



Ultrasonography Diagnosis and Imaging-Based Management of Thyroid Nodules: Revised Korean Society of Thyroid Radiology Consensus Statement and Recommendations

Jung Hee Shin, MD¹, Jung Hwan Baek, MD², Jin Chung, MD³, Eun Ju Ha, MD⁴, Ji-hoon Kim, MD⁵, Young Hen Lee, MD⁶, Hyun Kyung Lim, MD⁷, Won-Jin Moon, MD⁸, Dong Gyu Na, MD, PhD⁹, Jeong Seon Park, MD¹⁰, Yoon Jung Choi, MD¹¹, Soo Yeon Hahn, MD¹, Se Jeong Jeon, MD¹², So Lyung Jung, MD¹³, Dong Wook Kim, MD¹⁴, Eun-Kyung Kim, MD¹⁵, Jin Young Kwak, MD¹⁵, Chang Yoon Lee, MD¹⁶, Hui Joong Lee, MD¹⁷, Jeong Hyun Lee, MD², Joon Hyung Lee, MD¹⁸, Kwang Hui Lee, MD¹⁹, Sun-Won Park, MD²⁰, Jin Young Sung, MD²¹;
 Korean Society of Thyroid Radiology (KSThR) and Korean Society of Radiology

¹Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 06351, Korea; ²Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul 05505, Korea; ³Department of Radiology, Ewha Womans University School of Medicine, Seoul 07985, Korea; ⁴Department of Radiology, Ajou University School of Medicine, Suwon 16499, Korea; ⁵Department of Radiology, Seoul National University College of Medicine, Seoul 03080, Korea; ⁶Department of Radiology, Ansan Hospital, Korea University College of Medicine, Ansan 15355, Korea; ⁷Department of Radiology, Soonchunhyang University Seoul Hospital, Seoul 04401, Korea; ⁸Department of Radiology, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul 05030, Korea; ⁹Department of Radiology, Human Medical Imaging and Intervention Center, Seoul 06524, Korea; ¹⁰Department of Radiology, Hanyang University College of Medicine, Hanyang University Hospital, Seoul 04763, Korea; ¹¹Department of Radiology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul 03181, Korea; ¹²Department of Radiology, Wonkwang University Hospital, Iksan 54538, Korea; ¹³Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul 06591, Korea; ¹⁴Department of Radiology, Busan Paik Hospital, Inje University College of Medicine, Busan 47392, Korea; ¹⁵Department of Radiology, Severance Hospital, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul 03722, Korea; ¹⁶Department of Radiology, Research Institute and Hospital, National Cancer Center, Goyang 10408, Korea; ¹⁷Department of Radiology, Kyungpook National University Hospital, Daegu 41944, Korea; ¹⁸Department of Radiology, Dong-A University Medical Center, Busan 49201, Korea; ¹⁹Department of Radiology, Newwoori Namsan Hospital, Busan 46224, Korea; ²⁰Department of Radiology, SMG-SNU Boramae Medical Center, Seoul National University College of Medicine, Seoul 07061, Korea; ²¹Department of Radiology and Thyroid Center, Daerim St. Mary's Hospital, Seoul 07442, Korea

The rate of detection of thyroid nodules and carcinomas has increased with the widespread use of ultrasonography (US), which is the mainstay for the detection and risk stratification of thyroid nodules as well as for providing guidance for their biopsy and nonsurgical treatment. The Korean Society of Thyroid Radiology (KSThR) published their first recommendations for the US-based diagnosis and management of thyroid nodules in 2011. These recommendations have been used as the standard guidelines for the past several years in Korea. Lately, the application of US has been further emphasized for the personalized management of patients with thyroid nodules. The Task Force on Thyroid Nodules of the KSThR has revised the recommendations for the ultrasound diagnosis and imaging-based management of thyroid nodules. The review and recommendations in this report have been based on a comprehensive analysis of the current literature and the consensus of experts.

Index terms: *Thyroid nodule; Thyroid neoplasm; Lymph nodes; Ultrasonography; Multidetector computed tomography; Ablation techniques*

Received January 15, 2016; accepted after revision January 22, 2016.

These guidelines were funded by the Korean Society of Radiology without any support from commercial sources.

Corresponding author: Dong Gyu Na, MD, PhD, Department of Radiology, Human Medical Imaging and Intervention Center, 621 Gangnam-daero, Seocho-gu, Seoul 06524, Korea.

• Tel: (822) 512-6695 • Fax: (822) 512-6646 • E-mail: nndgna@gmail.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

The management of thyroid nodules has become a controversial issue with the increasing incidence of thyroid carcinomas. The prevalence of thyroid nodules is 2–6% with palpation, 19–68% with ultrasonography (US), and 8–65% in autopsy specimens (1-3). The rate of malignancy was approximately 5–15% among the nodules detected by palpation or US (3-5). The rate of malignancy was 8–12% of the nonpalpable nodules evaluated by fine-needle aspiration (FNA) (4, 5), and 1.6% among the patients with thyroid nodules in a population-based study (6). The rate of detection of thyroid carcinoma has increased lately with the widespread use of US for its diagnosis (7). Micropapillary thyroid carcinoma is the leading cause for the recent increase in incidence of thyroid cancer in South Korea and the United States (8, 9). Lately, the role of US has been further emphasized for the personalized management of patients with thyroid nodules. First, the selection of patients for FNA of a thyroid nodule is primarily determined by the assessment of the US findings in most of the patients with asymptomatic thyroid nodules. Second, the management procedure of a thyroid nodule is mainly determined by the cancer probability and the prognostic risk factors estimated by US. Third, the US assessment is crucial for the preoperative evaluation as well as the postoperative surveillance in thyroid cancer. Fourth, the image-guided ablation methods such as chemical or thermal ablations are being increasingly used in the treatment of benign thyroid nodules (10).

The Korean Society of Thyroid Radiology (KSThR) had published consensus recommendations for the US-based management of thyroid nodules in 2011 (11). Recent many advances in the diagnosis and nonsurgical therapy of thyroid nodules have necessitated the revision of the original recommendations. The KSThR therefore organized a taskforce for the revision of the recommendations from September 2014 (Supplementary Tables 1-3 in the online-only Data Supplement). The major update of the revised KSThR recommendations includes the revised US malignancy risk stratification system for thyroid nodules, i.e., the Korean Thyroid Imaging Reporting and Data System (K-TIRADS), risk stratification of cervical lymph nodes (LN) on the basis of the US and computed tomography (CT) features, and recommendations for the image-guided ablation of benign thyroid nodules. A PubMed MEDLINE search was performed for retrieving publications from 1990

to October 2015 with the following keywords: thyroid nodule, thyroid carcinoma, cervical LN, US, CT, and ablation. Since clinical controversies over the issues exist in many of the areas, the recommendations regarding some of the issues are based on expert opinion. This limitation needs to be overcome in the near future when new evidences are accumulated. The goal of these recommendations is to provide the best scientific evidence available and a consensus expert-opinion regarding the US-based diagnosis and management of thyroid nodules in clinical practice.

Terminology and US Features in Thyroid Nodule

The US terminology of thyroid nodules should have feasibility for clinical application, utility for malignancy risk stratification, and low interobserver variability. The recommended terminology and definition of the US features are summarized in Table 1.

The Nodule Size

The size of a thyroid nodule should be measured in all three dimensions; however, only the maximal diameter of the nodule may be documented in small nodules (≤ 5 mm). The correlation between the nodule size and the risk for malignancy remains controversial. Although a recent systemic review suggested that the larger nodules present a higher pretest probability of malignancy (12), whether the malignancy risk is higher in the larger nodules and whether the nodule size could be a predictor for malignancy are still controversial (13-15). The growth of a nodule is not a reliable predictor of malignancy since many benign nodules can slowly grow over time (16-19). However, the rapid growth of a solid nodule can be a clinical manifestation of a high grade malignancy such as anaplastic thyroid carcinoma or lymphoma. The accurate estimation of the nodule growth is essential for deciding the management strategy for the follow-up of suspected or proven papillary thyroid microcarcinomas. It is also required for the follow-up management of the nodules with an indeterminate or benign cytology diagnosis. For the estimation of a significant size change of a nodule, we recommend defining a significant size change as the nodule growth with a 20% increase in at least two nodule dimensions and a minimal increase of 2 mm, or more than a 50% change in volume (20).

Internal Content

The internal content of a nodule is categorized in terms

of the ratio of the cystic portion to the solid portion in the nodule: solid (no obvious cystic content), predominantly solid ($\leq 50\%$ of the cystic portion), predominantly cystic ($> 50\%$ of the cystic portion), and cystic (no obvious solid content) (Supplementary Fig. 1 in the online-only Data Supplement). We recommend that the nodules with minimal cystic changes ($< 10\%$) be categorized as predominantly solid nodules because their malignancy risk seems to be

similar to that of the partially cystic (predominantly solid or predominantly cystic) nodules (21). Most of the malignant thyroid tumors are solid (81.6–93%) (22–25), and the malignancy risk of the solid nodules is higher (24.1–34.7%) than that of the partially cystic nodules (3.3–7.1%) (22, 24–26).

We suggest that the spongiform appearance of a nodule be defined as the aggregation of multiple microcystic

Table 1. Recommended US Terminology and Definition for Thyroid Nodules

US Characteristics	Category	Definition	Synonym
Internal content (composition)	Solid	No obvious cystic component	
	Predominantly solid	Cystic portion $\leq 50\%$	
	Predominantly cystic	Cystic portion $> 50\%$	
	Cystic	No solid portion	Pure cyst
Echogenicity	Marked hypoechogenicity	Hypoechoic relative to adjacent anterior neck muscle	
	Mild hypoechogenicity	Hypoechoic relative to thyroid parenchyma	
	Isoechogenicity	Same echogenicity as that of thyroid parenchyma	
	Hyperechogenicity	Hyperechoic relative to thyroid parenchyma	
Shape	Round to oval	Round or oval regardless of orientation	
	Irregular	Neither round nor oval	
Orientation	Parallel	Anteroposterior diameter shorter or equal to transverse or longitudinal diameter	
	Nonparallel	Anteroposterior diameter longer than transverse or longitudinal diameter on transverse or longitudinal image	Taller-than-wide shape
Margin	Smooth	Obviously discernible smooth edge	Regular, circumscribed
	Spiculated/microlobulated	Obviously discernible, but non-smooth edge showing spiculation, microlobulation, or jagged appearance	Irregular, infiltrative, non-smooth
	Ill-defined	Poorly demarcated margin which cannot be obviously differentiated from adjacent thyroid tissue	Indistinct
Calcification	Microcalcification	Echogenic foci of 1 mm or less with or without posterior acoustic shadowing within solid portion	
	Macrocalcification	Echogenic foci larger than 1 mm with posterior acoustic shadowing	Coarse calcification
	Rim calcification	Peripheral curvilinear echogenic rim (complete or incomplete)	Egg shell calcification
Halo	Present or absent	Thin or thick hypoechoic rim surrounding nodule	
Spongiform	Present or absent	Isoechoic nodule with microcystic change greater than 50% of nodule	Honeycomb
Colloid (comet-tail artifact)	Present or absent	Echogenic foci with reverberation artifacts within cystic component	
Vascularity	Type 1 (none)	Absence of intranodular or perinodular vascularity	
	Type 2 (perinodular vascularity)	Presence of circumferential vascularity at margin of nodule	
	Type 3 (mild intranodular vascularity)	Intranodular vascularity with or without perinodular vascularity (lesser than 50%)	
	Type 4 (marked intranodular vascularity)	Marked intranodular vascularity with or without perinodular vascularity (greater than 50%)	

US = ultrasonography

components in more than 50% of the isoechoic partially cystic nodule (Supplementary Fig. 2 in the online-only Data Supplement). An isoechoic spongiform nodule can be regarded as a benign nodule with a malignancy risk less than 1% (27-30). Spongiform appearance is rarely found in papillary carcinomas (30, 31), and the presence of hypoechogenicity or microcalcification may increase the malignancy risk in the nodules with sponge-like areas (30).

