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Diagnostic Value of CT for the Detection of Cervical Lymph Node Metastases in Papillary Thyroid Carcinoma[1]

Kyu Ri Son, M.D., Dong Gyu Na, M.D.[2], Kee-Hyun Chang, M.D.[2]

Purpose: To determine the diagnostic accuracy of CT for the detection of cervical lymph node metastases in patients with papillary thyroid carcinoma (PTC).

Materials and Methods: Two hundred twelve consecutive patients with surgically proven PTC were included in this study. CT images were retrospectively evaluated to determine the presence of a node metastasis using morphologic CT criteria (at least one of the following: strong nodal enhancement without hilar vessel enhancement, heterogeneous enhancement, calcification, and cystic change). The diagnostic accuracy of CT for the diagnosis of a metastatic lymph node was assessed using a level-by-level analysis.

Results: The accuracy of the CT finding for strong nodal enhancement was greater than the other morphologic CT criteria (81.6% and 74.5-78.5%, respectively). The sensitivity, specificity, and accuracy were 64.4%, 91.4%, and 84.3% by the morphologic CT criteria, and were 34.6%, 93.9%, and 78.2% by size criteria, respectively.

Conclusion: The morphologic CT criteria are more accurate than the size criteria in the detection of cervical lymph node metastases in patients with papillary thyroid carcinoma; and, strong nodal enhancement on a CT scan is the most important factor for its diagnostic accuracy.

Index words : Thyroid neoplasms
Papillary carcinoma
Head and neck neoplasms, metastases
Tomography, X-ray computed

A papillary thyroid carcinoma is the most common neoplasm in the thyroid gland and accounts for approximately 70% of all thyroid carcinomas (1). Metastatic cervical lymphadenopathy is a common finding in patients with papillary thyroid carcinoma, and its detection is crucial for planning the surgical management of these patients (2-4). Many investigators have noted the sonographic differentiation between normal and abnormal lymph nodes (5-7). Although criteria for the diagnosis of abnormal nodes are well established, overlap between the criteria for metastasis and various other pathological conditions still exists.

Although many studies have described the ultrasonographic or MR imaging appearance of metastatic lymph nodes from papillary thyroid carcinoma (5-10), many

[1]Department of Radiology, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea.
[2]Department of Radiology, Seoul National University College of Medicine, Institute of Radiation Medicine, Seoul National University Medical Research Center, and Clinical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea.
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Address reprint requests to : Kyu Ri Son, M.D., Department of Radiology, SMG-SNU Boramae Medical Center, 39, Boramae Road, Dongjak-ku, Seoul, 156-707, Korea
Tel. 82-2-870-2544 Fax. 82-2-747-7418 E-mail: kyurad@gmail.com

practitioners are reluctant to use a contrast-enhanced CT scan as a diagnostic tool due to a concern about delayed subsequent radioiodine therapy. Recently, several investigators have reported that a CT scan increases the sensitivity of detecting metastatic lymph nodes from a papillary thyroid carcinoma (11, 12). The criteria of the CT findings for metastatic lymph nodes of papillary thyroid carcinomas; however, have not yet been established. In this study, we evaluated the usefulness of CT for the detection of cervical lymph node metastases in patients with papillary thyroid carcinomas, and assessed the optimal criteria for the detection of a nodal metastasis on CT images.

Materials and Methods

Patients

We retrospectively reviewed 212 patients with a papillary thyroid carcinoma that also underwent a neck dissection and a thyroidectomy. The subjects included 182 women and 30 men, ranging in age from 21 to 78 years (average age, 46 years). A contrast-enhanced neck CT was performed in all patients as a preoperative evaluation. The surgeons dissected all visible or palpable lymph nodes on a level-by-level basis according to the preoperative findings of clinical palpation and the CT findings.

CT Imaging

CT examinations were performed using a series of multi-detector row CT scanners. The CT scanners included a four-detector row CT scanner (MX 8000, Philips Medical Systems, Cleveland, OH U.S.A. (n = 68), an eight-detector row CT scanner (Light Speed Ultra, GE Medical Systems, Milwaukee, WI U.S.A.) (n = 46), a 16-detector row CT scanner (Sensation 16, Siemens, Erlangen, Germany) (n = 53), and a 64-detector row CT scanner (Brilliance 64, Philips Medical Systems) (n = 45). The respective scanning parameters used for the 4-, 8-, 16- and 64-multidetector row CT scanners were respectively as follows: the detector configurations were 4×2.5, 8×1.25, 16×0.75, and 64×0.625 mm; slice thicknesses, 3.2, 2.5, 3 and 3 mm; reconstruction intervals 3, 2.5, 3 and 2 mm; table speeds, 12.5, 13.5, 24, and 46 mm/rotation. The time interval between the CT examination and neck dissection ranged from one to sixty days (mean, 28 days).

