

Staging of Papillary Thyroid Carcinoma with Ultrasonography: Performance in a Large Series

Ji Soo Choi, MD¹, Woong Youn Chung, MD, PhD², Jin Young Kwak, MD, PhD¹, Hee Jung Moon, MD¹, Min Jung Kim, MD, PhD¹, and Eun-Kyung Kim, MD, PhD¹

¹Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea; ²Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

ABSTRACT

Background. This study was designed to evaluate the performance of ultrasonography (US) for the preoperative staging of papillary thyroid carcinoma (PTC) in a large series according to the TNM classification.

Methods. Preoperative US was performed for the evaluation of primary tumors and lymph node metastasis in 722 consecutive patients with cytologically proven PTC. Three experienced radiologists prospectively determined T and N categories of PTC. N categorization was based on compartments, including left and right lateral compartments (levels II–V) and central compartment (level VI). All patients underwent surgery and central compartment dissection. Lateral compartment dissection was selectively performed. We assessed the diagnostic performance of preoperative US for staging of PTC on the basis of pathologic findings of surgical specimens. Subgroup analysis according to suspicion of diffuse thyroid disease (DTD) on US was performed to compare US accuracies for N categorization.

Results. US predicted 61.7% (142/230) of patients with multifocal PTC and 67.1% (100/149) of patients with bilateral malignancy. Overall accuracy of US for T categorization was 69.7% (503/722) and that of US for N categorization was 59% (426/722). Accuracies of sonographic categorization for N0, N1a, and N1b were 66% (276/418), 33.3% (70/210), and 85.1% (80/94), respectively. Overall US accuracy for prediction of an N category was significantly lower in patients with US-indicated DTD

(51.1%, 67/131) than it was in patients without DTD (60.7%, 359/591; $P = 0.043$).

Conclusions. Preoperative US is a feasible technique for the preoperative staging of PTC and is helpful for the detection of lateral compartment metastasis. Presence of DTD can affect the staging of lymph node metastasis.

Papillary thyroid carcinoma (PTC), the most common histologic type of differentiated thyroid cancer, shows a good prognosis with a 10-year survival rate exceeding 90%; however, cervical lymph node metastasis occurs in more than 30% of patients.^{1–4} Although lymph node metastasis of PTC has little effect on overall survival, it has been identified as a risk factor of local tumor recurrence.^{5–7} In addition to lymph node metastasis, the size of the primary tumor and extrathyroidal extension are independent risk factors of tumor recurrence.^{7–9} Therefore, preoperative determinations of the presence of lymph node metastasis and the extent of primary tumor are important for optimal surgical management to reduce the recurrence rate.

High-resolution ultrasonography (US) is becoming a method of choice for preoperative imaging/staging of PTC, because it can depict and characterize thyroid nodules and detect lymph node metastasis as small as 5 mm.^{10–12} Also, the current management guidelines of the American Thyroid Association recommend neck US for preoperative imaging in patients with differentiated thyroid cancer.¹³ Recent studies have shown the feasibility of preoperative US in patients with PTC.^{11,12,14–20} Most of these studies, however, focused on the performance of US for prediction of lymph node metastasis with a small group of patients, and few studies have reported on the performance of preoperative US for determination of T category primary tumors in PTC patients.^{11,12,14–20}

The purpose of this study was to evaluate the diagnostic performance of US for preoperative staging of PTC according to the TNM classification system in a large series.

PATIENTS AND METHODS

Patients

Our institutional review board approved this retrospective study and waived the need for informed consent. This study included 722 patients (614 women, 108 men; mean age, 45 (range, 14–76) years) with PTC surgically diagnosed from May 2007 to January 2008. PTC had been confirmed preoperatively by using preoperative fine-needle aspiration biopsy in all patients. None of these patients had undergone a previous head or neck operation. The time interval between US examination and surgery was less than 2 months.

Imaging and Image Analysis

Thyroid US was performed prospectively by one of three radiologists with 8–12 years of experience and specialization in thyroid US. At the US examination for preoperative staging, the radiologists knew of the cytological results of malignancy in the thyroid masses. Both thyroid lobes and all neck levels (I–VI) were examined by using US with a 5- to 12-MHz linear transducer (iU22, Philips Healthcare) or a 7- to 15-MHz linear transducer (HDI 5000, Philips Healthcare).

