Original Article
pISSN 1738-2637 / eISSN 2288-2928
J Korean Soc Radiol 2015;72(4):271-281
http://dx.doi.org/10.3348/jksr.2015.72.4.271

대한영상의학회지

Comparative Study of Lymph Node Metastasis from Squamous Cell Carcinoma and Non-Squamous Cell Carcinoma on Neck CT

편평세포암과 비편평세포암 환자에서 경부 림프절 전이의 CT 영상소견 비교 연구

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Purpose: To assess the differential imaging findings of metastatic lymph nodes in squamous cell carcinoma (SCC) and non-squamous cell carcinoma (non-SCC) on neck CT and to facilitate the identification of primary focus before performing a biopsy.

Materials and Methods: We retrospectively analyzed 46 patients with SCC and 50 patients with non-SCC who underwent neck CT from January 2006 to January 2011. Patients were divided into two groups; SCC and non-SCC. The total number of lymph nodes was 204 in the SCC group and 530 in the non-SCC group. Two observers were asked to assess the characteristics of abnormal lymph nodes (number, margin types, enhancement patterns, size, bilaterality, calcification, fat infiltration, conglomeration, invasion of adjacent tissue, and nodal distribution). Nodal distribution was evaluated by imaging-based nodal classification on neck CT.

Results: Between the SCC group and the non-SCC group except for cases of thyroid cancer, the number of lymph nodes and the number of lymph nodes smaller than 3 cm in the non-SCC group except for cases of thyroid cancer were significantly greater than those in the SCC group ($p < 0.05$).

Conclusion: The number of lymph nodes, the number of lymph nodes smaller than 3 cm, and nodal distribution are helpful in differential diagnosis between SCC and non-SCC before performing a biopsy.

Index terms
Squamous Cell Carcinoma
Neck
Lymph Nodes
Computed Tomography

Received November 4, 2013; **Accepted** December 7, 2014

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INTRODUCTION

Cervical lymph node metastasis is frequently encountered on neck CT of patients with squamous cell carcinoma (SCC) and non-squamous cell carcinoma (non-SCC). The presence of lymph node metastasis is a well-known adverse prognostic factor in patients with head and neck cancers. Accurate information about cervical lymph node metastases is essential for choosing the most appropriate treatment. Imaging plays a critical role in addition to clinical evaluation towards improving the detection of nodal metastases. The most commonly used radiologic criteria to detect cervical lymph node metastasis on neck CT is the short axis diameter (> 1 cm). Morphologic features such as necrosis and indistinct margins have improved the detection of lymph node metastasis on neck CT. However, it is often difficult to diagnose cervical lymph node metastasis on neck CT. Metastasis in normal-sized lymph nodes can be missed and reactive lymph node enlargement cannot be reliably differentiated from metastatic involvement. Tuberculous lymphadenitis with intranodal necrosis can mimic metastatic lymphadenopathy. Therefore, numerous studies have been performed on the differential diagnosis between cervical lymph node metastasis and non-metastatic lymph node conditions on neck CT (1-4).

To the best of our knowledge, no prior published report has discussed the role of enhanced neck CT in differential diagnosis between SCC and non-SCC. SCC is the most common histolog-

ic type found in cervical lymph node metastasis followed by adenocarcinoma. Adenocarcinoma is the most common histological type in cervical lymph node metastasis from non-SCC. Differential diagnosis of SCC and non-SCC is important, because the treatment plan and prognosis are significantly different between the two disease conditions. Radiologic differential diagnosis is especially helpful and reliable when histologic examination is difficult or impossible. It is not always possible to obtain a definite pathologic confirmation. Reasons for not having confirmed pathologic diagnosis include indeterminate biopsy specimen in spite of repeated trials or inability to tolerate the procedure. Additional information about the cell type in nodal metastases is essential for choosing the most appropriate treatment in patients with lymph node metastasis without a definite primary site of origin. The chemotherapy regimen varies depending on the histologic type of cancer. The 5-year overall survival rate of patients with SCC that has metastasized to the cervical lymph nodes is about 68.5%. The survival rate of patients with metastatic non-SCC in the cervical lymph nodes is lower than that in patients with metastatic SCC in the cervical lymph nodes. The 5-year overall survival rate of patients with adenocarcinoma is about 9%.

The purpose of our study was to assess the differential imaging findings of metastatic lymph nodes in SCC and non-SCC on neck CT and to facilitate the identification of primary focus before performing a biopsy.

MATERIALS AND METHODS

Patients

We retrospectively analyzed 46 patients (35 men, 11 women, mean age 63 years) with SCC and 50 patients (21 men, 29 women, mean age 56 years) with non-SCC who underwent neck CT from January 2006 to January 2011. A diagnosis was established by percutaneous biopsy in 30 patients and open neck lymph node biopsy in 66 patients. Percutaneous biopsies were performed by a head and neck radiologist with 9 years experience (Observer 1) or by a radiology resident (Observer 2) using 16-gauge core biopsy needles. Open neck biopsies were performed by an otolaryngologist surgeon and a plastic surgeon.

The primary sites of SCC were cervix in 4 cases, esophagus in one case, hypopharynx in 6 cases, larynx in one case, lung in 6 cases, maxillary sinus in one case, metastasis of unknown origin (MUO) in 8 cases, nasal cavity in one case, nasopharynx in 8 cases, oral cavity in one case, oropharynx in one case, skin in one case, soft palate in one case, subglottis in one case, tongue in 2 cases, and tonsils in 3 cases.

The primary sites of non-SCC were breast in one case, cervix in 2 cases, colon in 2 cases, gallbladder in one case, lung in 11 cases, MUO in 4 cases, nasal cavity in one case, nasopharynx in 2 cases, oral cavity in one case, prostate in one case, salivary gland in one case, thyroid in 22 cases, and tongue in one case.