Unenhanced images were first obtained in a craniocaudal direction between an aorticopulmonary window level and the skull base. After acquiring unenhanced images, 90 ml of an iodinated contrast agent (Ultravist 370, Schering, Berlin, Germany) was injected at 3 ml/s using an automated injector and a scan delay time of 45 s. We additionally injected 45 ml of normal saline at 3 ml/s for saline flushing immediately after injection of the contrast agent to avoid artifacts induced by stagnated contrast agents within the subclavian or innominate vein, which may obscure the lymph nodes of the low central neck and supraclavicular fossa.

Image Analysis

The resected nodes were classified according to the nodal classification scheme of the American Joint Committee on Cancer level system (13). Accordingly, all cervical lymph nodes were divided into central (level VI) and lateral (Levels I-V) groups on each of the sides. Upon CT examination, the cervical lymph nodes were assessed on a level-by-level basis by two radiologists (D.K.N. and K.R.S.) with consensus. We could not reliably identify whether a node was positive or negative, as the nodes were too small to distinguish from other nodes of similar size. Therefore, the largest node was considered the representative of each nodal compartment and was used for CT and pathological correlation.

The CT images were retrospectively evaluated to determine the presence of node metastasis using the size, morphological CT, and combined criteria. We measured the short transverse diameter of the largest lymph node

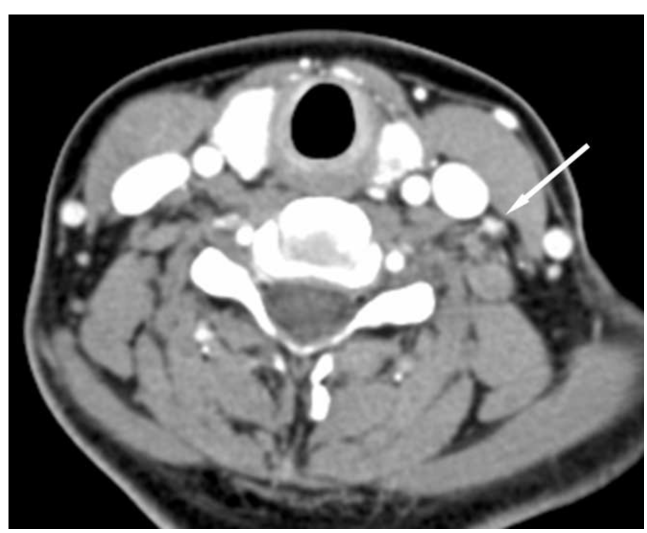

Fig. 1. A 38-year-old woman with papillary thyroid cancer in the left lobe of the thyroid gland. A CT demonstrates a small metastatic lymph node (arrow) with focal strong enhancement as adjacent neck vessels in left level IV. A pathologic specimen revealed metastatic papillary carcinoma in the lymph node.

at each neck level to determine the optimal size criteria. Morphological CT criteria for metastatic lymph nodes included strong nodal enhancement, cystic change, calcification, and heterogenous enhancement (Fig. 1-4). We considered nodes as being malignant based on morphological CT criteria if they had at least one out of these four findings. A lymph node with strong nodal enhancement was defined as a node showing higher enhancement than the adjacent sternocleidomastoid muscle without hilar vessel enhancement. A lymph node with heterogenous enhancement was defined as a node showing inhomonogenous enhancement without focal cystic change. A lymph node with strong nodal enhancement and hilar vessel enhancement was regarded as a reactive lymph node. We considered nodes as being malignant using the combined criteria if they were considered malignant by either size or morphological criteria.