Preoperative stagings of the primary tumor and regional lymph node were performed with US in accordance with the TNM classification of the American Joint Committee on Cancer and the International Union Against Cancer.²¹ T categories were as follows: T0, no evidence of primary tumor; T1, tumor \leq 2 cm in its greatest dimension and limited to the thyroid; T2, tumor 2–4 cm in its greatest dimension and limited to the thyroid; T3, tumor $>$ 4 cm in its greatest dimension and limited to the thyroid or any tumor with minimal extrathyroidal extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues); T4a, tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve; T4b, tumor invasion of the prevertebral fascia or encasement of the carotid artery or mediastinal vessels. N categories were as follows: N0, no regional lymph node metastasis; N1a, metastasis to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes); N1b, metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes.

For determination of T category, tumor size, extrathyroidal extension, and invasion of adjacent structures were

evaluated. The US criterion for extrathyroidal extension was contact with the adjacent thyroid capsule along more than 25% of the perimeter of the tumor.²² In the case of multiple malignant lesions, the most extensive tumor had priority in assignment of the T category.

Determination of the N category was based on compartments rather than individual levels, including the left and right lateral compartments (levels II–V) and the central compartment (level VI). The US criteria for lymph node metastasis were focal or diffuse hyperechogenicity, microcalcification, cystic change, round shape on transverse image, and abnormal vascular pattern (chaotic or peripheral).^{23–25}

The multifocality and bilaterality of the detected thyroid nodules also were evaluated. Multifocality was defined as the observation of multiple PTCs in one thyroid lobe, and bilaterality was defined as multiple PTCs in both thyroid lobes.²⁶

The presence of diffuse thyroid disease (DTD) was predicted preoperatively when the thyroid gland showed one or more of the following suspicious findings for DTD: heterogeneous echogenicity, micronodules, multiple linear echogenicity, and thyroid enlargement (AP diameter of thyroid on longitudinal scan $>$ 2 cm).^{27–29}

Surgical Procedures

A total of 491 patients underwent total or near-total thyroidectomy, and ipsilateral lobectomy was performed on 231 patients. All patients underwent dissection of the central compartment. Lateral compartment dissection was selectively performed on patients with nodes preoperatively categorized as N1b or on patients at high risk for lymph node recurrence. Preoperative fine-needle aspiration biopsy or intraoperative frozen biopsy was performed for suspicious lymph nodes. Surgeons dissected all suspicious lymph nodes by using a compartment-oriented approach based on the preoperative US findings and biopsy results. Of 722 dissected central compartments, 282 central compartments were pathologically proven to have metastatic nodes. Lateral compartment dissection was performed on 136 compartments in 116 patients, including unilateral dissection in 96 patients and bilateral dissection in 20 patients. Lymph nodes with metastasis were found in 106 of 136 lateral compartments dissected.

Follow-up

Of the 722 patients who underwent thyroid surgery, 6 patients did not follow-up after the initial operation, 453 patients (62.7%, 453/722) received postsurgical treatment with radioiodine (administered dose of ¹³¹I ranged from 30–150 mCi), and 263 patients were not treated with radioiodine. All patients received a suppressive dose of L-T4.

The follow-up period ranged from 15–28 (median, 21) months in 716 patients. All patients were examined at 6 and 12–18 months after initial treatment and yearly thereafter. The patients had a physical examination, neck US, and measurements of serum thyroid-stimulating hormone (TSH), free T4, thyroglobulin (Tg), and Tg antibody. ¹³¹I whole-body scintigraphy (WBS), chest computed tomography, or fluorodeoxyglucose positron emission tomography was performed only in selective cases (e.g., detectable serum Tg or persistent anti-Tg antibody without recurrence on US or WBS). WBS was performed after withdrawal of L-T4 for 2 or 3 weeks.

Recurrence was defined as reappearance of disease after initial treatment, as determined cytologically and histopathologically. The time to recurrence was defined as the duration from the date of thyroid surgery to the date of detection of recurrence using a diagnostic procedure. Patients with undetectable serum Tg during TSH suppression and no evidence of tumor on neck US or WBS were considered disease-free.