Echogenicity

We suggest that the nodule echogenicity be categorized on the basis of the relative echogenicity compared to the reference structures (thyroid parenchyma and anterior neck muscles). Nodule echogenicity is categorized as being markedly hypoechoic (hypoechoic relative to the anterior neck muscle), mildly hypoechoic (hypoechoic relative to the thyroid parenchyma, but not hypoechoic relative to the anterior neck muscles), isoechoic (same echogenicity as that of the thyroid parenchyma), or hyperechoic (more echogenic relative to the thyroid parenchyma) (Supplementary Fig. 3 in the online-only Data Supplement). When the echogenicity of a solid component is heterogeneous or mixed, the echogenicity of a nodule is defined by the predominant echogenicity. When the thyroid parenchyma shows abnormal hypoechogenicity in the case of thyroiditis, the nodule echogenicity should still be described relative to the same reference structures and the abnormal thyroid echogenicity should be described. A majority of the malignant thyroid tumors are hypoechoic (mild or marked) (62.5–87.2%), and the malignancy risk of the hypoechoic nodules is higher (20.6–70.4%) than that of the isoechoic (8.6–13.4%) or hyperechoic nodules (0–18.2%) (22, 24, 25, 27, 32). Although the markedly hypoechoic nodules are highly predictive of malignancy (27, 33), the malignancy risk of the markedly hypoechoic solid nodules without the presence of any other suspicious US features was only intermediate, and not as high as that of the mildly or markedly hypoechoic solid nodules with other suspicious US features present (25).

Nodule Shape and Orientation

We suggest that the shape of a nodule be categorized as round to ovoid and irregular. The orientation of the direction of growth of a nodule is categorized as parallel (when the anteroposterior diameter of a nodule is equal to or less than its transverse or longitudinal diameter) or non-parallel (when the anteroposterior diameter of a nodule

is longer than its transverse or longitudinal diameter) on a transverse or longitudinal plane (Supplementary Fig. 4 in the online-only Data Supplement). The orientation is categorized according to the relationship of the long axis of a nodule to the long axis of thyroid gland on imaging plane regardless of the nodule shape (oval to round or irregular). The nonparallel orientation presents the same US feature as the taller-than-wide shape defined previously (11, 33). This finding indicates that the malignant nodules grow across the normal tissue plane in a centrifugal manner, while benign nodules do the same in a parallel fashion (33-35). Although the nodules with round to ovoid shape or parallel orientation are more frequently found in benign nodules, the features are not specific for benign nodules, and are commonly found in follicular carcinomas or the follicular variant of papillary thyroid carcinoma (PTC) (36-38). A nodule with an irregular shape is not specific for benign or malignant nodules (27, 39, 40). The nonparallel orientation (taller-than-wide) feature is less sensitive, but highly specific for malignancy, with a specificity of 88.4–98.7% and a positive predictive value of 71.2–77.5% (24, 25, 27).

Nodule Margin

The US terminology for the nodule margin is controversial (11, 27, 41-44), and many different terminologies have been used to describe the margins of the malignant tumors. We suggest the margin of a nodule be categorized as smooth, spiculated/microlobulated, or ill-defined (Supplementary Fig. 5 in the online-only Data Supplement). An obviously discernible margin is categorized as either a smooth or a spiculated/microlobulated margin. When the margin of any portion of a nodule is obviously spiculated/microlobulated, it is categorized as a spiculated/microlobulated margin. A smooth margin is mostly found in the hypoechoic nodules, isoechoic nodules with hypoechoic halo, and nodules of heterogeneous composition. A spiculated or microlobulated margin is mostly found in the infiltrating malignant tumors, which are mostly found in the hypoechoic nodules and rarely in the isoechoic nodules with a partly hypoechoic portion or hypoechoic rim (Supplementary Fig. 6 in the online-only Data Supplement). While a smooth margin is not specific for benign or malignant nodules, a spiculated/microlobulated margin is highly suggestive of a malignancy, with a specificity of 90.8–98.4% and a positive predictive value of 79.8–86.7% (25, 27, 39). Meanwhile, the margin of a nodule might be indistinct in the isoechoic nodules when the periphery of the nodule has similar echogenicity and

composition as the surrounding normal gland, as is typically found in the isoechoic hyperplastic nodules without encapsulation (40). An ill-defined margin is also found in some hypoechoic nodules, including focal thyroiditis (45, 46) and infiltrative malignant tumors.

A nodule sometimes shows an accompanying hypoechoic thin or thick halo. Histologically, the halo sign or hypoechoic rim surrounding a nodule is comprised of the nodule capsule or pseudocapsule, compressed thyroid tissue, and caused by chronic inflammatory changes (47-50). Although the halo sign is more frequently found in the benign nodules, it is not highly specific for the benignity (40, 51) and frequently found in follicular neoplasm (36, 52), and the absence of the halo is less specific for malignancy (53, 54).

Calcification, Echogenic Foci

The calcifications are categorized as microcalcifications (punctuate echogenic foci of 1 mm or less either with or without posterior shadowing; brighter echo than the surrounding thyroid tissue), macrocalcifications (echogenic foci greater than 1 mm in size with posterior shadowing), and rim calcifications (peripheral curvilinear or eggshell calcification at the nodule margin) (Supplementary Fig. 7 in the online-only Data Supplement). The punctuate echogenic foci found within the solid portion may be either true microcalcification or colloid material. Pathologically, a microcalcification is a psammoma body comprised of 10–100 μm round, laminar, crystalline, calcified deposits, which is very specific for thyroid carcinoma and, especially, for PTC. The echogenic foci are sometimes accompanied by reverberation artifacts within the cystic portion—the so-called comet-tail artifacts; these artifacts are caused by the colloid materials, and are almost always suggestive of benignity (55-57). We recommend that the US features of the comet-tail artifacts be used for diagnosis only when they are found within the cystic portion of a nodule, because the comet-tail artifacts within the solid portion are not reliably differentiated from the microcalcifications, and are not specific for a benign nodule (57). Large nodular or linear echogenic foci without posterior shadowing at the septa or the wall of the cystic nodules are mostly found in benign cystic nodules, and should not be considered as calcifications (56).

Microcalcification has been reported to be highly suggestive of malignancy, with a reported specificity of 84–97% and a positive predictive value of 33–78% (4,

22, 24, 25, 27, 58). However, it should be noted that the malignancy risk of the microcalcifications is high in the solid hypoechoic nodules, but intermediate in the partially cystic or isohyperechoic nodules (25). Although the presence of macrocalcifications might increase the malignancy risk (27, 40), they are not specific for malignancies and present a variable malignancy risk (23.9–64.8%) (25, 27, 59). Although the malignancy risk of the isolated macrocalcifications composed of entirely calcified nodules without any solid portions may be low (0–16%) (59, 60), a PTC with an aggressive behavior may rarely manifest as an isolated macrocalcification (60). An isolated macrocalcification may be considered as an intermediate suspicion nodule. However, there is not enough evidence. Although the rim or eggshell calcifications are not significantly associated with malignancy (22, 27, 40), the presence of a hypoechoic halo or a solid portion accompanying the disruption of the eggshell or rim calcifications may increase the malignancy risk (61, 62).

Nodule Vascularity

Color Doppler or power Doppler US can be used for the evaluation of the vascularity of thyroid nodules. The vascularity patterns of thyroid nodules can be categorized as four types according to the patterns of the nodular vascularity: type 1, absence of nodule vascularity; type 2, perinodular vascularity only (presence of circumferential vascularity at the margin of a nodule); type 3, mild intranodular vascularity with or without perinodular vascularity (vascularity lesser than 50%); type 4, marked intranodular vascularity with or without perinodular vascularity (vascularity greater than 50%). The presence of intranodular vascularity is variably observed in 16.7–91.7% of the malignant tumors (4, 51, 63-67) and 30.7–65.3% of the benign nodules (63-67). Although the presence of intranodular vascularity might increase the risk of malignancy (4, 64), there are no consistent results regarding the association of an intranodular vascularity pattern with the risk of malignancy (63, 66-68). Recent studies reported that the presence of intranodular vascularity was not predictive of the malignancy (25, 67), and that it could not provide an added value over that of the gray-scale US alone for the prediction of the malignancies of the overall thyroid nodules (67). Additionally, higher resistive index (RI) or pulsatility index Doppler index values might be predictive of malignancy. However, the cutoff value of each of the indices and their complementary role in the diagnosis of malignancies has

not yet been established (68). Although the presence of a marked intranodular vascularity pattern might be predictive of malignancy in the follicular lesions or follicular neoplasm (69-73), the hypothesis remains controversial (74).

US Elastography

Ultrasonographic elastography is a new technique for the measurement of the elasticity of the tissues. The tissue of the carcinoma is usually harder and firmer than that of the normal thyroid parenchyma or a benign nodule. There are two representative elastography techniques to quantify the tissue strain. The first is "strain elastography", which evaluates the degree of tissue deformation induced by compression or acoustic forces. The second method of elastography is the "shear wave" speed measurement, where the shear waves propagate in a direction orthogonal to the direction of the tissue displacement. The propagation speed is generally higher in the malignant thyroid nodules than in the benign ones (75, 76). Although several studies (77, 78) have reported that US elastography performed the same or better than the gray-scale US, the clinical efficiency or the complementary role of elastography in the diagnosis of thyroid nodules is still controversial (79). Recently, several studies (80-84) reported the potential role of US elastography in the diagnosis of thyroid nodules with indeterminate or non-diagnostic cytology as well as those with indeterminate US features. Further investigations are required for establishing the supplementary role of US elastography in the risk stratification of thyroid nodules.

US-Risk Stratification and the Korean Thyroid Imaging Reporting and Data System

The US stratification of the malignancy risk has an essential role in deciding for or against FNA of thyroid nodules. Recent meta-analysis studies (53, 54, 85) have consistently demonstrated that the gray-scale US features of microcalcification, spiculated/microlobulated margins, and nonparallel orientation (taller-than-wide) are strongly predictive of malignancy, with a high specificity (greater than 80%) and a high positive likelihood ratio (greater than 3); the US features of the solid internal content and hypoechogenicity have also been shown to be predictive of malignancy, with an intermediate specificity and a modest likelihood ratio for the thyroid malignancies. Although these US features are independent predictors of malignancy, any single US predictor does not have both high sensitivity

and high specificity for the detection of malignancies (24, 25, 53, 54, 85). Since the malignancy risk estimated by US is not determined by a single US predictor, it should be assessed by a combination of the US features. The US-malignancy risk stratification system of the thyroid nodules, TIRADS, was initially proposed by Horvath et al. (86). It has been investigated for its ability for the quantitative estimation of the malignancy risk using scoring systems based on the categorization of the US patterns (25, 86, 87) or based on the calculation of the number of suspicious US features and US risk scores (24, 39, 88). Previous reports suggest that the malignancy risk or the US features predicting the malignancy might differ according to the solidity (26, 89-91) and echogenicity (40) of the thyroid nodules. Most thyroid society guidelines (20, 92-95) suggest risk stratification systems based on the categorization of the US patterns for thyroid nodules. However, there has been no standardized malignancy risk stratification system for thyroid nodules.

A recent retrospective multicenter study (25) demonstrated that the predictability of the suspicious US features demonstrated a heterogeneous dependency on the solidity and echogenicity of the thyroid nodules. The presence of any suspicious US features in the solid hypoechoic nodules revealed a high malignancy risk (79%), and that in the partially cystic or isohyperechoic nodules revealed an intermediate risk (25%). We recommend a simplified clinically feasible K-TIRADS for the malignancy risk stratification of thyroid nodules (Fig. 1) (25). Thyroid nodules are categorized as high suspicion, intermediate suspicion, low suspicion, and benign nodules based on their malignancy risks stratified by the US patterns composed of the integrated solidity, echogenicity, and suspicious US features (Table 2, Figs. 2-5). Although the color Doppler US features of the intranodular vascularity and the elastography findings are potentially useful in the differentiation of the benign and malignant nodules, further studies are required to establish their complementary role in the risk stratification of thyroid nodules.