Non-SCCs included 23 adenocarcinomas, 2 malignant neuroendocrine tumors, 2 medullary thyroid carcinomas, 20 papillary thyroid carcinomas, 1 salivary duct carcinoma, 1 small cell carcinoma, and 1 undifferentiated carcinoma.

Computed Tomography

All CT scans were performed with 8 channel (GE LightSpeed Ultra; GE Medical Systems, Waukesha, WI, USA) and 64 channel (GE LightSpeed VCT; GE Healthcare, Milwaukee, WI, USA) equipments. Scanning parameters were as follows: 1 table pitch, 120 kVp, 140 mAs, and 5 mm thickness. After acquisition of unenhanced images, 100 mL of nonionic contrast material (Iomeron 350; Braco, Milan, Italy/Omnipaque 350; Nycomed, Oslo, Norway/GE Healthcare, Milwaukee, WI, USA) was injected at 1.5 mL/s followed by a 20 mL saline flush.

Image Analysis

A head and neck radiologist with 9 years experience (Observer 1) and a radiology resident (Observer 2) independently reviewed two sets (SCC and non-SCC) of neck CT. Two observers were asked to assess the characteristics of the abnormal lymph nodes (number, margin types, enhancement patterns, size, bilaterality, calcification, fat infiltration, conglomeration, invasion of adjacent tissue, and nodal distribution).

Observers counted the total number of abnormal lymph nodes greater than 1 cm in the short diameter identified on neck CT. Enlarged lymph nodes with normal fatty hilum or normal ovoid shape (long to short axis ratio > 2) were considered to be reactive lymph nodes, even if the size of the lymph node was larger than 1 cm. The observers counted "conglomerate" nodal metastasis as one metastatic lymph node. Following the 'N' staging of the American Joint Committee on Cancer 6th edition TNM staging manual, the specific 'count' was considered to have minimal sig-

nificance with large mass potentially representing multiple matted lymph nodes (1). The margin of the lymph nodes was classified as well-defined smooth, well-defined irregular, or ill-defined. Observers counted the number of each type of lymph node and calculated the ratio of each type of lymph node to the total number of lymph nodes assessed.

The enhancement pattern of the lymph nodes was categorized into non-necrotic and necrotic lymph nodes. Lymph nodes showing a central region of low "water" attenuation [below 25 Hounsfield units (HU)] with peripheral enhancement were defined as necrotic lymph nodes in this article. Necrotic lymph nodes were further classified as those with thin regular (< 1 mm) and thick irregular wall enhancement. Non-necrotic lymph nodes were further classified as those showing homogeneous or heterogeneous enhancement. A lymph node was regarded as showing heterogeneous enhancement when 2 selected regions of interest having the highest and the lowest attenuation values differed by more than 20 HU. Observers counted the number of lymph nodes with each enhancement pattern and calculated the ratio of lymph nodes with each enhancement pattern to the total lymph nodes.

Observers measured the diameter of the largest lymph node in the neck. The size of the lymph nodes was further categorized into three groups (smaller than 3 cm, between 3 cm to 6 cm, larger than 6 cm). Observers counted the number of lymph nodes in each group.

Bilaterality was defined as metastatic involvement of any number of lymph nodes on the contralateral neck. Conglomeration of lymph nodes was considered as juxtaposed lymph nodes that cannot be clearly delineated from each other. Fat infiltration was considered to be present when there was obliteration of the adjacent fat plane or there was increased perinodal attenuation on CT scan. Observers recorded the presence of fat infiltration and conglomeration. The invasion of adjacent tissue, when present, was categorized into four groups (bone invasion, direct soft tissue invasion, dural invasion, and great vessel invasion). Nodal distribution was evaluated by imaging-based nodal classification on neck CT.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 14.0 (SPSS Statistics, Chicago, IL, USA). Independent *t*-test was used to compare the number of lymph nodes, the ratio of lymph nodes with each margin type to total lymph nodes, the ratio of lymph nodes with each enhancement pattern to total lymph nodes, the diameter of the largest lymph node, the number of lymph nodes in each group, and patient age between the two cancer groups. The chi-square test was used to compare bilaterality, presence of calcification, fat infiltration, conglomeration, invasion of adjacent tissue, and patient sex between the two cancer groups. The independent *t*-test was also used to compare the nodal distribution between the two groups. Considering the high proportion of cases with thyroid cancer in the non-SCC group, an additional analysis was performed between the SCC group and the non-SCC group, except for cases of thyroid cancer. In order to exclude the influence of thyroid cancer, independent *t*-test and chi-square test were additionally applied to variables that showed a significant difference between the SCC and non-SCC groups.

Inter-observer agreement was evaluated using intraclass correlation coefficient (ICC) with the two way random-effects model and simple kappa statistic. ICC values were calculated between the two observers for assessing continuous variables such as the number of lymph nodes, the ratio of lymph nodes with each margin type to total lymph nodes, the ratio of lymph nodes with each enhancement pattern to total lymph nodes, the diameter of the largest lymph node, and the number of lymph nodes in each group. We used a scale for interpretation of ICC, which was introduced in a previous literature: ICC values of less than 0.40 indicated poor reproducibility, ICC values of 0.40–0.75 indicated fair-to-good reproducibility, and ICC values greater than 0.75 indicated excellent reproducibility.

The kappa values were calculated for the two observer pairs for assessing categorical variables such as bilaterality and presence of calcification, fat infiltration, conglomeration, adjacent tissue invasion, and nodal distribution. According to the Landis and Koch guideline, the agreement was rated as follows: kappa values of 0–0.2 indicated slight agreement, 0.21–0.4 indicated fair agreement, 0.41–0.60 indicated moderate agreement, 0.61–0.8 indicated substantial agreement, and 0.81 or greater indicated excellent agreement.