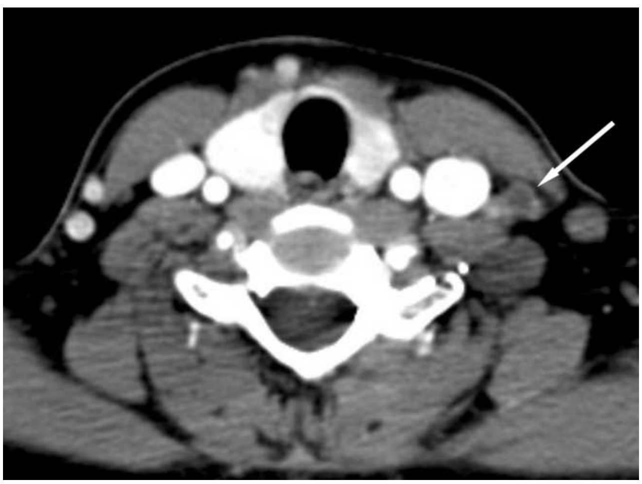

Fig. 2. A 47-year-old man woman with papillary thyroid cancer in the left lobe of the thyroid gland. A CT demonstrates a small lymph node (arrow) with a focal cystic change in left level IV revealed to be a metastatic lymph node.

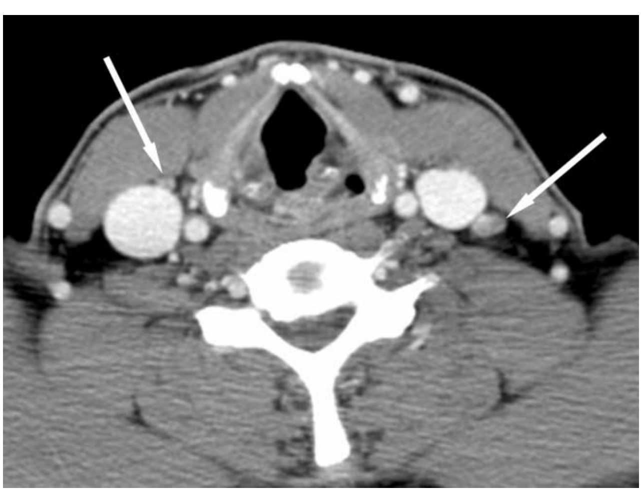

Fig. 3. A 55-year-old man with papillary thyroid cancer in the left lobe of the thyroid gland. A CT demonstrates small heterogeneously enhancing lymph nodes (arrows) in both level IVs. A pathologic specimen revealed metastatic papillary carcinoma in the lymph node.

Statistical Analysis

The size of malignant and benign nodes was compared using the t-test. The optimal cutoff value for the short transverse diameter in terms of differentiating metastatic from benign lymph nodes was calculated using the receiver operating characteristic curve analysis in the central and lateral neck compartment. The sensitivity, specificity, and accuracy for the detection of lymph node metastases were calculated on a level-by-level basis for all neck levels or the central and lateral nodal compartment using each of the three previously mentioned criteria (size, morphological criteria and combined criteria). The three criteria were compared using the McNemar test. A univariate analysis was performed to identify the parameters that were used to differentiate malignant and benign nodes. A multivariate analysis was performed using the multiple logistic regression to determine if these parameters were useful in distinguishing malignant from benign lymph nodes if they are independent of each other. The odds ratios and 95% confidence intervals were determined. For all statistical analyses, a p-value less than 0.05 was considered to indicate a significant difference. The data were ana-

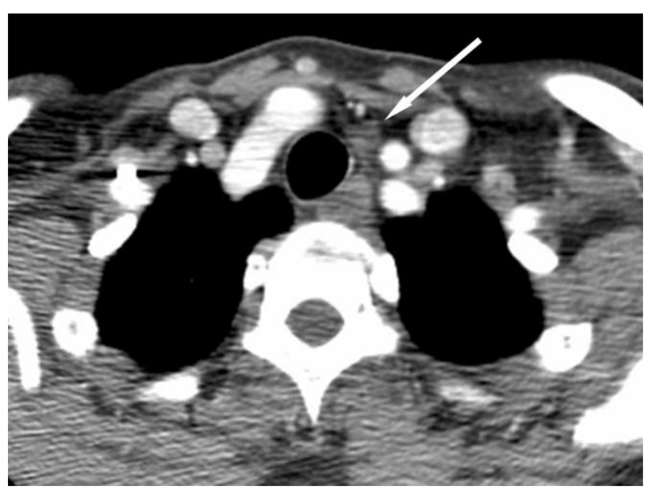

Fig. 4. A 50-year-old woman with papillary thyroid cancer in the right lobe of the thyroid gland. A CT demonstrates a lymphadenopathy (arrow) in the left level VI, which is regarded to be positive when applying size criteria, and negative when applying morphologic criteria. The formal report suggested possible lymph node metastasis, but pathologic exam revealed a reactive lymphadenopathy.

lyzed using the SPSS statistical software (version 10.0; SPSS, Chicago, IL, U.S.A.).