US Assessment of Extrathyroidal Tumor Extension

Extrathyroidal extension (ETE) of the primary tumor occurs in 11.5–30% of the differentiated thyroid carcinomas, and it increases the risk of recurrence and mortality (96, 97). The ETE can be minimal (pT3) or extensive (massive; pT4a), and the two types of ETE vary in their recurrence rates and

disease-free survival odds (97, 98). The clinical outcome is worse in the patients with a gross ETE than in those with a microscopic local invasion (99). Microscopic ETE is considered to be an intermediate risk factor, and gross ETE, a high risk factor for differentiated thyroid cancers; this

difference can affect the treatment decision of surgery and RI therapy (20).

The US assessment of the ETE shows a wide range of diagnostic sensitivities (15.0–88.9%), specificities (27.2–97.6%), and accuracy values (56.0–84.8%) for

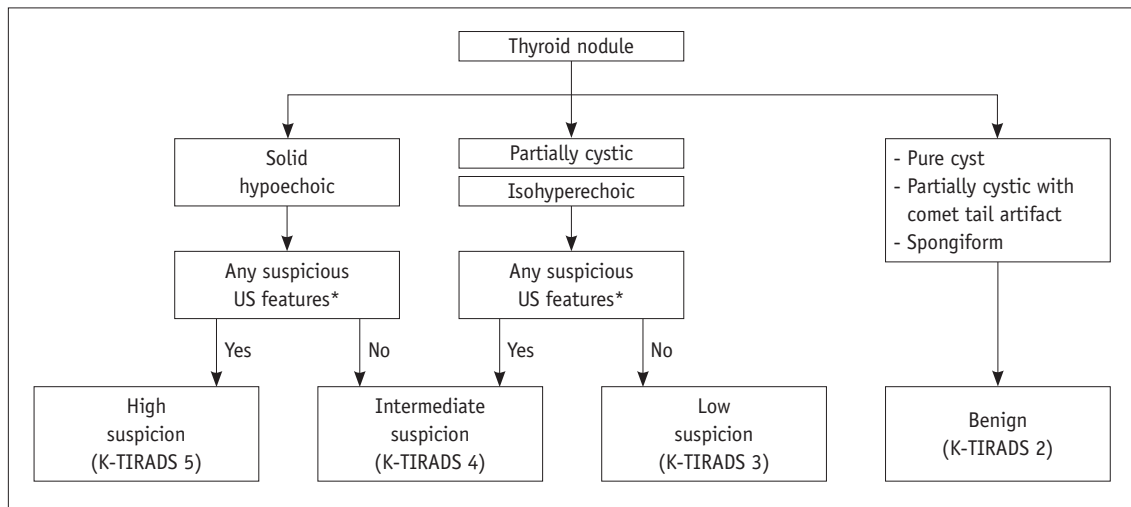


Fig. 1. Algorithm of K-TIRADS for malignancy risk stratification based on solidity and echogenicity of thyroid nodules. Modified from Na et al. *Thyroid* 2016;26:562-572 (25). *Microcalcification, nonparallel orientation, spiculated/microlobulated margin. K-TIRADS = Korean Thyroid Imaging Reporting and Data System, US = ultrasonography

Table 2. Malignancy Risk Stratification According to Korean Thyroid Imaging Reporting and Data System (K-TIRADS) and FNA Indications

Category	US Feature	Malignancy Risk (%)	Calculated Malignancy Risk (%), Overall (LV, HV)	Calculated Sensitivity for Malignancy (%), Overall (LV, HV)	FNA [§]
5 High suspicion	Solid hypoechoic nodule with any of 3 suspicious US features*	> 60	79.3 (60.9, 84.9)	51.3 (35.9, 56.7)	≥ 1 cm (> 0.5 cm, selective)
4 Intermediate suspicion	1) Solid hypoechoic nodule without any of 3 suspicious US features* or 2) Partially cystic or isohyperechoic nodule with any of 3 suspicious US features*	15–50	25.4 (15, 33.6)	29.5 (29.9, 29.4)	≥ 1 cm
3 Low suspicion	Partially cystic or isohyperechoic nodule without any of 3 suspicious US features*	3–15	7.8 (6, 10.3) [†]	19.2 (34.2, 13.9)	≥ 1.5 cm
2 Benign [‡]	1) Spongiform 2) Partially cystic nodule with comet tail artifact 3) Pure cyst	< 3 < 1	0 0	0 0	≥ 2 cm NA
1 No nodule	-	-	-	-	NA

LV and HV indicate low and high cancer volume data, respectively. Solid hypoechoic nodules include solid nodules with marked or mild hypoechoogenicity. *Microcalcification, nonparallel orientation (taller-than-wide), spiculated/microlobulated margin, [†]Malignancy risk calculated from nodules excluding spongiform or partially cystic nodules with comet tail artifacts, [‡]K-TIRADS 2 (benign category) includes partially cystic nodules with spongiform appearance or comet tail artifacts which do not have any suspicious US feature, [§]FNA is indicated regardless of size and US feature of nodule in presence of poor prognostic factors including suspected lymph node metastasis by US or clinical evaluation, suspected extrathyroidal tumor extension, patients with diagnosed distant metastasis from thyroid cancer. Modified from Na et al. *Thyroid* 2016;26:562-572 (25). FNA = fine-needle aspiration, NA = not applicable for FNA, US = ultrasonography

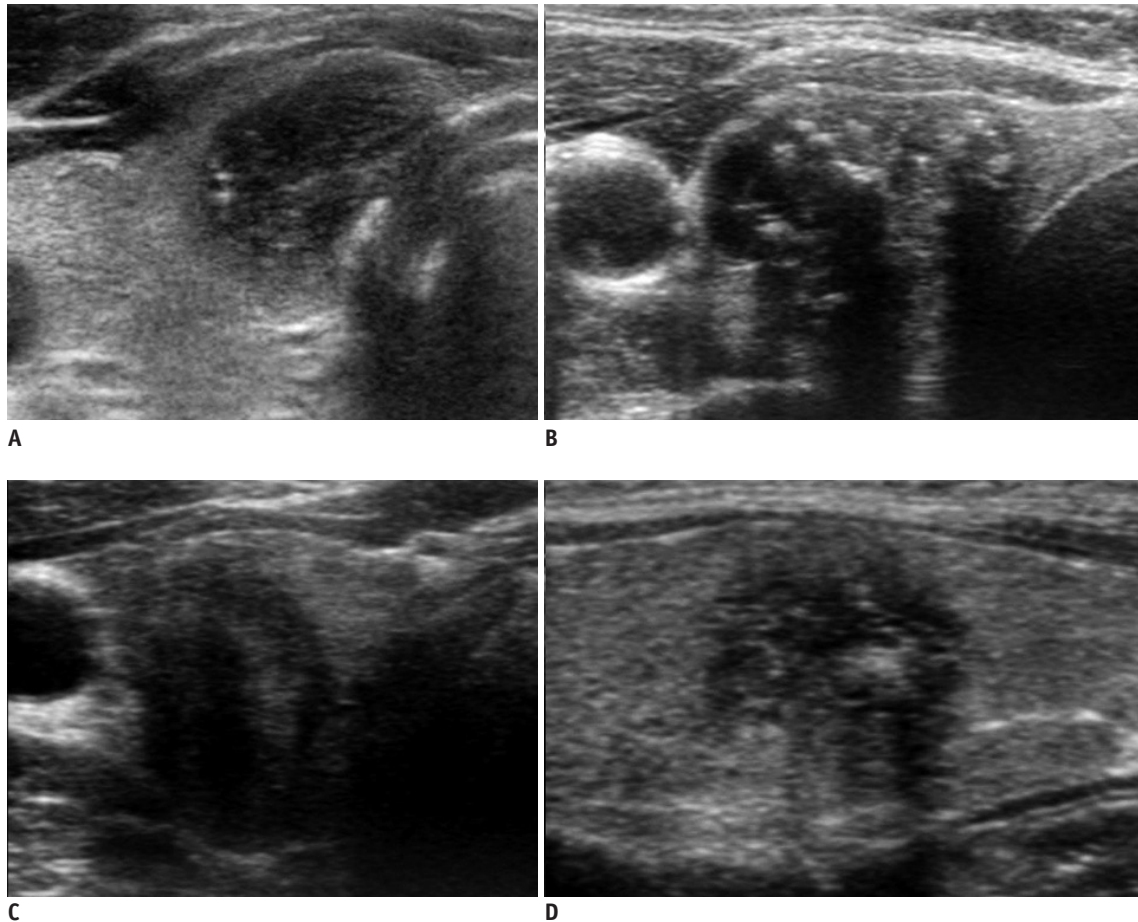


Fig. 2. Korean Thyroid Imaging Reporting and Data System 5 (high suspicion).

A. Solid hypoechoic nodule with microcalcifications. **B.** Solid hypoechoic nodule with multiple microcalcifications and macrocalcifications. **C.** Solid hypoechoic nodule with non-parallel orientation. **D.** Solid hypoechoic nodule with spiculated/microlobulated margin. Diagnosis: papillary carcinoma (A-D).

the diagnosis of the ETE (100-106). Although, the direct tumor invasion of the muscles or other organs around the thyroid gland is the hallmark of the gross ETE, the US-based diagnostic criteria for ETE is somewhat subjective and has not been established yet. The US features predictive of the ETE can be categorized as the presence of the capsular protrusion, disruption, and abutment (Supplementary Fig. 8 in the online-only Data Supplement). Capsular protrusion is defined as the bulging into the adjacent structures with the loss of the normal tissue boundaries (102). The disruption of the capsular margin is defined as loss of the perithyroidal echogenic line at the site of contact with the thyroid cancer (100, 101). Capsular abutment is defined as the lack of intervening tissue between the thyroid cancer and the thyroid capsule (100), which can be graded by the perimeter ratio (abutment perimeter/nodule perimeter \times 100%) (101, 103) or the diameter ratio (abutting diameter/whole tumor diameter \times 100%) (104). If the perimeter

ratio is greater than 25%, the possibility of ETE should be considered. The US-based diagnostic criteria for ETE remains debatable, and further, well-organized, prospective studies are required to determine the diagnostic accuracy of the US criteria for ETE. According to a recent study (107) of the low-risk papillary thyroid microcarcinomas, tracheal tumor invasion was found only in the subcapsular tumors attached to the trachea at the right or obtuse angles, and the tumor invasion of the recurrent laryngeal nerve was found only in the subcapsular tumors with the loss of intervening normal parenchyma in the direction of the recurrent laryngeal nerve (Supplementary Figs. 8, 9 in the online-only Data Supplement).