RESULTS

The results were significantly different between the two ob-

servers with respect to the ratio of lymph nodes with ill-defined margins to total lymph nodes, the ratio of lymph nodes with thick irregular wall enhancement to total lymph nodes, the number of lymph nodes larger than 6 cm in size, and invasion of adjacent tissue.

The number of lymph nodes in the non-SCC group was significantly greater than that in the SCC group ($p < 0.05$) (Tables 1, 2). The number of lymph nodes smaller than 3 cm was significantly greater in the non-SCC group than in the SCC group ($p < 0.05$).

With respect to the non-necrotic lymph nodes, the ratio of

Table 1. Comparison with Variables between Two Groups (Observer 1)

	SCC	Non-SCC	*p* Value
Number of lymph node (mean number)	4.43 (1–32)	10.62 (1–72)	< 0.05
Margin of lymph node (mean ratio)			
Well-smooth	0.59	0.61	0.26
Well-irregular	0.31	0.24	0.56
Ill-defined	0.09	0.13	0.21
Enhancement pattern (mean ratio)			
Non-necrotic			
Homogeneous	0.47	0.48	0.48
Heterogeneous	0.08	0.25	< 0.05
Necrotic			
Thin-regular	0.17	0.17	0.29
Thick-irregular	0.27	0.09	< 0.05
Size of lymph node (cm)	3.05 (1.0–7.0)	2.56 (1.0–8.5)	0.90
Size of lymph node (mean number)			
Below 3 cm	3.85	10.1	< 0.05
3–6 cm	0.57	0.48	0.78
Above 6 cm	0.02	0	NA
Age (year)	63.0	56.1	< 0.05
Sex (M:F)	35:11	21:29	< 0.05

Note.—The number of lymph node above 6 cm was too small to obtain significant result.
NA = not available, SCC = squamous cell carcinoma

Table 2. Comparison with Variables between Two Groups (Observer 2)

	SCC	Non-SCC	*p* Value
Number of lymph node (mean number)	4.72 (1–28)	8.76 (1–64)	< 0.05
Margin of lymph node (mean ratio)			
Well-smooth	0.64	0.64	0.40
Well-irregular	0.27	0.31	0.12
Ill-defined	0.08	0.03	< 0.05
Enhancement pattern (mean ratio)			
Non-necrotic			
Homogeneous	0.45	0.55	0.18
Heterogeneous	0.10	0.09	< 0.05
Necrotic			
Thin-regular	1.09	1.16	0.13
Thick-irregular	1.15	1.50	0.24
Size of lymph node (cm)	3.01 (1.0–6.4)	2.72 (1.0–9.4)	0.86
Size of lymph node (mean number)			
Below 3 cm	4.09	8.22	< 0.05
3–6 cm	0.57	0.42	0.93
Above 6 cm	0.02	0.04	NA

Note.—The number of lymph node above 6 cm was too small to obtain significant result.
NA = not available, SCC = squamous cell carcinoma

lymph nodes with heterogeneous enhancement to total lymph nodes in the non-SCC group was significantly greater than that in the SCC group ($p < 0.05$) (Fig. 1). Among the necrotic lymph nodes analyzed, the ratio of lymph nodes with thick irregular wall enhancement to total lymph nodes in the SCC group was significantly higher than that in the non-SCC group ($p < 0.05$) (Fig. 2). The patients in the SCC group were significantly older than those in the non-SCC group ($p < 0.05$).

The incidence of calcification was significantly higher in the non-SCC group than in the SCC group ($p < 0.05$) (Fig. 3). The incidence of adjacent tissue invasion in the non-SCC group was significantly higher than that in the SCC group ($p < 0.05$) (Tables 3, 4).

There was no significant difference in the ratio of lymph nodes with each margin type to total lymph nodes, the diameter of the largest lymph node, bilaterality, fat infiltration, and conglomeration between the two groups (Figs. 4, 5).

The number of lymph nodes larger than 6 cm in size and the number of level IIA, VI, and paratracheal groups of lymph nodes were too small to draw statistical conclusions. For example, there were only three lymph nodes larger than 6 cm in size in both groups (1 in the SCC group, 2 in the non-SCC group). Statistical results of these items are marked as 'not available' in this article.

Between the SCC group and the non-SCC group except for cases of thyroid cancer, the number of lymph nodes and the number of lymph nodes smaller than 3 cm in the non-SCC group except for cases of thyroid cancer were significantly greater than those in the SCC group ($p < 0.05$). There was no significant difference in the ratio of lymph nodes with heterogeneous enhancement to total lymph nodes, the ratio of lymph nodes with thick irregular wall enhancement to total lymph nodes, age, incidence of calcification, and adjacent tissue invasion between the SCC group and the non-SCC group, except for cases of thyroid cancer.

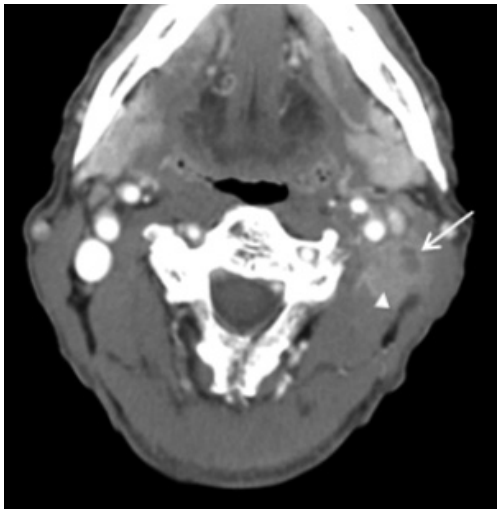


Fig. 1. Cervical lymph node metastasis in a 69-year-old man who present with palpable left sided neck mass. Axial CT images show enlarged lymph node in the left neck at level IIB. Attenuations value of the highest enhancement portion (arrowhead) and the lowest enhancement portion (arrow) are 96 Hounsfield units (HU) and 67 HU, respectively. Because the attenuation values differed by over 20 HU, the enhancement pattern is defined as heterogeneous enhancement. Percutaneous needle biopsy is performed and the histologic diagnosis is metastatic squamous cell carcinoma. The primary focus was unknown.