Statistical Analysis

The final assignments of T and N categories were based on histopathologic interpretations of surgical specimens. Because of the resolution of US, PTCs more than 1 mm in diameter were included for the analysis of this study. The accuracy of US in preoperative assignments of T and N categories was analyzed for each category on a “per patient” analysis.

Subgroup analysis according to existence of DTD was performed to compare US accuracies for N categorization because DTD can be accompanied by cervical lymphadenopathy.³⁰ Existence of DTD was based on the pathologic reports for surgical specimens. We used Chi-square test to compare US accuracies between two subgroups. Statistical significance was assumed when the two-sided *P* value was <0.05. Statistical analysis was performed with SPSS software package.

RESULTS

The mean tumor size was 9.3 (range, 1–60) mm according to histopathologic examination. The final T and N categories are summarized in Table 1. In 505 patients with PTC, the tumors were confirmed as microcarcinoma (≤1 cm, 69.9%). One or more PTC lesions were found in all patients; multifocality was identified in 230 patients (31.9%) and bilaterality was found in 149 patients (20.6%). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of preoperative US were 61.7% (142/230), 87.6% (431/492), 69.9%

TABLE 1 Final T and N categories confirmed via surgery according to tumor size

Final category	Tumor size				Total
	≤1 cm	1–2 cm	2–4 cm	>4 cm	
T stage					
T1	263	53	0	0	316
T2	0	0	8	0	8
T3	241	123	27	6	397
T4a	1	0	0	0	1
N stage					
N0	341	72	4	1	418
N1a	128	67	13	2	210
N1b	36	37	18	3	94
Total	505	176	35	6	722

(142/203), 83% (431/519), and 79.4% (573/722), respectively, for predicting multifocality, and 67.1% (100/149), 94.2% (540/573), 75.2% (100/133), 91.7% (540/589), and 88.6% (640/722), respectively, for predicting bilaterality. In 186 cases, DTD was diagnosed pathologically, and the PPV for expecting DTD on US was 95.4% (125/131). There were 181 chronic lymphocytic thyroiditis (97.3%) and 5 Hashimoto thyroiditis (2.7%)

Assignment of T Category

Sonographic versus pathologic T category results are summarized in Table 2. The overall accuracy of preoperative US for T categorization was 69.8% (504/722). The accuracies of sonographic T categorization for T1, T2, T3, and T4 cancers were 47.4% (150/316), 25% (2/8), 88.4% (351/397), and 100% (1/1), respectively. Extrathyroidal extension was found in 398 of the 722 patients (55.1%). The sensitivity, specificity, PPV, NPV, and accuracy of US in predicting of extrathyroidal extension were 88.9% (354/398), 47.2% (153/324), 67.4% (354/525), 77.7% (153/197), and 70.2% (507/722), respectively.

TABLE 2 Sonographic versus pathologic T categories

Pathologic stage	US stage				Total
	T1	T2	T3	T4	
T1	150	1	164	1	316
T2	0	2	6	0	8
T3	44	0	351	2	397
T4	0	0	0	1	1
Total	194	3	521	4	722

US ultrasonography

TABLE 3 Sonographic versus pathologic N categories

Pathologic stage	US stage			Total
	N0	N1a	N1b	
N0	276	67	75	418
N1a	97	70	43	210
N1b	8	6	80	94
Total	381	143	198	722

US ultrasonography

TABLE 4 Sonographic versus pathologic N categories according to suspicion of DTD on US

Pathologic stage	US stage					
	US-DTD (–) (<i>n</i> = 591)			US-DTD (+) (<i>n</i> = 131)		
	N0	N1a	N1b	N0	N1a	N1b
N0 (<i>n</i> = 418)	236	43	57	40	24	18
N1a (<i>n</i> = 210)	91	53	30	6	17	13
N1b (<i>n</i> = 94)	7	4	70	1	2	10
Total (<i>n</i> = 722)	334	100	157	47	43	41

US ultrasonography, DTD diffuse thyroid disease

TABLE 5 Accuracies of US in preoperative N categorization according to suspicion of DTD on US