Indications for US-Guided Fine-Needle Aspiration

Fine-needle aspiration has been established as a safe,

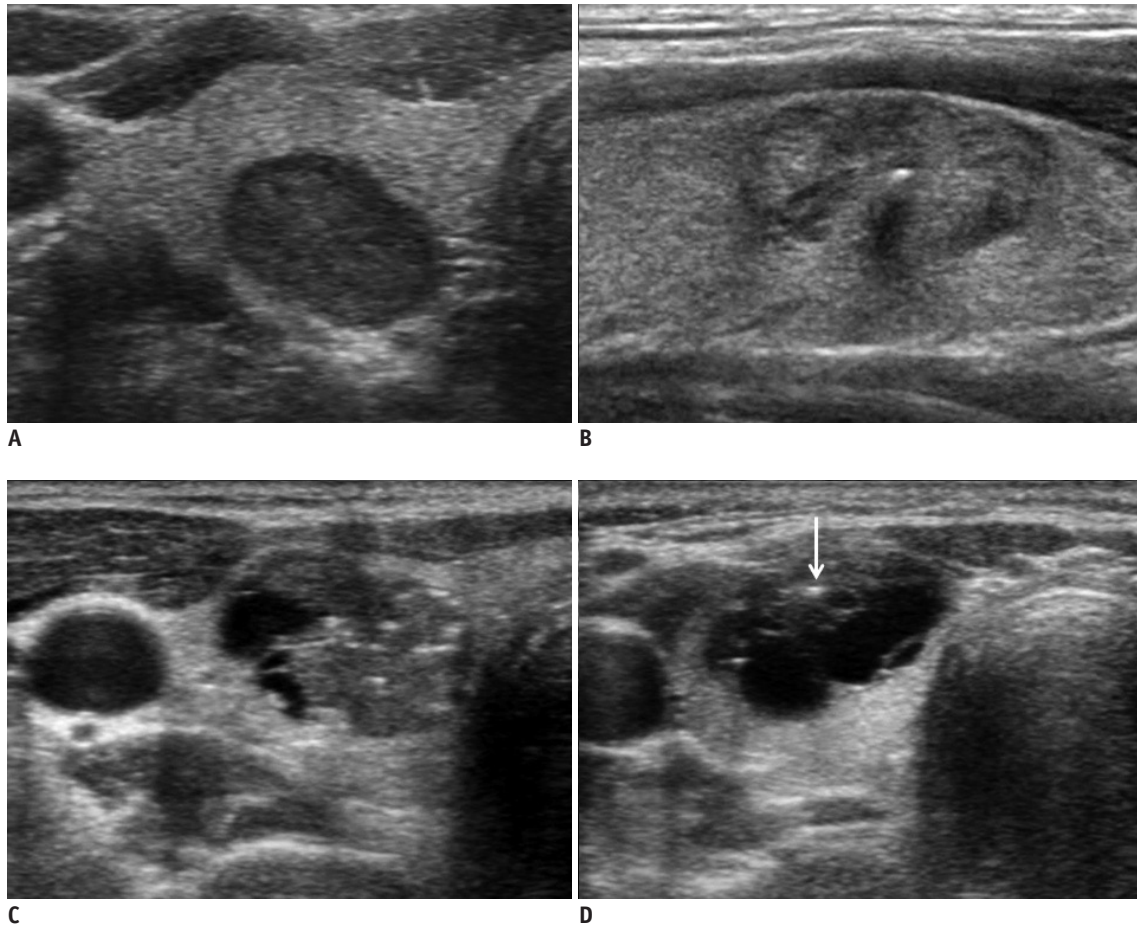


Fig. 3. Korean Thyroid Imaging Reporting and Data System 4 (intermediate suspicion).

A. Solid hypoechoic nodule without suspicious US features. Diagnosis: benign follicular nodule. **B.** Solid isoechoic (predominantly isoechoic) nodule with microcalcification. Diagnosis: benign follicular nodule. **C.** Predominantly solid hypoechoic nodule with multiple microcalcifications. Diagnosis: papillary carcinoma. **D.** Predominantly cystic hypoechoic nodule with microcalcification (arrow). Diagnosis: papillary carcinoma. US = ultrasonography

reliable, and effective method for the diagnosis of the thyroid malignancies. The decision to perform FNA needs to be based on the malignancy and prognostic risks of a thyroid nodule. In the cases with poor prognostic risk factors including suspected cervical LN metastases, ETE, and confirmed distant metastases of thyroid cancer, FNA of the thyroid nodules should be performed regardless of the nodule size. In the patients without the abovementioned poor prognostic factors, we recommend that FNA of the thyroid nodules be performed on the basis of the cancer probability estimated by US and the nodule size (Table 2). Although whether the nodule size could be a predictor for malignancy is controversial (13-15), the primary tumor size of the thyroid cancer is closely related to the prognosis, and the cancer-specific mortality rate and the rate of recurrence is proportional to the size of the thyroid tumor (108, 109). If the nodule has a high or intermediate risk of malignancy (K-TIRADS 5 or 4), FNA is routinely recommended when

the nodule size is ≥ 1 cm; if the nodule has a low risk of malignancy (K-TIRADS 3), FNA is recommended when the nodule size is ≥ 1.5 cm, in order to reduce unnecessary FNA procedures. If the nodule is in the benign condition (K-TIRADS 2), diagnostic FNA may be selectively considered for a spongiform nodule when the nodule size is ≥ 2 cm. Additionally, FNA may be performed for the therapeutic drainage of the cystic content as well as for diagnosis prior to ablation therapy in a pure cyst or a partially cystic nodule with comet-tail artifacts. With the FNA criteria of K-TIRADS categories 4 or 5 for nodules ≥ 1 cm and K-TIRADS 3 for nodules ≥ 1.5 cm, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for overall malignancy were 94.5%, 26.8%, 27.5%, 94.3%, and 42.2%, respectively according to a recent study where 85.5% of the malignant tumors were PTC (25).

Although it is undetermined whether the known clinical risk factors for thyroid cancer including worrisome symptom,

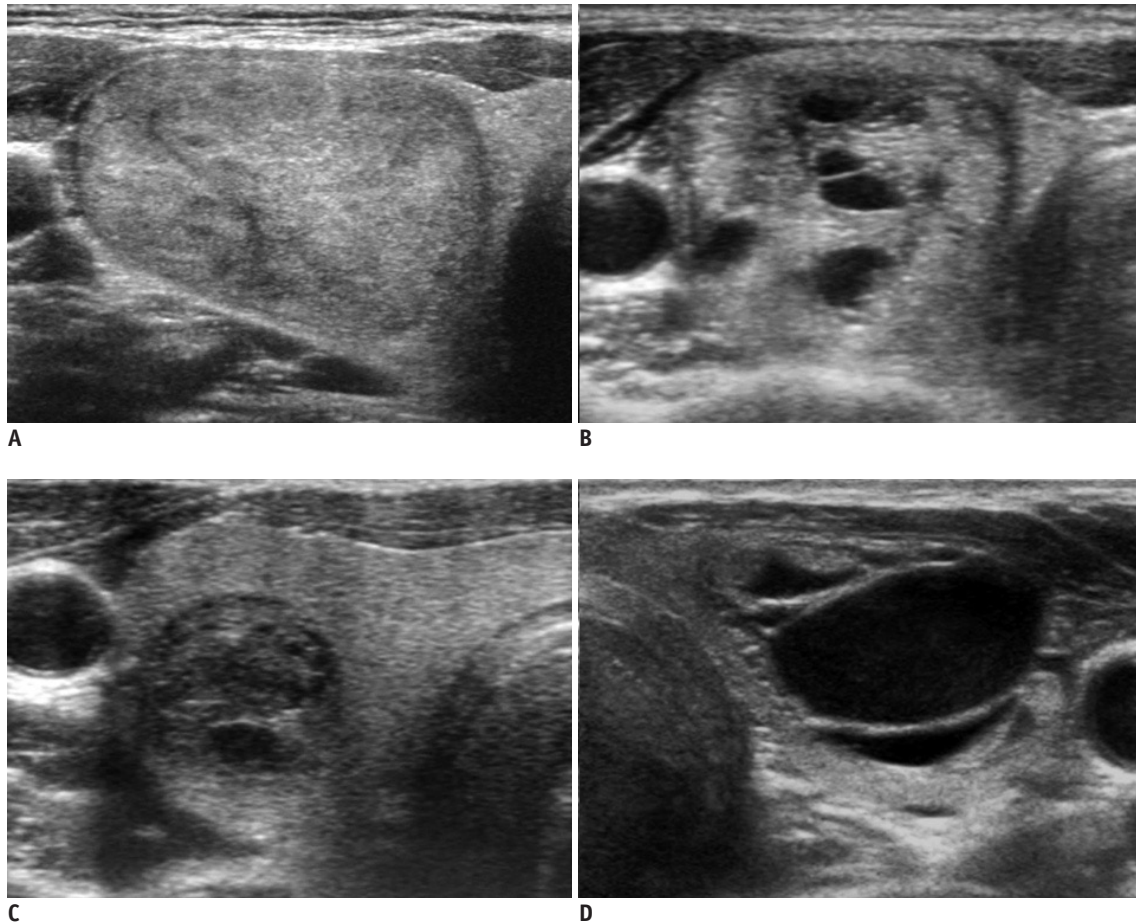


Fig. 4. Korean Thyroid Imaging Reporting and Data System 3 (low suspicion).

None of nodules have any suspicious US features such as microcalcification, non-parallel orientation, and spiculated/microlobulated margins. **A.** Solid isoechoic nodule. Diagnosis: follicular variant papillary carcinoma. **B.** Predominantly solid and isoechoic nodule. Diagnosis: benign follicular nodule. **C.** Predominantly solid and hypoechoic nodule. Diagnosis: benign follicular nodule. **D.** Predominantly cystic and isoechoic nodule. Diagnosis: benign follicular nodule. US = ultrasonography

history of childhood radiation therapy, familial thyroid cancer, increased level of calcitonin, and incidentalomas with ^{18}F -fluorodeoxyglucose uptake incrementally increase the malignancy risk estimated by a US pattern, FNA may be considered at lower size cutoffs of nodules with intermediate or low suspicion pattern in the clinical risk group. The current K-TIRADS categories are based on the US features of the nodules, irrespective of the clinical background. Although the US features of some nodules might correspond to the K-TIRADS categories 4 or 5, FNA may be avoided when they have serially correlated images or a typical clinical history such as degenerating nodule, post-ablation state, and subacute thyroiditis (110-112).

The decision to perform FNA is controversial in the cases with low-risk subcentimeter nodules without poor prognostic factors such as ETE and nodal or distant metastasis. For this category of nodules, we recommend that FNA can be selectively considered only for those

nodules larger than 5 mm in size, with a high suspicion US pattern (K-TIRADS 5). The decision for the FNA of the subcentimeter nodules depends on the management strategy of the thyroid microcarcinomas. Active surveillance instead of immediate surgery could be considered in adult patients (> 18 years) with low-risk papillary thyroid microcarcinomas (113-118). Among the patients with the subcentimeter nodules, FNA of the nodules should be performed for the patients with risk factors requiring immediate surgery, who have poor prognostic factors such as ETE and nodal or distant metastasis, subcapsular nodules with possible tumor invasion of the trachea or the recurrent laryngeal nerve, or evidence of tumor progression (≥ 3 mm) upon serial examination (114, 117, 118). Immediate FNA may be deferred for the older patients (> 60 years) without risk factors requiring immediate surgery, considering the very low risk of disease progression and the relatively shorter follow-up periods in these patients (118); FNA may also be