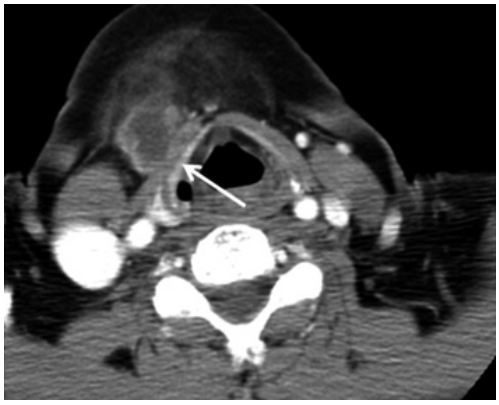
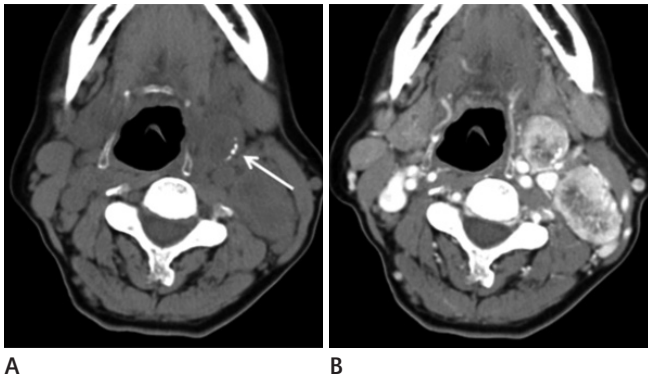


Fig. 2. Cervical lymph node metastasis in a 78-year-old woman. Axial image reveals enlarged lymph nodes in the right neck level IA, IB. The lymph node shows central water attenuation (below 25 Hounsfield units) with peripheral enhancement, enhancement pattern is defined as peripheral thick wall enhancement (> 1 mm). Invasion of the anterior belly of the digastric muscle is also noted (arrow). Percutaneous needle biopsy is performed and the histologic diagnosis is metastatic squamous cell carcinoma. Primary focus was tongue cancer.



A **B**

Fig. 3. Cervical lymph node metastasis in a 70-year-old woman. Precontrast axial image reveals intranodal calcification (arrow in **A**). Postcontrast axial image **(B)** shows enlarged lymph nodes with heterogeneous enhancement noted in left neck level II. Percutaneous needle biopsy is performed and histologic diagnosis is metastatic medullary carcinoma. Primary focus is medullary thyroid carcinoma.

Table 3. Comparison with Variables between Two Groups (Observer 1)

	SCC (%)	Non-SCC (%)	*p*-Value
Bilaterality	8/46 (17.4)	13/50 (26.0)	0.22
Calcification	1/46 (2.2)	7/50 (14.0)	< 0.05
Fat infiltration	13/46 (28.3)	9/50 (18.0)	0.17
Conglomeration	20/46 (43.5)	16/50 (32.0)	0.17
Invasion to adjacent tissue	8/46 (17.4)	18/50 (36.0)	< 0.05

Note.—SCC = squamous cell carcinoma

Table 4. Comparison with Variables between Two Groups (Observer 2)

	SCC (%)	Non-SCC (%)	*p*-Value
Bilaterality	8/46 (17.4)	14/50 (28.0)	0.16
Calcification	1/46 (2.2)	7/50 (14.0)	< 0.05
Fat infiltration	16/46 (34.8)	15/50 (30.0)	0.40
Conglomeration	16/46 (34.8)	26/50 (52.0)	0.06
Invasion to adjacent tissue	12/46 (26.1)	13/50 (26.0)	0.59

Note.—SCC = squamous cell carcinoma

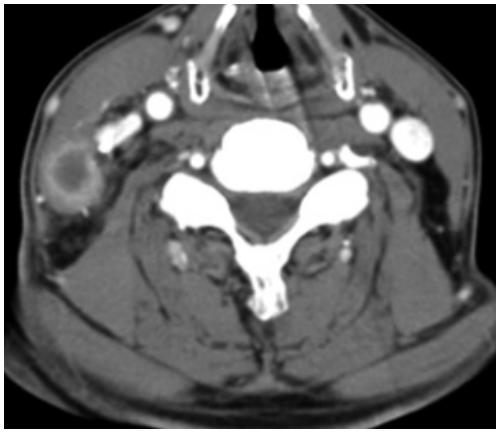


Fig. 4. Cervical lymph node metastasis in a 64-year-old man. Axial image shows enlarged lymph node with peripheral thick wall enhancement in right neck level III. Perinodal fat tissue infiltration is also noted. Percutaneous needle biopsy is performed and the histologic diagnosis is metastatic papillary carcinoma. Primary focus is papillary thyroid carcinoma.

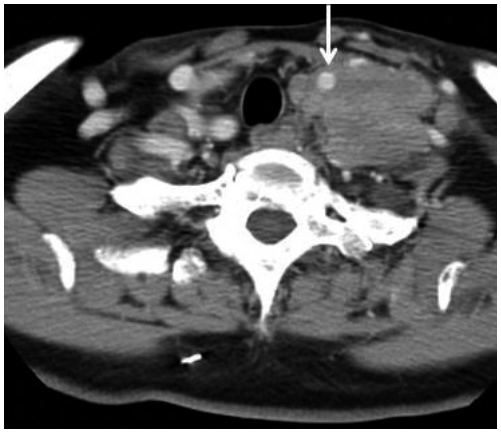


Fig. 5. Cervical lymph node metastasis in a 78-year-old woman who present with palpable left neck mass. Axial image shows conglomerated lymph node with homogeneous enhancement in the left neck at supraclavicular level. Left internal jugular vein is not clearly visible due to tumor invasion. Encasement of left internal carotid artery is also noted (arrow). Percutaneous needle biopsy is performed and the histologic diagnosis is metastatic squamous cell carcinoma. Primary focus is bladder cancer.