	US-DTD (–) (%)	US-DTD (+) (%)	<i>P</i>
Overall	359/591 (60.7)	67/131 (51.1)	0.043
N0 = N0	236/336 (70.2)	40/82 (48.8)	<0.001
N1a = N1a	53/174 (30.5)	17/36 (47.2)	0.052
N1b = N1b	70/81 (86.4)	10/13 (77)	0.372
Total	591	131	

US ultrasonography, DTD diffuse thyroid disease

Assignment of N Category

Sonographic versus pathologic N category results are summarized in Table 3. The overall accuracy of US for N categorization was 59% (426/722). The accuracies of sonographic categorization for N0, N1a, and N1b were 66% (276/418), 33.3% (70/210), and 85.1% (80/94), respectively. The overall US accuracy for prediction of N category was significantly lower in patients with DTD (51.1%, 67/131) than in patients without DTD (60.7%, 359/591) ($P = 0.043$; Tables 4, 5). US accuracy for N0 category was significantly lower in patients with DTD (48.8%, 40/82) than in patients without DTD (70.2%, 236/336; $P < 0.001$); however, accuracies for N1a and N1b were not significantly different between patients with DTD and those without DTD (0.052 and 0.372, respectively).

Follow-up Results

Among the 716 patients who received follow-up after initial treatment, 715 patients were disease-free during the follow-up period (range, 15–28 months). Of these 715 patients, 123 patients had no recurrence for more than 2 years after thyroid surgery. One patient had a recurrence in an ipsilateral lateral lymph node during follow-up (20 months after total thyroidectomy and ipsilateral lateral compartment dissection), which was detected using neck US and confirmed via fine-needle aspiration cytology. This patient, initially staged as T3N1b at histopathologic examination, underwent surgical removal of the lymph node metastasis.

DISCUSSION

Despite debate about the extent of surgery, total or near-total thyroidectomy is usually recommended for surgical treatment of PTC.^{3,5,31} Total thyroidectomy, however, can have a higher surgical complication rate, including hypoparathyroidism or recurrent laryngeal nerve injury compared with that of lobectomy. Thus, lobectomy may be an appropriate treatment for low-risk patients with small (<1 cm), unifocal, intrathyroidal carcinoma.¹³ For lymph node dissection of PTC, the lateral compartment is selectively dissected only in patients preoperatively suspected of having lateral lymph node metastasis or in patients with risk factors of lymph node recurrence.^{32,33} Therefore, accurate preoperative evaluation of tumor size, extrathyroidal extension, multifocality, and cervical lymph node metastasis is necessary to determine the optimal surgical extent for patients with PTC.

In this study, we evaluated the performance of US for the preoperative evaluations of primary tumor and lymph node metastasis in a large series of 722 patients with PTC. Bilateral malignancy was found in 20.6% of patients at pathologic examination, which is consistent with results from previous reports (19.1–23%).^{15,18} Prediction of bilaterality is important to determine the extent of surgery, because total thyroidectomy is not needed for T1N0M0 carcinoma with no pathological lesions in the contralateral lobe.³⁴ Our data showed high accuracy (88.6%) and specificity (94.2%) of preoperative US for predicting bilaterality.

The histopathologic examination in this study revealed a high proportion of papillary thyroid microcarcinoma (69.9%), but a large proportion of the tumors were confirmed as category T3 (54.9%). The majority of PTCs of category T3 were <2 cm in maximum diameter but pathologically demonstrated extrathyroidal extension. Lymph node metastasis was found in 304 patients (42.1%), and lateral lymph node metastasis was confirmed in 94 patients (13.0%). Preoperative US detected extrathyroidal extension

with an accuracy of 70.2% and lateral lymph node metastasis with an accuracy of 81.7% in the current study. The follow-up results showed that only one patient had lymph node recurrence after initial treatment, whereas 715 patients were disease-free. These findings suggest that preoperative US evaluation of the neck may lead to proper surgical treatment in patients with PTC.