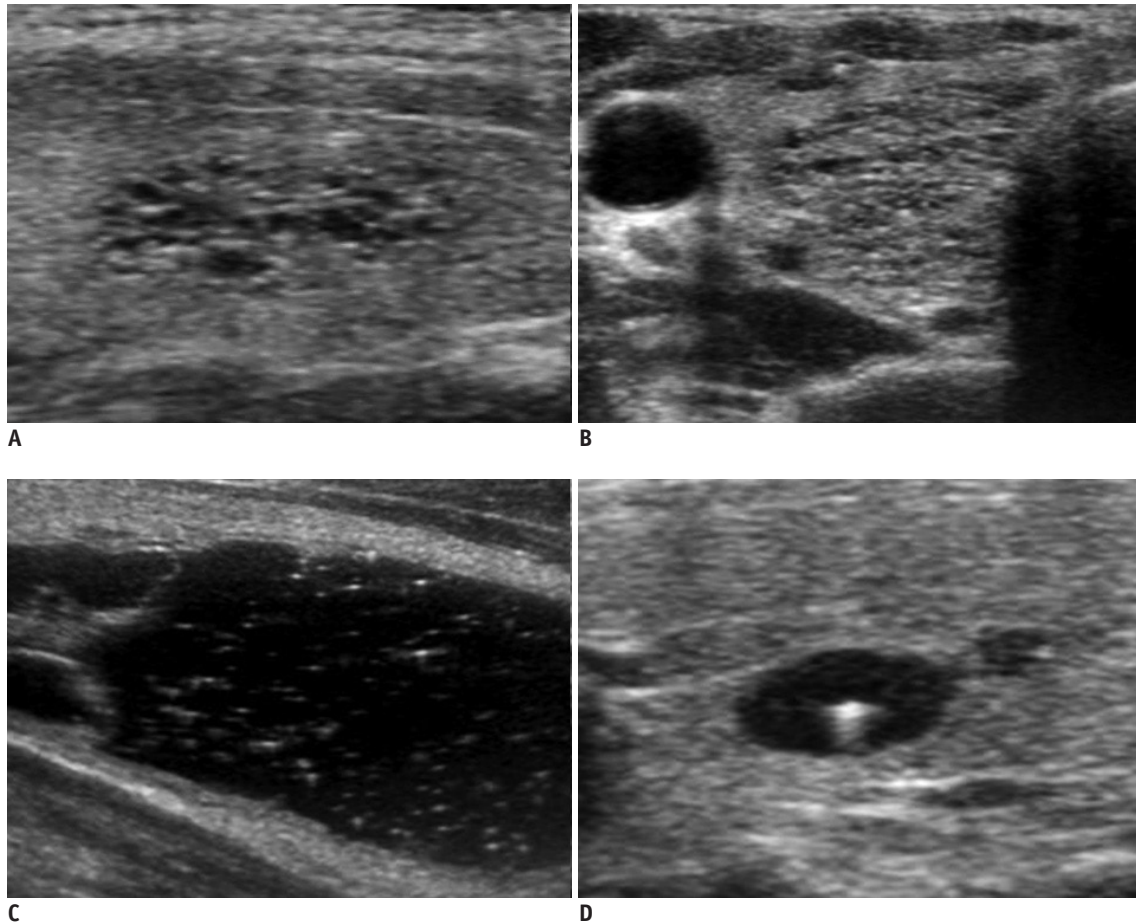


Fig. 5. Korean Thyroid Imaging Reporting and Data System 2 (benign).

A. Spongiform nodule. Diagnosis: benign (FNA not performed). **B.** Spongiform nodule with tiny microcystic changes. Diagnosis: benign follicular nodule. **C.** Predominantly cystic nodule with multiple comet tail artifacts. Diagnosis: benign follicular nodule with colloid. **D.** Cyst with comet-tail artifact. Diagnosis: benign (colloid cyst, FNA not performed). FNA = fine-needle aspiration

deferred for patients who have a high surgical risk because of co-morbid conditions and a relatively short life.

Although it is controversial, FNA may be selectively performed for the subcentimeter nodules (> 5 mm) with high suspicion US pattern by shared decision making in the young or middle-aged adult patients who are not candidates for immediate surgery. A recent American Thyroid Association guideline (20) discourages the FNA of asymptomatic subcentimeter thyroid nodules even when the nodules are highly suspicious for malignancy on the US images, in order to avoid an immediate admittance for surgical treatment because of a definite diagnosis of thyroid cancer; the guideline recommends FNA only when there is evidence of the disease progression in these patients (118). However, we can avoid unnecessary long-term active surveillance of some of the patients with benign nodules showing high suspicion US pattern (approximately 20–40% of nodules with high suspicion pattern); moreover, the

FNA findings of the high-grade malignancies may change the management strategy from that of active surveillance to surgery, although such cases are rare. The nodule size threshold of 5 mm for FNA has no reliable evidence, and it was not a predictor of the tumor progression of the low-risk thyroid microcarcinomas in an observational study (114). However, the PTCs larger than 5 mm might potentially exhibit aggressive behavior such as clinically apparent metastatic nodes (cN1) (119), distant metastases (120, 121), and tumor recurrence (122), although these issues are controversial (123, 124).

In the case of multiple thyroid nodules, we recommend the FNA of one or more nodules that meet the FNA criteria based on the malignancy risk and nodule size. When lobectomy is considered in a patient with bilateral nodules, and a malignant tumor is diagnosed only in one of the lobes, FNA may be preoperatively performed for the contralateral nodule on the basis of a clinical decision.

Management of Thyroid Nodules after FNA

The follow-up and post-FNA management strategies should be determined on the basis of the US and clinical features, as well as the FNA results. The combined use of the US-based risk stratification and the Bethesda system could make possible a more timely detection of thyroid cancer, and might be useful for arriving at an optimal management decision after FNA in thyroid nodules (Table 3) (125-128).

Non-Diagnostic or Unsatisfactory Cytology

The estimated malignancy rate of the nodules with nondiagnostic FNA results is 1–4% (125). In a recent meta-analysis (129), the malignancy rate was 2.7% of all nodules with nondiagnostic FNA results and 16.8% of surgically resected nodules. Since the malignancy rate of the nodules with nondiagnostic FNA results is low, but not negligible, FNA should be repeated with US guidance for the nodules of this category (20, 92, 125). Thyroid nodules with high suspicion US pattern should be followed-up with US-FNA within 3–6 months of the initial treatment, and those with intermediate or low suspicion US pattern may be followed-up with US-FNA within 6–12 months, depending on the nodule size and clinical features. The waiting period of 3 month for the repeat FNA might be unnecessary, depending

on the patient's risk evaluation or the clinician's preference (130, 131). Core needle biopsy (CNB) can be performed by an experienced operator in order to achieve a higher diagnostic adequacy with regard to the nodules with initial or repeated nondiagnostic cytological results (92, 132-135).

Benign Cytology

When the cytological results indicate benign tumors, the follow-up strategy should be determined by risk stratification based on the US features (135-143). The estimated malignancy rate of the nodules with benign cytological results is 3.7%, according to the findings of a meta-analysis based on surgical diagnosis (129), and 1–2% based on the repeat FNA results or a long-term follow-up (127, 144, 145). Whether the false negative rates of FNA are higher (12, 146-148) or similar (13, 15, 149-151) in the large nodules is a matter of controversy. However, the false negative rates of the initial benign findings of FNA are quite different, and are relatively high (11.3–56.6%) for thyroid nodules with suspicious US features (127, 136-142). Therefore, thyroid nodules with high suspicion US pattern should undergo repeat FNA within 6–12 months after the initial FNA. Thyroid nodules with intermediate or low suspicion US pattern are indicated for a follow-up US evaluation 1–2 years after FNA, and may be followed-up every 2–4 years, thereafter (152). When a nodule with

Table 3. Recommended Management Based on FNA Results and US Patterns in Thyroid Nodules

FNA Diagnosis	US Patterns (K-TIRADS)	Management
Nondiagnostic	High suspicion	Repeat FNA or CNB* within 3–6 months [†]
	Intermediate or low suspicion	Repeat FNA or CNB* within 6–12 months [†]
Benign	High suspicion	Repeat FNA within 6–12 months
	Intermediate or low suspicion	US follow-up at 12–24 months
AUS/FLUS	High suspicion	Repeat FNA within 3–6 months
	Intermediate or low suspicion	Repeat FNA within 6–12 months [‡]
FN/SFN	All nodules	Diagnostic surgery (lobectomy) [§]
	Suspicious malignancy	High or intermediate suspicion Surgery Repeat FNA or surgery Active surveillance
Malignant	All nodules	Low suspicion Surgery Active surveillance

*CNB may be considered instead of repeat FNA if experienced operator is available, [†]Optimal timing of repeat FNA or CNB should be determined by clinical decision based on consideration of nodule size, presence of poor prognostic factors such as suspected nodal metastasis or gross extrathyroidal extension, and clinical factors as well as US features, [‡]Close follow-up may be considered depending on clinical risk factors, US features, patient preference, and, when possible, results of molecular studies. If repeat FNA cytology findings are inconclusive, close follow-up or diagnostic surgery can be considered, [§]Close follow-up instead of immediate surgery may be considered in some selected patients based on consideration of clinical factors, nodule size, US features, and, when possible, results of molecular study, ^{||}Active surveillance with close follow-up instead of immediate surgery may be considered in adult patients with probable or proven low-risk papillary microcarcinoma. AUS = atypia undetermined significance, CNB = core needle biopsy, FLUS = follicular lesions of undetermined significance, FN = follicular neoplasm, FNA = fine-needle aspiration, K-TIRADS = Korean Thyroid Imaging Reporting and Data System, SFN = suspicious for a follicular neoplasm, US = ultrasonography

a benign FNA result is found to have increased in size at the follow-up, repeat FNA is not routinely recommended; it is, however, selectively performed depending on the malignancy risk estimated on the basis of the US findings, because of the low malignancy risk of these growing nodule (153).

AUS/FLUS Cytology

The risk of malignancy for thyroid nodules with cytological results indicating atypia/follicular lesions of undetermined significance (AUS/FLUS) is estimated to be 5–15% (125). The reported malignancy rates of the AUS/FLUS nodules are variable; they were estimated to be 15.9% by a meta-analysis study (129), and might have a range of 26.6–37.8% (154). Although this diagnostic category has been recommended for a limited use of less than 7% (125), the AUS/FLUS are diagnosed in 0.8–27.2% of all of the thyroid FNA samples (129). For the nodules diagnosed as the AUS/FLUS, a repeat FNA is recommended, which results in a more definitive interpretation and might avoid diagnostic surgery in many cases (129, 155). The risk for malignancy for the AUS/FLUS nodules with suspicious US features is much higher, and is reported to be as high as 60–80% (128, 156–159). Therefore, we recommend that FNA be repeated within 3–6 months for thyroid nodules with high suspicion US pattern, and within 6–12 months for those with indeterminate or low suspicion US pattern, instead of immediate surgery or surveillance. If the repeat FNA cytology findings are inconclusive, a close follow-up or diagnostic surgery can be decided upon. The utility of the repeat FNA is controversial because of its high rates (up to 67%) of repeatedly inconclusive results (156, 160–162) and high false negative rates of benign diagnosis (163, 164). The malignancy risk of the AUS/FLUS category of nodules might vary according to their subcategory; the AUS/FLUS subcategory presenting nuclear atypia has a higher malignancy risk than those presenting architectural or other atypia (154, 161, 165). Although further investigations are necessary, the management strategy based on the subtype and US features of the nodules might be helpful for arriving at an optimal management decision (128). The CNB method might be more useful for obtaining more conclusive results for the AUS/FLUS nodules than repeat FNA (134, 166–169). Molecular testing is currently not recommended for routine use; however, their use may be considered in selected cases, in order to supplement the findings of malignancy risk assessment (170, 171).

Follicular Neoplasm or Suspicious for a Follicular Neoplasm Cytology

Diagnostic surgery is generally recommended for the nodules with follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN) cytological results (20, 92, 95, 125). However, close follow-up can be considered instead of immediate surgery upon considering the clinical risk factors, US features, and results of the molecular study. The US features of the follicular adenomas and carcinomas overlap substantially, and there is insufficient data regarding the malignancy risk stratification of the nodules of this category, based on the US features. A recent study (153) suggests that if a FNA-diagnosed FN/SFN nodule is found to be growing at the follow-up, its malignancy risk is higher compared to that of the FN/SFN nodules that have been treated by immediate surgery.

Suspicious for Malignancy

Surgical treatment is recommended for the nodules with suspicious malignant cytological results (20, 92, 95, 125). If a nodule has a low suspicion or benign US pattern, repeat FNA may be considered before surgery, given the possibility of false positive results in the nodules without suspicious US features (172).

Malignancy

Surgical treatment is recommended for the nodules with malignant cytological results. However, surgery should be carefully determined on an individual basis for each patient according to the risk-benefit ratio. Active surveillance by means of close follow-ups can be considered as an alternative to immediate surgery in adult patients with low-risk thyroid microcarcinomas without aggressive features or high-grade malignant tumors (113, 114, 117, 118). Close follow-up may also be preferred instead of immediate surgery considering the risk-benefit ratio of surgery in the cases where the patient has a high surgical risk because of co-morbid conditions, relatively short life, or concurrent medical or surgical issues.