Observer 1 recorded that lymphadenopathies in the SCC group were significantly more common in level IA, IB, and III (3.3%, 9.1%, 17.7%, respectively) groups of lymph nodes compared to the non-SCC group (0.5%, 3.2%, 8.5%, respectively). Lymphadenopathies in the non-SCC group were significantly more common in level IIB and IV (27.2%, 25.0%, respectively) groups of lymph nodes compared to the SCC group (14.9%, 12.3%, respectively) (Table 3). Observer 2 recorded that lymphadenopathies in the SCC group were more common in level IA, IB, and III (3.3%, 8.7%, 17.7%, respectively) groups of lymph nodes compared to the non-SCC group (0.5%, 3.2%, 7.5%, respectively). Lymphadenopathies in the non-SCC group were significantly more common in level IIB and IV (27.0%, 28.4%, respectively) groups of lymph nodes compared to the SCC group (15.2%, 17.3%, respectively).

There were no significant interobserver differences in both continuous and categorical variables (Tables 5, 6).

DISCUSSION

Evaluation of the primary focus and cell type are crucial steps in treating patients with lymph node metastasis. Radiologic dif-

Table 5. Interobserver Agreements between Two Groups in Continuous Variables

Continuous Variables	ICC Value
LN number	0.96
LN size	0.94
< 3 cm	0.96
3–6 cm	0.85
> 6 cm	0.50
Margin	
Well-defined smooth	0.87
Well-defined irregular	0.92
Ill-defined	0.84
Enhancement pattern	
Homogeneous	0.95
Heterogeneous	0.60
Thin irregular	0.83
Thick irregular	0.50

Note.—ICC = intraclass correlation coefficient, LN = lymph nodes

Table 6. Interobserver Agreements between Two Groups in Categorical Variables

Categorical Variables	Kappa Value
Bilaterality	0.91
Calcification	1.00
Fat infiltration	0.54
Conglomeration	0.53
Adjacent tissue invasion	0.70
Nodal distribution	
Level IA	0.85
Level IB	0.81
Level IIB	0.70
Level III	0.73
Level IV	0.62
Level VA	0.63
Level VB	0.60
Supraclavicular	0.47

ferential diagnosis is reliable and unavoidable when histologic examination is difficult or impossible. However, the differential diagnosis of cervical lymph node metastasis between SCC and non-SCC still remains difficult.

The number of lymph nodes in the non-SCC group and the number of lymph nodes smaller than 3 cm were greater than those in the SCC group. There also were significant differences between the SCC group and the non-SCC group except for cases of thyroid cancer. Conglomeration of at least three lymph nodes has been used as a morphologic criteria for the diagnosis of SCC of the head and neck region (5, 6). In this study, we counted "conglomerate" nodal metastasis as one lymph node with metastatic involvement and conglomeration was more frequently observed in the SCC group (55.6%) than in the non-SCC group (44.4%). As the conglomeration of lymph nodes increases, the number of total lymph nodes may decrease, similar to a negative correlation. The higher frequency of lymph node conglomeration in the SCC group may have resulted in counting of a larger number of metastatic lymph nodes in the non-SCC group than in the SCC group.

To the best of our knowledge, there has been no report that compared the characteristics of lymph nodes with heterogeneous enhancement between the SCC and non-SCC groups. In our study, the ratio of lymph nodes with heterogeneous enhancement to total lymph nodes was significantly larger in the non-SCC group than in the SCC group. However, there was no significant difference in the ratio of lymph nodes with heterogeneous enhancement to total lymph nodes between the SCC group and the non-SCC group except for cases of thyroid cancer. Metastasis from SCC is commonly seen as solid masses in the neck. Tumor cells replacing the medulla of the lymph nodes commonly show less contrast enhancement than the remaining nodal cortex, resulting in a heterogeneous appearance. This heterogeneous enhancement has been known as the characteristic appearance of both metastatic SCC and non-SCC (7, 8). However, there has been no comparative study assessing the enhancement pattern of metastasis from SCC and non-SCC. There are two possible interpretations of the above result. First, necrotic lymph nodes were included in the group showing heterogeneous enhancement in previous studies. Because necrotic lymph nodes were not included in the group showing heterogeneous enhancement pattern in this study, the frequency of heterogeneous enhancement in the SCC group may have been underestimated compared to that in other studies. Second, we suggested that the broad spectrum of imaging findings in the SCC group can explain the lower frequency of heterogeneous enhancement in the SCC group than in the non-SCC group. Homogeneous enhanced metastasis in the SCC group has not been commonly reported. Sumi et al. (3) reported that substantial number of lymph nodes with metastasis displayed homogeneous staining patterns after contrast enhancement on CT. Homogeneous enhancement of lymph nodes on CT can be seen in either lymph nodes with metastasis or benign reactive lymph nodes. It is a nonspecific CT finding that has little value in the detection of lymph node me-

tastasis in SCC patients (7). Cystic metastasis with thin regular wall enhancement has not been commonly reported (9-13). Goldenberg previously stated that cystic metastasis with thin regular wall enhancement can be explained by a malignant process in the lymphoepithelial tissue of Waldeyer's ring or a relationship with human papillomavirus in tonsil/tongue SCC (14, 15). Regauer et al. (16) reported that cystic change can be present at a microscopic level in as many as 50% of metastasis from a primary SCC in the Waldeyer's ring. In our study, thin regular wall enhancement of SCC was noted in 17% of the cases (13/46).