Recent studies have shown low sensitivity (9.5–61%) of US for central lymph nodes and high sensitivity (64–93.9%) for lateral lymph nodes in preoperative detection of lymph node metastasis from PTC.^{15,16,18,19} Based on our data, preoperative US also showed low sensitivity for the detection of central compartment metastasis (N1a) but high sensitivity for prediction of lateral compartment metastasis (N1b). The low sensitivity of US in the detection of central compartment metastasis may be due to possible limitations of US in this area of the neck as a result of surrounding structures, such as the clavicle, sternum, and tracheal air shadow.³⁵ However, in terms of the performance of preoperative US for detection of lymph node metastasis in PTC patients, high sensitivity of US in the detection of lateral compartment metastasis may overcome this low sensitivity in the central compartment, because the type of therapeutic lymph node dissection is strongly influenced by the presence of lateral compartment metastasis on preoperative examination,^{32,33} whereas the central compartment is routinely dissected at many institutions for both therapy for and prevention of recurrence of PTC.^{36–39}

We additionally evaluated the effect of DTD on US accuracy in preoperative N categorization. This study showed lower accuracy for prediction of N category in the DTD group compared with that in the group without DTD on US, which was due to the lower accuracy for prediction of the N0 category in the DTD group (48.8%) compared with that in the group without DTD (70.2%). This finding may result from difficulties in distinguishing metastatic lymph nodes from cervical lymphadenopathy-associated DTD. A recent study showed that 23% of DTD cases diagnosed via fine-needle aspiration cytology (FNAC) were associated with single or multiple cervical lymphadenopathy, and FNAC of these lymph nodes was consistent with reactive hyperplasia.³⁰ Accordingly, careful examination of neck compartments is needed and US-guided FNAC of suspicious lymphadenopathy may be helpful for determination of N category, when a patient with PTC is suspected to have coexistent DTD based on preoperative US.

Sugitani et al. reported that patients with PTC demonstrating a large primary tumor (>4 cm) or distant metastasis were high-risk for recurrence in the lateral compartment, despite normal findings on preoperative US evaluation of the lateral compartment.⁴⁰ In addition, those authors reported primary tumor in the upper part of the thyroid lobe and extrathyroidal extension as risk factors for

lymph node recurrence. Therefore, accurate T categorization may be needed for the determination of prophylactic lateral lymph node dissection or close follow-up after surgery. Few studies, however, have been conducted to evaluate the performance of preoperative US with regard to T categorization in patients with PTC. In the present study, we found high accuracies for preoperative US in T categorization and prediction of extrathyroidal extension. Consequently, preoperative US can be useful for the prediction of lymph node metastasis as well as for the evaluation of the extent of the primary tumor.

The present study had several limitations. First, only 41 patients had primary tumors that were >2 cm in diameter, and one patient had a tumor with tracheal invasion (T4a). The high proportion of early thyroid cancer may be due to screening US for thyroid or carotid arteries.^{41,42} Thus, the accuracy of US for preoperative evaluation of PTC with large size or T4 category could not be determined in this study. Second, we analyzed lymph node metastasis by using a compartment-oriented approach, because each involved compartment is usually dissected as a single unit. Therefore, we could not directly correlate radiologic findings of suspected lymph node metastasis with findings at pathological evaluation. The findings of this study should be confirmed with other analytic methods (e.g., node by node or level by level). Third, lateral compartment dissections were performed selectively only when necessary. This may have decreased the reliability in our determination of specificity for detection of lateral lymph node metastasis. However, we believe that this limitation is unavoidable because routine prophylactic lateral compartment dissection is not advocated in the treatment of PTC.^{32,33} Finally, the postoperative follow-up period of this study was not long (median, 21 months), and cervical recurrence was rare. Recently, Marshall et al. reported follow-up (median, 41 months) results of patients with PTC in whom preoperative US was used to stage accurately.⁴³ They found less cervical recurrences in recent years during which there was increased US specialization and concluded that preoperative US followed by compartment-oriented surgery may decrease recurrence rates in PTC patients. Nonetheless, long-term outcome of PTC patients who underwent preoperative US and primary surgery should be further evaluated to determine the effect of preoperative US in the treatment of PTC.

In conclusion, high-resolution US is a good technique for preoperative staging of PTC and is helpful for accurate prediction of extrathyroidal tumor extension and lateral lymph node metastasis. The presence of DTD on US can affect the staging of lymph node metastasis in PTC patients.

DISCLOSURE No competing financial interests exist.