US and CT Diagnosis of Cervical Lymph Node Metastasis

The frequency of metastasis to the cervical LNs in PTC has been estimated to be as high as 60–70% (173, 174), and the presence of the LN metastases is known to be highly correlated with the loco-regional recurrence rather than the

disease-specific mortality (175, 176). US is the established primary imaging modality for the assessment of the LNs in the patients with thyroid nodules and proven thyroid cancers. Contrast-enhanced CT has not been routinely applied for the preoperative evaluation of thyroid cancer,

and the use of iodine-based contrast media was strictly restricted before surgery because of the concerns over the disturbed radioactive iodine uptake for months and the delay of radioiodine treatment (177, 178). However, recent studies have demonstrated that the delaying of the

Table 4. Imaging-Based Risk Stratification of Cervical Lymph Nodes for Nodal Metastasis

Category	US	CT
Suspicious*	Cystic change	Cystic change
	Calcification (micro/macro)	Calcification (micro/macro)
	Hyperechogenicity (focal or diffuse)	Heterogeneous enhancement
	Abnormal vascularity (peripheral or diffuse)	Strong enhancement (focal or diffuse)
Indeterminate [†]	Loss of central hilar echo and absence of central hilar vascularity	Loss of central hilar fat and absence of central hilar vessel enhancement
Benign [‡]	Central hilar echo	Central hilar fat
	Central hilar vascularity	Central hilar vessel enhancement

*Lymph nodes with any imaging feature for suspicious lymph nodes are included for this category regardless of presence of any imaging feature for benign or indeterminate lymph nodes, [†]Lymph nodes not included in suspicious or benign categories, [‡]Lymph nodes with any imaging feature of either central hilar fat or central hilar vessels are considered as benign category if there is no imaging feature of suspicious lymph nodes. US = ultrasonography

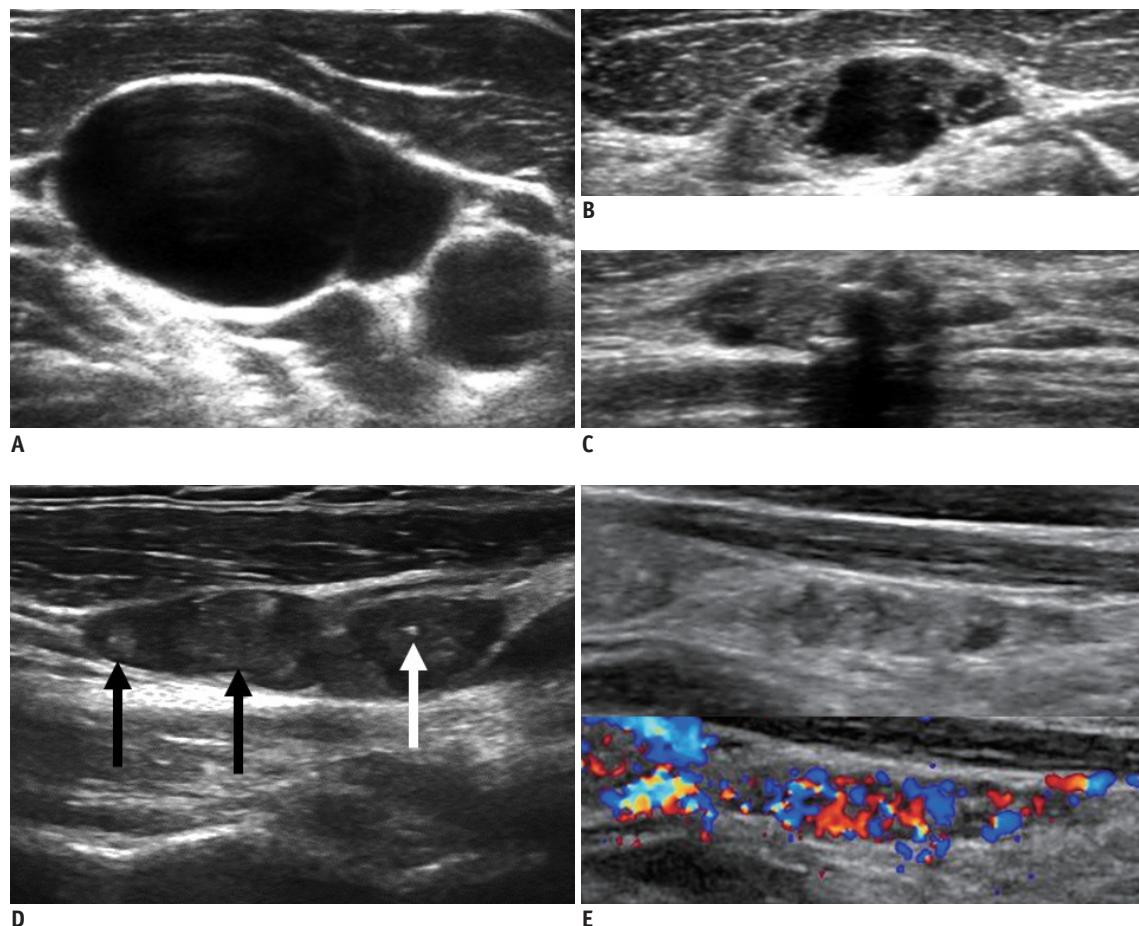


Fig. 6. Suspicious lymph nodes (ultrasonography features).

A. Large cystic nodal mass. **B.** Small focal cystic change and hyperechogenicity in lymph node. **C.** Hyperechogenicity and macrocalcifications in lymph node. **D.** Multifocal hyperechogenicity (black arrows) and microcalcification (white arrow) in lymph node. **E.** Hyperechogenicity, microcalcification, and abnormal hypervascularity in lymph node. Diagnosis: metastatic papillary carcinoma (**A-E**).

radioiodine therapy is not necessary in the patients who have undergone preoperative contrast-enhanced CT, and that the body iodine content is not an important determinant of thyroid ablation (179-183). Contrast-enhanced CT has a complementary role in the preoperative assessment of the extent of the primary tumors and nodal metastases (184-188). We recommend preoperative contrast-enhanced CT for the patients with a suspected invasive primary tumor or cervical LN metastasis. Although the added value of the routine preoperative use of the neck CT for the detection of the LN metastases has been reported in the patients with PTC (184, 186), there is insufficient data and it remains controversial (189).

US and CT Classification of the Cervical Lymph Nodes According to the Risk of Nodal Metastasis

Based on the US and CT features, cervical LNs can be classified into three categories—suspicious, indeterminate, benign—based on the risk of the LN metastasis (190)

(Table 4, Figs. 6-9). The US criteria for suspicious LNs have been reported to be highly specific and predictive of LN metastases (approximately 80–90%) in node-by-node correlation studies (191, 192). The CT criteria for suspicious LNs have been also reported to have high specificity (70–90%) and positive predictive value (70–80%) for LN metastases in level-by-level studies (184, 185). Benign LNs are defined as the LNs which do not have imaging features of suspicious LNs and show any typical imaging feature of benign nodes including US feature of either a central echogenic hilum or a central radiating hilar vascularity and CT feature of either a central hilar fat or a central hilar vessel enhancement. Indeterminate LNs are defined as the LNs which have no imaging feature of suspicious or benign LNs. Indeterminate LNs include the LNs with an eccentric or deformed configuration of the hilum or hilar vessels as well as the LNs with loss of both central hilar fat and central hilar vascularity on US or CT regardless of nodal shape (ovoid or round shape). These imaging features for indeterminate

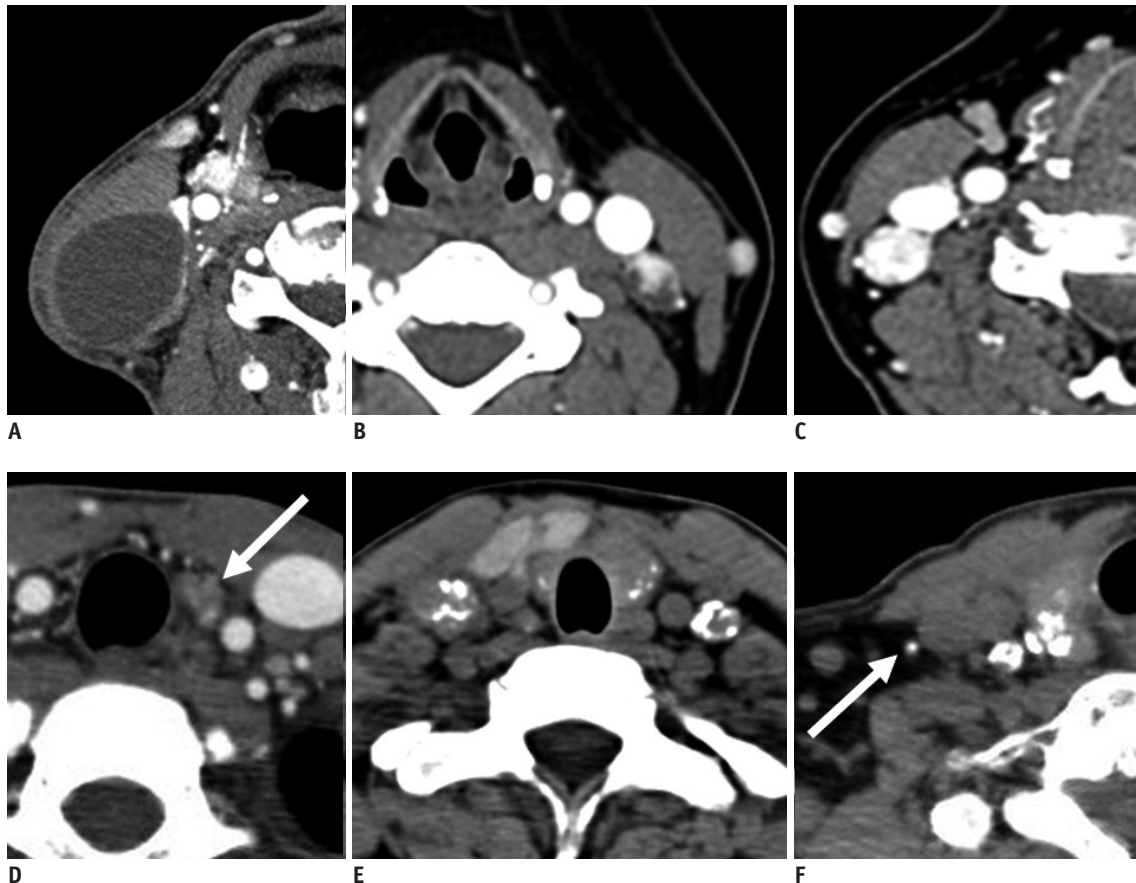


Fig. 7. Suspicious lymph nodes (CT features).

A. Large nonenhancing cystic nodal mass. **B.** Small focal cystic change and strong enhancement in lymph node. **C.** Diffuse, strong enhancement in lymph node. **D.** Heterogeneous mild enhancement in lymph node (arrow). **E, F.** Multiple variable-sized nodal calcifications and tiny nodal calcification (**F**, arrow) on unenhanced CT image. Diagnosis: metastatic papillary carcinoma (**A-F**).

LNs are not specific for the metastatic nodes (190, 192). However, it is likely that these criteria for indeterminate LNs could be helpful to distinguish the malignant LNs from the benign if they can be applied along with the size criteria, which should be verified in future studies (192).

Ultrasonography has been regarded as an insufficient imaging modality because of its relatively low sensitivity for the detection of the metastatic LNs, especially in the central compartment (173, 193-195). The low sensitivity may be explained by the presence of the overlying thyroid gland in the central neck and that of nodal micrometastases (less than 2 mm in diameter), which are mostly undetected by US. The macroscopic metastatic nodes present a high risk of postoperative recurrence; however, the microscopic metastatic nodes have no significant association with the risk of recurrence, and the recurrence rate is similar to that of the pathologically negative nodes (176, 196-200).