There was a significant difference in counting of the number of lymph nodes larger than 6 cm in size between the two observers. Because the size criteria was thought to be relatively clear, the observers wondered why there was a difference in their results. During the second review of these cases, there was a difference in the determination of presence of conglomeration between the two observers. There are no objective criteria for conglomeration of lymph nodes, including numeric values or parameters. Because observers considered "conglomerate" nodal metastasis as one lymph node with metastasis and measured the entire diameter of the conglomerated mass, the ambiguity in criteria for determining the presence of conglomeration had a very large effect on the number of lymph nodes larger than 6 cm in size. If the imaging criteria for determining conglomeration were clearly defined, it is thought that there would be a minimal or no significant difference between the two observers.

The incidence of calcification in the non-SCC group (14.0%, 7/50) was significantly higher than that in the SCC group (2.2%, 1/46). This result was probably due to high proportion of thyroid cancer cases in the non-SCC group (22/50). Among the 22 cases with primary thyroid cancer, 7 cases showed calcified metastatic lymphadenopathy. This finding was compatible with that in previous studies of metastatic lymphadenopathy in primary thyroid cancer (17-19). There was no significant difference in the incidence of calcification between the SCC group and the non-SCC group except for cases of thyroid cancer in this study. Eisenkraft and Som (20) stated that nodal calcification is not a reliable predictor of either benign or malignant disease. However, nodal calcification suggests a limited differential diagnosis that most commonly includes tuberculosis, treated lymphoma, and metastatic adenocarcinoma, or squamous cell carcinoma. In our study, all cases with calcification in the non-SCC group were of thyroid cancer (7/7, 100%). Therefore, calcification can be used for the detection of lymph nodes affected by metastasis from thyroid cancer. However, it cannot be used for the differentiation of lymph nodes with metastasis between the SCC and non-SCC groups. The imaging features of tuberculous lymphadenitis are diverse and nonspecific, although rim enhancement or calcification, if present, can be a strong indicator of tuberculosis (21). Choi et al. (22) reported cases of tuberculous cervical lymphadenitis mimicking lymph nodes with metastasis in papillary thyroid carcinoma. Fine-needle aspiration cytology may be indicated for suspicious metastatic cervical nodes in patients with papillary thyroid carcinoma, especially in those who have a previous tuberculosis history (23).

Previous reports have demonstrated that the detection of nodal necrosis in patients with primary head and neck tumor is the most reliable sign of a node with metastasis (24-28). Necrosis is frequently found in nodal metastases from SCC of the head and neck, and it has been used as a criteria for diagnosis (8, 29, 30). To the best of our knowledge, there have been no reports comparing the necrosis pattern between the SCC and non-SCC groups. In this study, there was no significant difference in the presence of necrosis between the two groups, but the ratio of lymph nodes with thick irregular wall enhancement to total lymph nodes was higher in the SCC group (mean number: 0.27) than in the non-SCC group (mean number: 0.09). There was no significant difference in the ratio of lymph nodes with thick irregular wall enhancement to total lymph nodes between the SCC group and the non-SCC group except for cases of thyroid cancer. Wunderbaldinger et al. (31) revealed that a thickened outer wall was present in 35.2% of complex metastatic lymph nodes in patients with papillary thyroid carcinoma. Our results suggested that necrosis itself cannot be used as single criteria for differentiation between SCC and non-SCC groups.

The incidence of adjacent tissue invasion in the non-SCC group (36.0%, 18/50) was significantly higher than that in the SCC group (17.4%, 8/46). Various invaded tissues were identified in this study. In the SCC group, great vessel [internal jugular vein (IJV), common carotid artery] invasion, bone (hyoid bone) invasion, and soft tissue (sternocleidomastoid muscle, digastric muscle, submandibular gland) invasion were noted. In the non-SCC group, great vessel (IJV, internal carotid artery) invasion, bone (spine and rib, mandible) invasion, and soft tissue (sterno-

cleidomastoid muscle, prevertebral muscle, longus colli muscle, parotid gland, thyroid, esophagus) invasion were noted. Tumor cell types in the non-SCC group with adjacent tissue invasion included papillary thyroid carcinoma, medullary thyroid carcinoma, adenocarcinoma, and salivary duct carcinoma. Papillary carcinoma was the predominant tumor type in the non-SCC group with adjacent tissue invasion (7/21, 33.3%). As a result, there was no significant difference in adjacent tissue invasion between the SCC group and the non-SCC group except for cases of thyroid cancer. Yamashita et al. (32, 33) stated that extracapsular invasion of lymph node metastasis is an indicator of distant metastasis and poor prognosis in patients with papillary thyroid carcinoma. They identified lymph node metastasis in 202 patients with papillary microcarcinoma. In their study, the incidence of extracapsular invasion of lymph node metastasis was 30.7%; 62 patients among the 202 patients had lymph node metastasis.

The patients in the SCC group (36–89 yrs, mean: 63.0 yrs) were significantly older than those in the non-SCC group (16–81 yrs, mean: 56.1 yrs). While various primary cancers were included in this study, the high proportion of thyroid cancer cases in the non-SCC group (22/50) played an important role in this result. There was no significant difference in age between the SCC group and the non-SCC group except for cases of thyroid cancer. Thyroid cancer can occur at any age but it often affects younger patients. The median age at the time of diagnosis of thyroid cancer was 50 years in a previous study (34, 35). In our study, the mean age of patients with primary thyroid cancer in the non-SCC group was 52 years.