REFERENCES

- Noguchi S, Noguchi A, Murakami N. Papillary carcinoma of the thyroid. I. Developing pattern of metastasis. *Cancer*. 1970;26:1053–60.
- Samaan NA, Maheshwari YK, Nader S, et al. Impact of therapy for differentiated carcinoma of the thyroid: an analysis of 706 cases. *J Clin Endocrinol Metab*. 1983;56:1131–8.
- Sherman SI. Thyroid carcinoma. *Lancet*. 2003;361:501–11.
- Tubiana M, Schlumberger M, Rougier P, et al. Long-term results and prognostic factors in patients with differentiated thyroid carcinoma. *Cancer*. 1985;55:794–804.
- Cady B, Rossi R. An expanded view of risk-group definition in differentiated thyroid carcinoma. *Surgery*. 1988;104:947–53.
- Mazzaferri EL, Kloos RT. Clinical review 128: current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab*. 2001;86:1447–63.
- Yamashita H, Noguchi S, Murakami N, Toda M, Uchino S, Watanabe S, Kawamoto H. Extracapsular invasion of lymph node metastasis. A good indicator of disease recurrence and poor prognosis in patients with thyroid microcarcinoma. *Cancer*. 1999;86:842–9.
- Ito Y, Higashiyama T, Takamura Y, et al. Risk factors for recurrence to the lymph node in papillary thyroid carcinoma patients without preoperatively detectable lateral node metastasis: validity of prophylactic modified radical neck dissection. *World J Surg*. 2007;31:2085–91.
- Shaha AR. TNM classification of thyroid carcinoma. *World J Surg*. 2007;31:879–87.
- Antonelli A, Miccoli P, Ferdeghini M, et al. Role of neck ultrasonography in the follow-up of patients operated on for thyroid cancer. *Thyroid*. 1995;5:25–8.
- Gonzalez HE, Cruz F, O'Brien A, et al. Impact of preoperative ultrasonographic staging of the neck in papillary thyroid carcinoma. *Arch Otolaryngol Head Neck Surg*. 2007;133:1258–62.
- Ito Y, Tomoda C, Urano T, et al. Preoperative ultrasonographic examination for lymph node metastasis: usefulness when designing lymph node dissection for papillary microcarcinoma of the thyroid. *World J Surg*. 2004;28:498–501.
- Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167–214.
- Ahn JE, Lee JH, Yi JS, et al. Diagnostic accuracy of CT and ultrasonography for evaluating metastatic cervical lymph nodes in patients with thyroid cancer. *World J Surg*. 2008;32:1552–8.
- Choi JS, Kim J, Kwak JY, Kim MJ, Chang HS, Kim EK. Preoperative staging of papillary thyroid carcinoma: comparison of ultrasound imaging and CT. *AJR Am J Roentgenol*. 2009;193:871–8.
- Kim E, Park JS, Son KR, Kim JH, Jeon SJ, Na DG. Preoperative diagnosis of cervical metastatic lymph nodes in papillary thyroid carcinoma: comparison of ultrasound, computed tomography, and combined ultrasound with computed tomography. *Thyroid*. 2008;18:411–8.
- Kouvaraki MA, Shapiro SE, Fornage BD, et al. Role of preoperative ultrasonography in the surgical management of patients with thyroid cancer. *Surgery*. 2003;134:946–54; discussion 54–5.
- Park JS, Son KR, Na DG, Kim E, Kim S. Performance of preoperative sonographic staging of papillary thyroid carcinoma based on the sixth edition of the AJCC/UICC TNM classification system. *AJR Am J Roentgenol*. 2009;192:66–72.
- Roh JL, Park JY, Kim JM, Song CJ. Use of preoperative ultrasonography as guidance for neck dissection in patients with papillary thyroid carcinoma. *J Surg Oncol*. 2009;99:28–31.
- Stulak JM, Grant CS, Farley DR, et al. Value of preoperative ultrasonography in the surgical management of initial and reoperative papillary thyroid cancer. *Arch Surg*. 2006;141:489–94; discussion 94–6.
- Greene FL, Page DL, Fleming ID, et al. *AJCC cancer staging manual*. 6th ed. New York: Springer-Verlag; 2002.