Results

A central neck dissection was performed at 198 levels (right and left central neck levels). Of the 198 dissected central neck levels, 48 (24%) were proven pathologically to have metastatic nodes. Lateral neck dissection was performed at 183 levels [level I (n = 6), level II (n = 47), level III (n = 71), level IV (n = 44) and level V (n = 15)]. Metastatic lymph nodes were found at 53 (29%) lateral neck levels [level I (n = 2), level II (n = 9), level III (n = 22), level IV (n = 17) and level V (n = 1)]. Overall, metastatic lymph nodes were shown to be present after surgery at 101 levels (27%) of the 381 dissected neck levels in 212 patients on a level-by-level analysis.

Table 1. The Size Distribution of Lymph Nodes in the Central and Lateral Neck

	Malignant Nodes(*mm)	Benign Nodes (*mm)	p value
Central group	5.73 ± 2.63	3.95 ± 1.38	0.00003
Lateral group	6.78 ± 3.56	5.07 ± 1.97	0.0008

Mean ± standard deviation
The size (*mm) refers to the transverse minimal diameter

Malignant nodes were larger than benign nodes in the central and lateral neck compartments (Table 1). A short transverse diameter of 5 mm and 8 mm were determined as the cutoff values for the discrimination of metastatic nodes from benign nodes at the central neck and lateral neck levels by ROC analysis, respectively.

Table 2 shows the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of four morphological CT findings for the detection of metastatic cervical lymph nodes on all neck levels. The morphological CT criteria revealed a sensitivity of 64% and a specificity of 91% for the diagnosis of metastatic nodes. The accuracy of the CT finding for strong nodal enhancement was higher than that of the other morphologic CT criteria (81.6% and 74.5–78.5%, respectively).

The detection of nodal metastasis, sensitivity, specificity, and accuracy when the short transverse diameter of 5 mm for the central neck levels and 8 mm for the lateral neck levels was used as the threshold were 34.6%, 93.9% and 78.2%, respectively (Table 3). When the morphological characteristics were analyzed, sensitivity, specificity, and accuracy were found to be 64.4%, 91.4%, and 84.3%, respectively (Table 3). The morpho-

Table 2. Comparison of the Diagnostic Accuracy of Morphologic CT Findings at All Levels of the Neck

CT Findings	Diagnostic Values				
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Strong enhancement	43 (43/101)	96 (268/280)	78 (43/55)	82 (268/326)	81.6 (311/381)
Cystic change	23 (23/101)	99 (276/280)	85 (23/27)	78 (276/354)	78.5 (299/381)
Calcification	6 (6/101)	99 (278/280)	75 (6/8)	75 (278/373)	74.5 (284/381)
Heterogenous enhancement	20 (20/101)	96 (269/280)	65 (20/31)	77 (269/350)	75.9 (289/381)
*Morphologic criteria	64 (65/101)	91 (256/280)	73 (65/89)	88 (256/292)	84.3 (321/381)

PPV, positive predictive value, NPV, negative predictive value, * Morphologic criteria means at least one of four morphologic CT findings

Table 3. Diagnostic Accuracy of CT For Nodal Staging Using the Sensitivity, Specificity, and Accuracy on a Level-by-Level Basis

Group	Parameter	Size*	Morphology*	Combined*	Size vs Morphology†	Size vs Combined†	Morphology vs Combined†
All group	Sensitivity	34.6(35/101)	64.4(65/101)	65.3(66/101)	0.000	0.000	1.0
	Specificity	93.9(263/280)	91.4(256/280)	87.5(245/280)	0.265	0.000	0.001
	Accuracy	78.2(298/381)	84.3(321/381)	81.6(311/381)	0.005	0.086	0.006
Central group	Sensitivity	39.6(19/48)	52.1(25/48)	52.1(25/48)	0.031	0.031	1.0
	Specificity	93.3(140/150)	92.7(139/150)	89.3(134/150)	1.0	0.031	0.063
	Accuracy	80.3(159/198)	82.8(164/198)	80.3(159/198)	0.332	1.0	0.063
Lateral group	Sensitivity	30.2(16/53)	75.5(40/53)	77.4(41/53)	0.000	0.000	1.0
	Specificity	94.6(123/130)	90(117/130)	85.4(111/130)	0.238	0.000	0.031
	Accuracy	75.9(139/183)	85.8(157/183)	83.1(315/381)	0.01	0.049	0.125

* Data are in percentage. The numbers in parentheses are raw data.
† p-values were calculated using the McNemar test.