In our study, SCC was more frequent in men than in women (female to male ratio, 11:35) and non-SCC was relatively more frequent in women than in men (female to male ratio, 29:21). Thyroid cancer was noted in 22 patients, who accounted for a high proportion of non-SCC cases (22/50). Thyroid cancer was much more frequent in females than in males (female to male ratio, 18:4). In the previous reports, Parkin and Muir (34) and Voutilainen et al. (35) stated that the female-to-male ratio of thyroid cancer ranged from 2:1 to 5:1 in most populations. The higher frequency of non-SCC in women than in men was suspected to be due to the high proportion of thyroid cancer cases in the non-SCC group.

This study had several limitations. First, the total sample size and the number of cases in both the SCC and non-SCC groups were limited. Second, this was a retrospective review of patients who underwent imaging investigations as part of the assessment for head and neck metastasis. Third, we only analyzed MDCT findings without MRI correlation. Fourth, not all lymph nodes included in this study were pathologically confirmed by biopsy. Biopsy was performed only on a few selected lymph nodes in patients with multiple cervical lymph node metastases. In conclusion, large number of lymph nodes, heterogeneous enhancement pattern, large number of lymph nodes smaller than 3 cm in size, presence of calcification, and presence of adjacent tissue invasion suggest non-SCC rather than SCC. The presence of thick irregular wall enhancement pattern in lymph nodes with metastasis suggests SCC rather than non-SCC. The age of patients in the SCC group was higher than that of patients in the non-SCC group. SCC was more frequent in men than in women, and non-SCC was relatively more frequent in women than in men. Lymphadenopathies associated with SCC were more common in levels IA, IB, and III groups of lymph nodes, while lymphadenopathies associated with non-SCC were more common in levels IIB and IV groups of lymph nodes on neck CT.

In conclusion, the number of lymph nodes, the number of lymph nodes smaller than 3 cm, and nodal distribution are helpful in differential diagnosis between SCC and non-SCC before performing a biopsy.

REFERENCES

1. Seethala RR. Current state of neck dissection in the United States. *Head Neck Pathol* 2009;3:238-245
2. van den Brekel MW, Stel HV, Castelijns JA, Nauta JJ, van der Waal I, Valk J, et al. Cervical lymph node metastasis: assessment of radiologic criteria. *Radiology* 1990;177:379-384
3. Sumi M, Ohki M, Nakamura T. Comparison of sonography and CT for differentiating benign from malignant cervical lymph nodes in patients with squamous cell carcinoma of the head and neck. *AJR Am J Roentgenol* 2001;176:1019-1024
4. de Bondt RB, Nelemans PJ, Bakers F, Casselman JW, Peutz-Kootstra C, Kremer B, et al. Morphological MRI criteria improve the detection of lymph node metastases in head

and neck squamous cell carcinoma: multivariate logistic regression analysis of MRI features of cervical lymph nodes. *Eur Radiol* 2009;19:626-633
5. Dammann F, Horger M, Mueller-Berg M, Schlemmer H, Claussen CD, Hoffman J, et al. Rational diagnosis of squamous cell carcinoma of the head and neck region: comparative evaluation of CT, MRI, and 18FDG PET. *AJR Am J Roentgenol* 2005;184:1326-1331
6. Curtin HD, Ishwaran H, Mancuso AA, Dalley RW, Caudry DJ, McNeil BJ. Comparison of CT and MR imaging in staging of neck metastases. *Radiology* 1998;207:123-130
7. Yuasa K, Kawazu T, Nagata T, Kanda S, Ohishi M, Shirasuna K. Computed tomography and ultrasonography of metastatic cervical lymph nodes in oral squamous cell carcinoma. *Dentomaxillofac Radiol* 2000;29:238-244
8. Anzai Y, Brunberg JA, Lufkin RB. Imaging of nodal metastases in the head and neck. *J Magn Reson Imaging* 1997;7:774-783
9. Burgess KL, Hartwick RW, Bedard YC. Metastatic squamous carcinoma presenting as a neck cyst. Differential diagnosis from inflamed branchial cleft cyst in fine needle aspirates. *Acta Cytol* 1993;37:494-498
10. Verma K, Mandal S, Kapila K. Cystic change in lymph nodes with metastatic squamous cell carcinoma. *Acta Cytol* 1995;39:478-480
11. Flanagan PM, Roland NJ, Jones AS. Cervical node metastases presenting with features of branchial cysts. *J Laryngol Otol* 1994;108:1068-1071
12. Gourin CG, Johnson JT. Incidence of unsuspected metastases in lateral cervical cysts. *Laryngoscope* 2000;110(10 Pt 1):1637-1641
13. Unal M, Pata YS, Akbaş Y, Aydin O. Cervical cystic metastasis of squamous cell carcinoma: a case report with an unusual presentation. *Eur Arch Otorhinolaryngol* 2005;262:387-389
14. Goldenberg D, Sciubba J, Koch WM. Cystic metastasis from head and neck squamous cell cancer: a distinct disease variant? *Head Neck* 2006;28:633-638
15. Goldenberg D, Begum S, Westra WH, Khan Z, Sciubba J, Pai SI, et al. Cystic lymph node metastasis in patients with head and neck cancer: an HPV-associated phenomenon. *Head Neck* 2008;30:898-903
16. Regauer S, Mannweiler S, Anderhuber W, Gotschuli A, Berghold A, Schachenreiter J, et al. Cystic lymph node metastases of squamous cell carcinoma of Waldeyer's ring origin. *Br J Cancer* 1999;79:1437-1442
17. Choi YJ, Yun JS, Kook SH, Jung EC, Park YL. Clinical and imaging assessment of cervical lymph node metastasis in papillary thyroid carcinomas. *World J Surg* 2010;34:1494-1499
18. Sohn YM, Kwak JY, Kim EK, Moon HJ, Kim SJ, Kim MJ. Diagnostic approach for evaluation of lymph node metastasis from thyroid cancer using ultrasound and fine-needle aspiration biopsy. *AJR Am J Roentgenol* 2010;194:38-43
19. Rosário PW, de Faria S, Bicalho L, Alves MF, Borges MA, Purisch S, et al. Ultrasonographic differentiation between metastatic and benign lymph nodes in patients with papillary thyroid carcinoma. *J Ultrasound Med* 2005;24:1385-1389
20. Eisenkraft BL, Som PM. The spectrum of benign and malignant etiologies of cervical node calcification. *AJR Am J Roentgenol* 1999;172:1433-1437
21. Moon WK, Han MH, Chang KH, Im JG, Kim HJ, Sung KJ, et al. CT and MR imaging of head and neck tuberculosis. *Radiographics* 1997;17:391-402
22. Choi EC, Moon WJ, Lim YC. Case report. Tuberculous cervical lymphadenitis mimicking metastatic lymph nodes from papillary thyroid carcinoma. *Br J Radiol* 2009;82:e208-e211
23. Iqbal M, Subhan A, Aslam A. Papillary thyroid carcinoma with tuberculous cervical lymphadenopathy mimicking metastasis. *J Coll Physicians Surg Pak* 2011;21:207-209
24. Mancuso AA, Harnsberger HR, Muraki AS, Stevens MH. Computed tomography of cervical and retropharyngeal lymph nodes: normal anatomy, variants of normal, and applications in staging head and neck cancer. Part II: pathology. *Radiology* 1983;148:715-723
25. Yousem DM, Som PM, Hackney DB, Schwaibold F, Hendrix RA. Central nodal necrosis and extracapsular neoplastic spread in cervical lymph nodes: MR imaging versus CT. *Radiology* 1992;182:753-759
26. King AD, Tse GM, Ahuja AT, Yuen EH, Vlantis AC, To EW, et al. Necrosis in metastatic neck nodes: diagnostic accuracy of CT, MR imaging, and US. *Radiology* 2004;230:720-726
27. Trotta BM, Pease CS, Rasamny JJ, Raghavan P, Mukherjee