Therefore, while the preoperatively identified macroscopic metastatic LNs have a nodal prognostic significance and are regarded as clinically apparent nodes (cN1), most of the microscopic metastatic nodes undetected by imaging might have little clinical significance (176).

FNA Indication for the Cervical Lymph Nodes

The clinical role of US or CT in the preoperative evaluation of the cervical LNs is to detect the clinically apparent and macroscopic metastatic LNs, which are the targets of surgical therapy. Therefore, accurate preoperative imaging is crucial for the complete surgical removal of the macroscopic metastatic LNs in the patients with thyroid cancers. In contrast, an insufficient preoperative assessment of the cervical LNs would eventually lead to a recurrent or persistent disease in the neck. We recommend FNA for the treatment of the suspicious LNs with a short diameter > 3-5

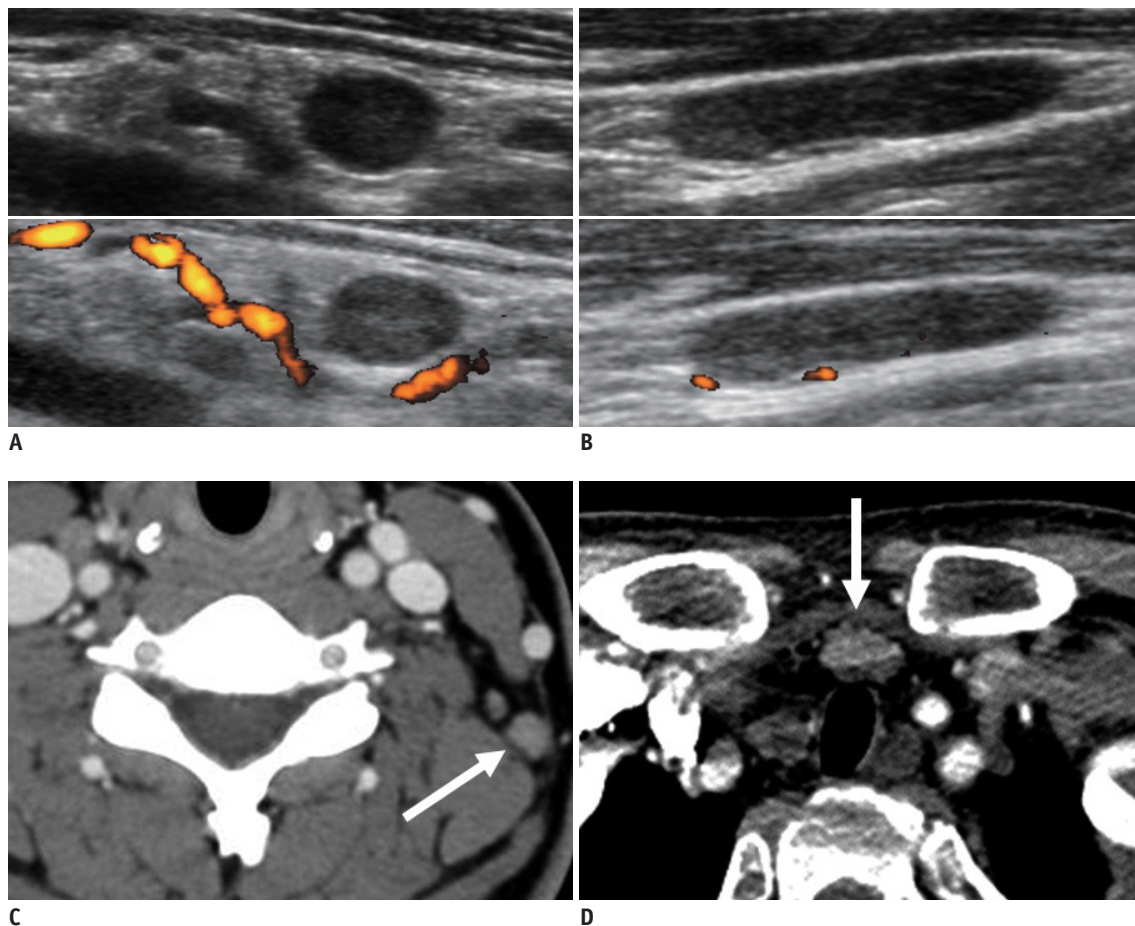


Fig. 8. Indeterminate lymph nodes.

A, B. US features of indeterminate lymph nodes. US images show ovoid and elongated lymph nodes which show loss of central echogenic hilum and central hilar vascularity. Note absence of any suspicious US feature in these nodes. Diagnosis: probable benign lymph node (FNA not performed). **C, D.** CT features of indeterminate lymph nodes. CT images show lymph nodes that do not have central fat hilum and central hilar vessel enhancement. Note absence of any suspicious CT feature in these nodes. Diagnosis: probably benign lymph node (arrow) (C, FNA not performed), metastatic papillary carcinoma (arrow) (D). FNA = fine-needle aspiration, US = ultrasonography

mm and the indeterminate LNs with a short diameter > 5 mm in the preoperative patients with suspected or proven thyroid cancer (Table 5).

Recent studies reported that the postoperative suspicious lesions in the thyroid bed or lateral necks usually remain stable, and have a low potential for structural disease progression (201, 202). In these studies, surgical resection at the time of structural disease progression was successful without evidence of local invasion or distant metastases. These data suggest that appropriately selected patients can be offered a strategy for close monitoring with serial serum thyroglobulin (Tg) measurements and the US evaluation of the suspicious lesions. The decision to perform US-guided FNA for the treatment of cervical LNs should be made based on whether the results of the biopsy will lead to an appropriate and reasonable therapeutic intervention. Therefore, considering the low efficacy of the reoperation

and the less aggressive nature of the recurred nodes, the suspicious or indeterminate LNs > 8–10 mm at the short axial diameter could be a reasonable indication for US-guided FNA in the postoperative evaluation of the cervical LNs (Table 5). However, when the LN is close to the vital organ or the non-surgical treatment including image-guided ablation (ethanol or radiofrequency) are taken into account, FNA could be performed even for the smaller LNs.

US-Based Minimally Invasive Nonsurgical Ablation Therapy

Minimally invasive treatments are indicated in thyroid nodules with clinical problems such as obvious symptoms, cosmetic concerns, and hyperfunction (203). Chemical (ethanol) or thermal (laser and radiofrequency) ablation modalities can be considered for the improvement of

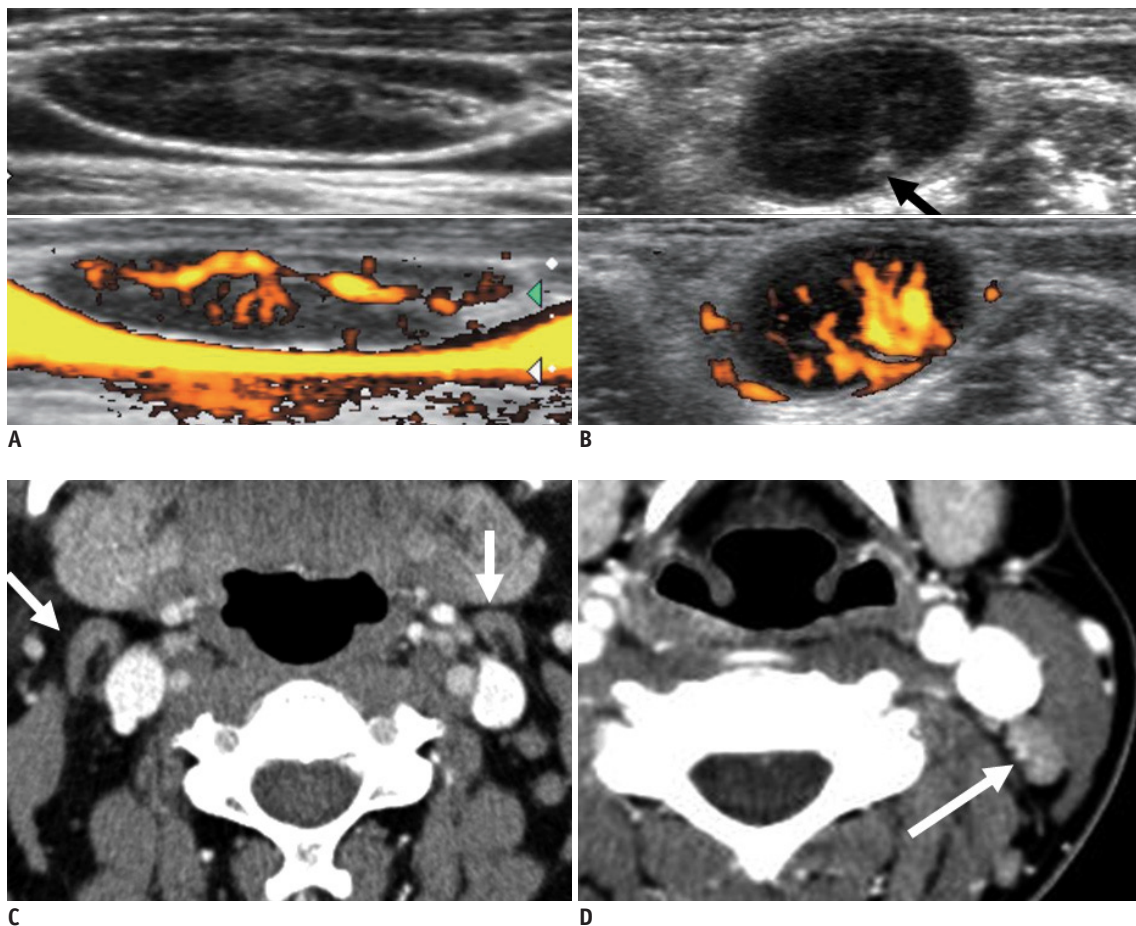


Fig. 9. Benign lymph nodes.

A, B. US features of benign lymph nodes. US image shows elongated lymph node with prominent central echogenic hilum and central hilar vascularity (**A**). US image shows ovoid lymph node with small deformed echogenic hilum (arrow), however, color-Doppler US shows prominent typical central hilar vascularity (**B**). **C, D.** CT features of benign lymph nodes. CT image shows lymph node with central hilar fat (**C**, arrows) and enhanced lymph node with central hilar vessel enhancement (**D**, arrow). Diagnosis: benign lymph node (**A-D**, FNA not performed). FNA = fine-needle aspiration, US = ultrasonography

Table 5. Recommended FNA Indications for Cervical Lymph Nodes in Patients with Possible or Proven Thyroid Carcinomas

Indication of US-FNA: preoperative evaluation*
1) Suspicious lymph node: size > 3–5 mm (short diameter on US and CT images)
2) Indeterminate lymph node: size > 5 mm (short diameter on US and CT images)
Indication of US-FNA: postoperative surveillance*
Suspicious or indeterminate lymph node: size > 8–10 mm (short diameter on US and CT images) [†]

*Measurement of tissue-washout thyroglobulin is recommended for lymph nodes in lateral neck and selectively in central neck, [†]When lymph node is close to vital organ or non-surgical treatment including image-guided ablation (ethanol or radiofrequency) is taken into account, FNA could be performed even for smaller lymph nodes. FNA = fine-needle aspiration, US = ultrasonography

Table 6. Recommendations for US-Guided Ablation of Thyroid Nodules

To reduce volume of benign thyroid nodules, chemical (ethanol) or thermal (laser and radiofrequency) ablation modalities may be considered
Recurrent cystic thyroid nodules after simple aspiration can be treated by ethanol ablation, depending on compressive symptoms and cosmetic concerns
Thermal ablation (radiofrequency or laser) shows high efficacy and safety in treatment of benign solid thyroid nodules, and may be considered as valid alternative to surgery

US = ultrasonography

the clinical problems by reducing the volume of benign thyroid nodules (10). The recommendations for the minimally invasive treatment of benign thyroid nodules are summarized in Table 6.