Table 4. CT Findings Discriminating Malignant from Benign Cervical Lymph Nodes in Patients with Papillary Thyroid Carcinoma

Variable		Pathology		*p* Value at Univariate Analysis	Multiple Logistic Regression			
		Benign	Malignant		*p* value	Odds Ratio	Confidence interval	
Strong enhancement	absent	268	58	0.000	0.000	10.0	4.4	22.9
	present	12	43					
Cystic change	absent	276	78	0.000	0.033	3.8	1.1	12.7
	present	4	23					
Calcification	absent	278	95	0.005	0.041	6.9	1.1	43.6
	present	2	6					
Heterogenous enhancement	absent	269	81	0.000	0.000	6.6	2.7	15.8
	present	11	20					
size	≤5 mm (central group) or ≤8 mm (lateral group)	263	66	0.000	0.02	2.6	1.2	5.7
	>5 mm (central group) or >8 mm (lateral group)	17	35					

logical criteria showed better sensitivity and accuracy than the size criteria without any significant decrease in specificity.

A univariate analysis and multiple logistic regression analysis demonstrated that the four morphologic CT findings and size were significant parameters for depicting malignant nodes (Table 4).

Discussion

The frequency of regional node metastases in patients with papillary carcinomas is reported to vary from 39% to 90% (2–4, 10), depending on the surgical method undertaken and the population studied. In this study, morphological findings on CT images were more important for the detection of cervical lymph node metastases in patients with papillary thyroid carcinoma. Compared with the size criteria alone, the morphological criteria showed a higher sensitivity of 52.1% at the central neck level and 75.5% at the lateral neck level. A multivariate analysis demonstrated that the four morphological criteria and the size criteria were found to be significant predictors for the identification of nodal metastases; however, strong nodal enhancement (odds ratio, 10.0) and calcification (odds ratio, 6.9) had higher odds ratios.

Most of primary thyroid cancers appeared as relatively low attenuated lesions on CT scans because of the high level of vascularity in normal thyroid tissue (13–15). Although the contrast enhancement pattern for papillary thyroid carcinomas has been rarely reported, the presence of strong enhancement within a lymph node strongly suggests the presence of nodal metastasis from papillary thyroid carcinoma (9), which indicates that the papillary thyroid cancer itself has hypervasularity. Strong enhancement of lymph nodes showed relatively high sensitivity (43%) among the morphological CT findings, and a high odds ratio (10.0) by multivariate analysis. In clinical practice, lymph nodes with strong enhancement should be considered as malignant, even if the node is small in size. Unlike metastatic nodes, reactive lymphadenopathy occasionally demonstrates hilar vessel enhancement or central enhancement rather than peripheral enhancement (6, 7).

The various cystic nature of a metastatic papillary thyroid carcinoma has also been demonstrated on ultrasonography and MRI (10, 16). Cystic changes have been reported to be present in 70% of metastatic lymph nodes on ultrasonography (16) and in 33% of metastatic lymph nodes by MRI (10). Cystic changes consist of a small solitary cystic area, multiple peripheral cystic areas, or almost complete replacement of the node by cystic formation. These cystic changes represent liquefaction necrosis, and appear to be characteristic of a metastatic papillary thyroid carcinoma (16). In our study, 23% of the metastatic lymph nodes showed cystic changes on the CT images.

Microcalcification in the papillary thyroid carcinoma is a common ultrasonographic finding and is well known, histologically, as a psammomatous body (17–19). Microcalcification had been reported to be seen in approximately 60% of papillary thyroid carcinomas and metastatic lymph nodes by ultrasonography (8, 18, 19). The peripheral punctuate calcification in the cervical nodes is important for the diagnosis of metastatic papillary carcinomas of the thyroid (8); however, microcalcification can barely be detected on CT. In our study, only 6% of metastatic nodes showed calcification on CT images.