- Kwak JY, Kim EK, Youk JH, Kim MJ, Son EJ, Choi SH, Oh KK. Extrathyroid extension of well-differentiated papillary thyroid microcarcinoma on US. *Thyroid*. 2008;18:609–14.
- Na DG, Lim HK, Byun HS, Kim HD, Ko YH, Baek JH. Differential diagnosis of cervical lymphadenopathy: usefulness of color Doppler sonography. *Am J Roentgenol*. 1997;168:1311–6.
- Rosario PW, de Faria S, Bicalho L, et al. Ultrasonographic differentiation between metastatic and benign lymph nodes in patients with papillary thyroid carcinoma. *J Ultrasound Med*. 2005;24:1385–9.
- Ying M, Ahuja A, Metreweli C. Diagnostic accuracy of sonographic criteria for evaluation of cervical lymphadenopathy. *J Ultrasound Med*. 1998;17:437–45.
- Kim TY, Hong SJ, Kim JM, et al. Prognostic parameters for recurrence of papillary thyroid microcarcinoma. *BMC Cancer*. 2008;8:296.
- Kim DW, Eun CK, In HS, Kim MH, Jung SJ, Bae SK. Sonographic differentiation of asymptomatic diffuse thyroid disease from normal thyroid: a prospective study. *AJNR Am J Neuroradiol*. 2010;31:1956–60.
- Tessler FN, Tublin ME. Thyroid sonography: current applications and future directions. *AJR Am J Roentgenol*. 1999;173:437–43.
- Yeh HC, Futterweit W, Gilbert P. Micronodulation: ultrasonographic sign of Hashimoto thyroiditis. *J Ultrasound Med*. 1996;15:813–9.
- Paksoy N, Yazal K. Cervical lymphadenopathy associated with Hashimoto's thyroiditis: an analysis of 22 cases by fine needle aspiration cytology. *Acta Cytol*. 2009;53:491–6.
- Sosa JA, Udelsman R. Papillary thyroid cancer. *Surg Oncol Clin N Am*. 2006;15:585–601.
- Ito Y, Miyauchi A. Lateral lymph node dissection guided by preoperative and intraoperative findings in differentiated thyroid carcinoma. *World J Surg*. 2008;32:729–39.
- Newman JG, Chalian AA, Shaha AR. Surgical approaches in thyroid cancer: what the radiologist needs to know. *Neuroimaging Clin N Am*. 2008;18:491–504, viii.
- Ito Y, Masuoka H, Fukushima M, et al. Excellent prognosis of patients with solitary T1N0M0 papillary thyroid carcinoma who underwent thyroidectomy and elective lymph node dissection without radioiodine therapy. *World J Surg*. 2010;34:1285–90.
- Loevner LA, Kaplan SL, Cunnane ME, Moonis G. Cross-sectional imaging of the thyroid gland. *Neuroimaging Clin N Am*. 2008;18:445–61, vii.
- Ito Y, Tomoda C, Urano T, et al. Clinical significance of metastasis to the central compartment from papillary microcarcinoma of the thyroid. *World J Surg*. 2006;30:91–9.
- Martensson H, Terins J. Recurrent laryngeal nerve palsy in thyroid gland surgery related to operations and nerves at risk. *Arch Surg*. 1985;120:475–7.
- Roher HD, Simon D, Goretzki PE. [Guidelines in oncologic surgery—malignant thyroid tumors]. *Langenbecks Arch Chir Suppl Kongressbd*. 1997;114:142–5.
- Scheumann GF, Seeliger H, Musholt TJ, et al. Completion thyroidectomy in 131 patients with differentiated thyroid carcinoma. *Eur J Surg*. 1996;162:677–84.
- Sugitani I, Fujimoto Y, Yamada K, Yamamoto N. Prospective outcomes of selective lymph node dissection for papillary thyroid carcinoma based on preoperative ultrasonography. *World J Surg*. 2008;32:2494–502.

41. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA*. 2006;295:2164-7.
42. Trimboli P, Ulisse S, Graziano FM, et al. Trend in thyroid carcinoma size, age at diagnosis, and histology in a retrospective study of 500 cases diagnosed over 20 years. *Thyroid*. 2006;16:1151-5.
43. Marshall CL, Lee JE, Xing Y, Perrier ND, Edeiken BS, Evans DB, Grubbs EG. Routine pre-operative ultrasonography for papillary thyroid cancer: effects on cervical recurrence. *Surgery*. 2009;146:1063-72.