterior pharyngeal wall invasion, more than N2 stage, contralateral node metastasis, or ipsilateral multilevel involvement were correlated with RPLN metastasis. Bilateral neck dissection is mandatory for primary lesions close to the midline and advanced ipsilateral nodal disease. Elective RPLN dissection should be considered for patients with advanced neck and primary tumor, particularly for tumors with posterior pharyngeal wall invasion.

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### Introduction

Tonsillar squamous cell carcinoma (SCC) has a strong tendency to invade the cervical lymph nodes. Treatment failure with nodal metastases is an important prognostic factor for patients.<sup>1</sup> However, currently there is no data to determine a pattern of cervical lymph node metastasis in tonsil cancer especially for the retropharyngeal (RPLN) and contralateral lymph node metastasis. Because the majority of patients with tonsillar cancers undergo radiation therapy with or without chemotherapy for their primary treatment, there have been few reports about pattern of cervical metastasis. Moreover, only a handful of articles are available about the significance of RPLN in tonsil cancer, and most previous studies have focused on radiological assessment or included other primary sites as well. The purpose of this study was to determine the pattern of cervical lymph node metastasis in tonsil cancer including the retropharyngeal and contralateral nodal metastasis.

### Materials and methods

#### Patient population

This study was reviewed and approved by the ethics committee of our institution. Ninety-four patients with tonsil cancer who underwent surgery-based treatment at the Ilsong Memorial Institute Head and Neck Cancer, Hallym University Medical Center from 1997 through 2010 were enrolled in the study. Salvage cases ( $n = 11$ ) and patients with insufficient data ( $n = 7$ ) were excluded. Consequently, a total of 76 tonsillar squamous cell carcinoma patients were retrospectively analyzed in this study. The study group was composed of 67 men and nine women (mean age: 56.9 years; range 36–80 years). The follow-up period ranged from 6 to 197 (mean 41.4) months.

The tumors were classified as stage I in six patients, stage II in eight patients, stage III in nine patients, stage IVa in 48 patients, and stage IVb in five patients (stages III and IV were 81.6%; 62 out of 76 patients). The TNM stages of the patients are summarized in Table 1. Surgical treatment was followed by postoperative radiotherapy in 38 patients (more than pT3/N2, perineural invasion,

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**Table 1**  
Pathologic TNM staging for overall patient (n = 76).

	N0	N1	N2a	N2b	N2c	N3	Total
T1	6	0	0	8	2	1	17
T2	8	4	1	17	1	1	32
T3	4	2	1	5	4	1	17
T4a	2	1	0	3	0	0	6
T4b	0	0	0	1	1	2	4
Total	20	7	2	34	8	5	76

vascular embolism), and chemoradiation in 22 patients (extracapsular nodal spread, positive margin). Sixteen patients were treated with surgery only. All patients underwent neck dissection on at least one side. Overall, 71 therapeutic neck dissections (63 ipsilateral; eight contralateral) and 27 elective neck dissections (13 ipsilateral; 14 contralateral) were performed. Thirty-four patients underwent RPLN dissection during their surgical treatment based on preoperative inclusion criteria – clinically positive group (positive preoperative CT, MRI, or PET-CT) and potential risk of occult metastasis group (T3/4, posterior pharyngeal wall extension, or multiple level positive nodes).

#### Treatment and reconstruction of primary lesion

Primary tumor was removed using mandible sparing approach in 49 cases (10 transoral approach; 39 lateral pharyngotomy approach), paramedian mandibulotomy approach in 26 cases, and segmental mandibulectomy in one patient. The general principle of our approach is transoral for T1 or selected T2 cases. The mandible-saving approach such as lateral pharyngotomy (with or without transoral lateral oropharyngectomy) are preferred for more than T2 cases at our since 2004 except for lesions with significant lateral extension (pterygoid muscle invasion) or mandible invasion.

For reconstruction of the defective area, a radial forearm free flap was used in 49 cases, a lateral thigh free flap in 14, a pectoralis myocutaneous flap in three, a sternocleidomastoid muscle (SCM) rotation flap in three, and secondary healing was promoted in the remaining seven cases.