As the size of lymph nodes varies according to the various levels in the neck, and because small metastatic deposits inside lymph do not always cause enlargement of a lymph node, it is very difficult to define an optimal size criteria for determining malignancy (5, 20, 21). Any chosen size criterion is a compromise between high sensitivity and specificity. We suggested that the optimal size criteria (8 mm or more for the minimum transverse diameter in the lateral group and 5 mm or more in the central group) was slightly smaller than the minimum transverse diameter (10 mm) for a metastasis of a squamous cell carcinoma (5, 20–22).

The different anatomic levels in the neck may affect the performance of diagnostic imaging for identifying metastatic lymph nodes. Several CT and sonography studies have confirmed that enlarged nodes at different levels require different size criteria to predict whether the nodes are metastatic (20–22). Therefore, our results suggest specific size criteria for central or lateral neck node metastases in papillary thyroid carcinomas as well as the presence of smaller lymph node metastases compared to other head and neck malignancies.

The diagnosis of metastatic nodes using CT also depends on size determination and assessment of changes in the internal architecture. Within this context, Curtin et al. (23) studied the effect of size criteria and internal architectural changes of nodes for the diagnostic accuracy for metastatic nodes. These researchers showed that the addition of information on the internal architecture of a node resulted in a substantial improvement in the diagnostic performance of CT using a long axis length (maximum axial diameter). In this study, a multivariate analysis demonstrated that the four morphologic criteria and size criteria as significant parameters for diagnosing a nodal metastasis; however, strong nodal enhancement (odds ratio, 10.0) had the highest odds ratio among those factors.

CT requires the use of intravenous iodinated contrast agents to opacify normal vascular structures and delineate abnormal enhancement in patients with papillary thyroid carcinoma who may require a subsequent radioiodine ablation. The iodine load may alter radioactive iodine uptake for 6 weeks after its administration. Although the use of an iodinated contrast agent for CT has the potential to delay or reduce the effectiveness of subsequent radioiodine therapy, in our current practice (2–3 months after thyroidectomy), undergoing a CT examination seems to have no significant effect on the subsequent therapy.

There are several limitations in this study. First, we analyzed lymph node metastases based on the various neck levels; however, we did not perform a node-by-node analysis. We could not have full assurance that a possible metastatic lymph node demonstrated on CT completely matched the pathological results. Thus, the accuracy of the CT criteria could be over- or underestimated. However, the preoperative CT evaluation for lymph node metastases in papillary thyroid carcinomas provided an easy surgical approach by providing presurgical anatomical information. The use of the preoperative CT evaluation may be helpful for the establishment of a therapeutic plan as an assessment for mediastinal and cervical lymph node metastases. Second, we measured the short transverse diameter of the largest lymph node at each neck level on an axial CT scan. We did not measure the short transverse diameter of lymph node on the sagittal and coronal image. Thus, node size can be overestimated according to the axis of lymph node.

In conclusion, we found that morphologic CT criteria are more accurate than the size criteria in the detection of cervical lymph node metastases in patients with papillary thyroid carcinoma; and, strong nodal enhancement on CT scan is the most important predictive diagnostic factor.

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유두상 갑상선암의 경부림프절 전이의 진단을위한 CT의 진단능[1]

[1]서울시립보라매병원 영상의학과
[2]서울대학교 의과대학 방사선의학연구소, 임상의학연구소, 서울대병원 영상의학과

손규리 · 나동규[2] · 장기현[2]

목적: 유두상 갑상선암 환자에서 경부림프절 전이의 진단을 위한 CT의 진단의 정확성을 평가하고자 한다
대상과 방법: 수술로 유두상 갑상선암으로 증명된 총 212명의 연속된 환자를 대상으로 한다. 조영증강 CT를 수술 전 검사로 모든 환자에서 시행하였다. 형태적 CT 기준(다음 중 적어도 하나: 혈관의 조영증강 없이 강한 조영 증강, 불규칙한 조영증강, 석회화와 낭성변화)에 의해 림프절 전이를 후향적으로 분석하였다. 수준별 분석으로 림프절 전이에 대한 CT의 진단의 정확성을 결정하였다.
결과: 강한 조영증강의 정확도가 다른 기준보다 높았다(81.6%와 74.5-78.5%). 형태적 CT 기준의 민감도, 특이도, 정확도는 각각 64.4%, 91.4%, 84.3%이었고, 림프절 크기 기준으로는 각각 34.6%, 93.9%, 78.2%이었다.
결론: 유두상 갑상선암의 경부 림프절 전이를 예측하는 데 형태적 CT 기준이 림프절 크기보다 더 정확하며, 강한 조영증강이 가장 중요한 인자이다.