S. Oral cavity and oropharyngeal squamous cell cancer: key imaging findings for staging and treatment planning. *Radiographics* 2011;31:339-354
28. Som PM. Detection of metastasis in cervical lymph nodes: CT and MR criteria and differential diagnosis. *AJR Am J Roentgenol* 1992;158:961-969
29. Mancuso AA, Maceri D, Rice D, Hanafee W. CT of cervical lymph node cancer. *AJR Am J Roentgenol* 1981;136:381-385
30. Vandecaveye V, De Keyzer F, Vander Poorten V, Dirix P, Verbeken E, Nuyts S, et al. Head and neck squamous cell carcinoma: value of diffusion-weighted MR imaging for nodal staging. *Radiology* 2009;251:134-146
31. Wunderbaldinger P, Harisinghani MG, Hahn PF, Daniels GH, Turetschek K, Simeone J, et al. Cystic lymph node metastases in papillary thyroid carcinoma. *AJR Am J Roentgenol* 2002;178:693-697
32. Yamashita H, Noguchi S, Murakami N, Kawamoto H, Watanabe S. Extracapsular invasion of lymph node metastasis is an indicator of distant metastasis and poor prognosis in patients with thyroid papillary carcinoma. *Cancer* 1997;80:2268-2272
33. Yamashita H, Noguchi S, Murakami N, Toda M, Uchino S, Watanabe S, et al. Extracapsular invasion of lymph node metastasis. A good indicator of disease recurrence and poor prognosis in patients with thyroid microcarcinoma. *Cancer* 1999;86:842-849
34. Parkin DM, Muir CS. Cancer Incidence in Five Continents. Comparability and quality of data. *IARC Sci Publ* 1992;(120):45-173
35. Voutilainen PE, Multanen MM, Leppäniemi AK, Haglund CH, Haapiainen RK, Franssila KO. Prognosis after lymph node recurrence in papillary thyroid carcinoma depends on age. *Thyroid* 2001;11:953-957

편평세포암과 비편평세포암 환자에서 경부 림프절 전이의 CT 영상소견 비교 연구

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목적: 경부 CT상에서 편평상피세포암과 비편평상피세포암의 경부 림프절 전이의 감별 영상 소견을 알아보고, 조직 검사를 시행하기 전에 원발 병소의 규명을 용이하게 하기 위하여 본 연구를 시행하였다.

대상과 방법: 2006년 1월부터 2011년 1월까지 경부 CT를 시행하고, 조직 검사를 통해 전이성 편평상피세포암으로 진단된 환자 46명, 그리고 비편평상피세포암으로 진단된 환자 50명을 대상으로 후향적 연구를 시행하였다. 환자들을 편평상피세포암, 비편평상피세포암의 두 집단으로 구분하였다. 검사에 포함된 총 림프절의 수는 편평상피세포암 204개, 비편평상피세포암 530개였다. 두 명의 관찰자는 비정상적인 림프절의 특징들(숫자, 경계 양상, 조영증강 양상, 크기, 양측성, 석회화, 지방침윤, 괴상집적, 주변 조직으로의 침투, 분포양상)에 대하여 검토를 하였다. 림프절의 분포는 영상기준림프절분류법을 이용하여 평가하였다.

결과: 비편평상피세포암 집단과 갑상선암을 제외한 편평상피세포암 집단 사이에 림프절의 수, 3 cm 크기 이하의 림프절의 수는 의미 있는 차이를 보였다($p < 0.05$).

결론: 림프절의 수, 3 cm 크기 이하의 림프절의 수와 같은 영상 소견을 통해 조직 검사를 시행하기 전에 편평상피세포암과 비편평상피세포암의 경부 림프절 전이의 감별진단에 도움을 받을 수 있다.

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