#### Surgical approach to RPLN

The operating surgeon determined the type of surgical approach to be used for the RPLN dissection (mandibulotomy or lateral pharyngotomy) based on the surgical approach for resection of the primary tumor. Among the 34 RPLN dissection patients, mandibulotomy approach was used in 14 patients, and lateral pharyngotomy approach (with or without transoral lateral oropharyngectomy) in 20 patients. Since 2004, the authors prefer to use mandible-saving approaches such as the lateral pharyngotomy, and since then, mandibulotomy was only performed in seven patients where there was significant lateral extension (pterygoid muscle invasion).

In the case of lateral pharyngotomy approach, retropharyngeal lymph node dissection was generally undertaken at the completion of the primary resection and neck dissection, with retraction of the carotid artery laterally, pharynx medially, and the hypoglossal nerve superiorly. Division of the posterior belly of the digastric muscle and stylohyoid muscle was necessary. On the other hand, in cases where the mandibulotomy approach was used, dissection of the retropharyngeal space was easier because the retropharyngeal space had already been identified after removal of the primary tumor. The RPLN dissection specimens were labeled separately.

#### Analysis

Univariate analysis was performed using Fischer's exact test to analyze the relationships of clinical variables with ipsilateral, retropharyngeal and contralateral nodal metastasis. Multivariate analysis was performed by logistic regression using the SPSS statistical package (SPSS Inc, Chicago, IL, USA). A *p*-value less than 0.05 was considered significant.

#### Results

##### Spread of tonsil cancer

The frequency of adjacent site involvement was analyzed. Invasion was defined as involvement of more than 1/3 of each subsite on preoperative imaging studies. Thirty-four out of 76 patients (45%) had soft palate invasion. Base of tongue (BOT) and posterior pharyngeal wall invasion were present in 28 (37%), and 23 (30%) patients, respectively.

##### Results of neck dissection

Overall, 98 neck dissection specimens (71 therapeutic neck dissections and 27 elective neck dissections) were available for analysis, among which 64 (65.3%) had nodal metastases. This included 55/76 (72.4%) ipsilateral nodal metastases and 9/22 (40.9%) contralateral nodal metastases (Table 2). The distribution of the ipsilateral and contralateral nodal metastases according to the neck level based on pathologic reports is shown in Table 3. Ipsilateral level IIa was the most common site for nodal metastasis, followed by ipsilateral level III. For the contralateral nodal metastases, level IIa was the most common site, followed by level III (Table 3). Ipsilateral multiple level involvement was observed in 31/76 (40.8%) patients. Levels II and III multiple level positive were the most common pattern (13/31) followed by levels II–IV positive.

##### Ipsilateral nodal metastasis

The rate of ipsilateral occult cases was 8% (1 out of 13 patients, levels IIa and IV). The overall N-positive rate on pathology was 72.4% (55 out of 76 patients). Levels I, IIb, IV, and V metastases rate were 9% (7/76), 20% (15/76), 18% (14/76), and 13% (10/76), respectively. There were no cases of isolated levels I, IV or V metastasis. There was a statistically significant metastasis in level I, IV or V nodes, when the ipsilateral multilevel was positive, contralateral node was positive, more than pN2 stage, or RPLN was positive (Table 4).

##### Contralateral nodal metastasis

The rate of contralateral occult cases was 28.6% (4 among 14 patients) and occurred only in the levels IIa or III (level IIa in two cases, level III in one case, levels IIa and III in one case). Among the 14 patients that underwent the contralateral END for contralat-

**Table 2**  
Results of neck dissection.

Neck dissection	Ipsilateral	Contralateral	Total
Therapeutic	63 (82.9%)	8 (36.4%)	71
Metastasis rate	54/63 (85.7%)	5/8 (62.5%)	59/71 (83.1%)
Elective	13 (18.3%)	14 (63.6%)	27
Occult metastasis rate	1/13 (8%)	4/14 (28.6%)	5/27 (18.5%)
Total metastasis	55/76 (72.4%)	9/22 (40.9%)	64/98 (65.3%)

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