In cystic thyroid nodules (cystic portions > 90%) with symptomatic cosmetic problems, simple aspiration is the first-line management tool for both diagnostic and therapeutic purposes. However, the recurrence rate is as high as 80% after simple aspiration, depending on the number and volume of the aspirated cysts (204). Ethanol ablation can be considered for the treatment of the recurrent cystic thyroid nodules on the basis of the compressive symptoms and cosmetic concerns. Ethanol ablation has a therapeutic efficacy comparable to that of radiofrequency ablation, but is less expensive than the latter; it should be considered as the first-line treatment modality for cystic thyroid nodules (205-206).

Thermal ablation shows high efficacy and safety in the treatment of the benign solid thyroid nodules, and may be considered as a valid alternative to surgery (207-211). Recent systematic reviews and meta-analyses have demonstrated that both radiofrequency and laser ablation achieved a significant volume reduction in the benign solid thyroid nodules; however, radiofrequency ablation was revealed as having efficacy superior to that of laser ablation for volume reduction. The studies also showed that both the intervention modalities are devoid of major complications (212). Because of potential complications, thermal ablation procedures should be performed only by experienced operators.

Supplementary Materials

The online-only Data Supplement is available with this article at <http://dx.doi.org/10.3348/kjr.2016.17.3.370>.

REFERENCES

- Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Ann Intern Med* 1968;69:537-540
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 1977;7:481-493
- Mandel SJ. A 64-year-old woman with a thyroid nodule. *JAMA* 2004;292:2632-2642
- Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab* 2002;87:1941-1946
- Nam-Goong IS, Kim HY, Gong G, Lee HK, Hong SJ, Kim WB, et al. Ultrasonography-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings. *Clin Endocrinol (Oxf)* 2004;60:21-28
- Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, et al. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. *JAMA Intern Med* 2013;173:1788-1796
- Vaccarella S, Dal Maso L, Laversanne M, Bray F, Plummer M, Franceschi S. The impact of diagnostic changes on the rise in thyroid cancer incidence: a population-based study in selected high-resource countries. *Thyroid* 2015;25:1127-1136
- Ahn HY, Park YJ. Incidence and clinical characteristics of

- thyroid cancer in Korea. *Korean J Med* 2009;77:537-542
9. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA* 2006;295:2164-2167
 10. Gharib H, Hegedüs L, Pacella CM, Baek JH, Papini E. Clinical review: nonsurgical, image-guided, minimally invasive therapy for thyroid nodules. *J Clin Endocrinol Metab* 2013;98:3949-3957
 11. Moon WJ, Baek JH, Jung SL, Kim DW, Kim EK, Kim JY, et al. Ultrasonography and the ultrasound-based management of thyroid nodules: consensus statement and recommendations. *Korean J Radiol* 2011;12:1-14
 12. Shin JJ, Caragacianu D, Randolph GW. Impact of thyroid nodule size on prevalence and post-test probability of malignancy: a systematic review. *Laryngoscope* 2015;125:263-272
 13. Kamran SC, Marqusee E, Kim MI, Frates MC, Ritner J, Peters H, et al. Thyroid nodule size and prediction of cancer. *J Clin Endocrinol Metab* 2013;98:564-570
 14. McHenry CR, Huh ES, Machezano RN. Is nodule size an independent predictor of thyroid malignancy? *Surgery* 2008;144:1062-1068; discussion 1068-1069
 15. Shrestha M, Crothers BA, Burch HB. The impact of thyroid nodule size on the risk of malignancy and accuracy of fine-needle aspiration: a 10-year study from a single institution. *Thyroid* 2012;22:1251-1256
 16. Asanuma K, Kobayashi S, Shingu K, Hama Y, Yokoyama S, Fujimori M, et al. The rate of tumour growth does not distinguish between malignant and benign thyroid nodules. *Eur J Surg* 2001;167:102-105
 17. Alexander EK, Hurwitz S, Heering JP, Benson CB, Frates MC, Doubilet PM, et al. Natural history of benign solid and cystic thyroid nodules. *Ann Intern Med* 2003;138:315-318
 18. Erdogan MF, Gursoy A, Erdogan G. Natural course of benign thyroid nodules in a moderately iodine-deficient area. *Clin Endocrinol (Oxf)* 2006;65:767-771
 19. Ajmal S, Rapoport S, Ramirez Batlle H, Mazzaglia PJ. The natural history of the benign thyroid nodule: what is the appropriate follow-up strategy? *J Am Coll Surg* 2015;220:987-992
 20. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016;26:1-133
 21. Na DG, Kim JH, Kim DS, Kim SJ. Thyroid nodules with minimal cystic changes have a low risk of malignancy. *Ultrasonography* 2016;35:153-158
 22. Salmaslioglu A, Erbil Y, Dural C, İşsever H, Kapran Y, Ozarmağan S, et al. Predictive value of sonographic features in preoperative evaluation of malignant thyroid nodules in a multinodular goiter. *World J Surg* 2008;32:1948-1954
 23. Henrichsen TL, Reading CC, Charboneau JW, Donovan DJ, Sebo TJ, Hay ID. Cystic change in thyroid carcinoma: prevalence and estimated volume in 360 carcinomas. *J Clin Ultrasound* 2010;38:361-366
 24. Kwak JY, Han KH, Yoon JH, Moon HJ, Son EJ, Park SH, et al. Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk. *Radiology* 2011;260:892-899
 25. Na DG, Baek JH, Sung JY, Kim JH, Kim JK, Choi YJ, et al. Thyroid imaging reporting and data system risk stratification of thyroid nodules: categorization based on solidity and echogenicity. *Thyroid* 2016;26:562-572
 26. Lee MJ, Kim EK, Kwak JY, Kim MJ. Partially cystic thyroid nodules on ultrasound: probability of malignancy and sonographic differentiation. *Thyroid* 2009;19:341-346
 27. Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation--multicenter retrospective study. *Radiology* 2008;247:762-770
 28. Bonavita JA, Mayo J, Babb J, Bennett G, Oweity T, Macari M, et al. Pattern recognition of benign nodules at ultrasound of the thyroid: which nodules can be left alone? *AJR Am J Roentgenol* 2009;193:207-213
 29. Moon WJ, Kwag HJ, Na DG. Are there any specific ultrasound findings of nodular hyperplasia ("leave me alone" lesion) to differentiate it from follicular adenoma? *Acta Radiol* 2009;50:383-388
 30. Kim JY, Jung SL, Kim MK, Kim TJ, Byun JY. Differentiation of benign and malignant thyroid nodules based on the proportion of sponge-like areas on ultrasonography: imaging-pathologic correlation. *Ultrasonography* 2015;34:304-311
 31. Kobayashi K, Hirokawa M, Yabuta T, Fukushima M, Kihara M, Takamura Y, et al. Papillary thyroid carcinoma with honeycomb-like multiple small cysts: characteristic features on ultrasonography. *Eur Thyroid J* 2013;2:270-274
 32. Cappelli C, Castellano M, Pirola I, Cumetti D, Agosti B, Gandossi E, et al. The predictive value of ultrasound findings in the management of thyroid nodules. *QJM* 2007;100:29-35
 33. Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee JT, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *AJR Am J Roentgenol* 2002;178:687-691
 34. Alexander EK, Marqusee E, Orcutt J, Benson CB, Frates MC, Doubilet PM, et al. Thyroid nodule shape and prediction of malignancy. *Thyroid* 2004;14:953-958
 35. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995;196:123-134
 36. Jeh SK, Jung SL, Kim BS, Lee YS. Evaluating the degree of conformity of papillary carcinoma and follicular carcinoma to the reported ultrasonographic findings of malignant thyroid tumor. *Korean J Radiol* 2007;8:192-197
 37. Yoon JH, Kim EK, Hong SW, Kwak JY, Kim MJ. Sonographic features of the follicular variant of papillary thyroid carcinoma. *J Ultrasound Med* 2008;27:1431-1437
 38. Kim DS, Kim JH, Na DG, Park SH, Kim E, Chang KH, et al. Sonographic features of follicular variant papillary thyroid carcinomas in comparison with conventional papillary

- thyroid carcinomas. *J Ultrasound Med* 2009;28:1685-1692
39. Kwak JY, Jung I, Baek JH, Baek SM, Choi N, Choi YJ, et al. Image reporting and characterization system for ultrasound features of thyroid nodules: multicentric Korean retrospective study. *Korean J Radiol* 2013;14:110-117
 40. Seo H, Na DG, Kim JH, Kim KW, Yoon JW. Ultrasound-based risk stratification for malignancy in thyroid nodules: a four-tier categorization system. *Eur Radiol* 2015;25:2153-2162
 41. Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. *Radiology* 2005;237:794-800
 42. Andrioli M, Carzaniga C, Persani L. Standardized ultrasound report for thyroid nodules: the endocrinologist's viewpoint. *Eur Thyroid J* 2013;2:37-48
 43. Su HK, Dos Reis LL, Lupo MA, Milas M, Orloff LA, Langer JE, et al. Striving toward standardization of reporting of ultrasound features of thyroid nodules and lymph nodes: a multidisciplinary consensus statement. *Thyroid* 2014;24:1341-1349
 44. Grant EG, Tessler FN, Hoang JK, Langer JE, Beland MD, Berland LL, et al. Thyroid ultrasound reporting lexicon: white paper of the ACR thyroid imaging, reporting and data system (TIRADS) committee. *J Am Coll Radiol* 2015;12(12 Pt A):1272-1279
 45. Langer JE, Khan A, Nisenbaum HL, Baloch ZW, Horii SC, Coleman BG, et al. Sonographic appearance of focal thyroiditis. *AJR Am J Roentgenol* 2001;176:751-754
 46. Frates MC, Marqusee E, Benson CB, Alexander EK. Subacute granulomatous (de Quervain) thyroiditis: grayscale and color Doppler sonographic characteristics. *J Ultrasound Med* 2013;32:505-511
 47. Scheible W, Leopold GR, Woo VL, Gosink BB. High-resolution real-time ultrasonography of thyroid nodules. *Radiology* 1979;133:413-417
 48. Propper RA, Skolnick ML, Weinstein BJ, Dekker A. The nonspecificity of the thyroid halo sign. *J Clin Ultrasound* 1980;8:129-132
 49. Lu C, Chang TC, Hsiao YL, Kuo MS. Ultrasonographic findings of papillary thyroid carcinoma and their relation to pathologic changes. *J Formos Med Assoc* 1994;93:933-938
 50. Haber RS. Role of ultrasonography in the diagnosis and management of thyroid cancer. *Endocr Pract* 2000;6:396-400
 51. Chan BK, Desser TS, McDougall IR, Weigel RJ, Jeffrey RB Jr. Common and uncommon sonographic features of papillary thyroid carcinoma. *J Ultrasound Med* 2003;22:1083-1090
 52. Seo HS, Lee DH, Park SH, Min HS, Na DG. Thyroid follicular neoplasms: can sonography distinguish between adenomas and carcinomas? *J Clin Ultrasound* 2009;37:493-500
 53. Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. *J Clin Endocrinol Metab* 2014;99:1253-1263
 54. Remonti LR, Kramer CK, Leitão CB, Pinto LC, Gross JL. Thyroid ultrasound features and risk of carcinoma: a systematic review and meta-analysis of observational studies. *Thyroid* 2015;25:538-550
 55. Ahuja A, Chick W, King W, Metreweli C. Clinical significance of the comet-tail artifact in thyroid ultrasound. *J Clin Ultrasound* 1996;24:129-133
 56. Beland MD, Kwon L, Delellis RA, Cronan JJ, Grant EG. Nonshadowing echogenic foci in thyroid nodules: are certain appearances enough to avoid thyroid biopsy? *J Ultrasound Med* 2011;30:753-760
 57. Malhi H, Beland MD, Cen SY, Allgood E, Daley K, Martin SE, et al. Echogenic foci in thyroid nodules: significance of posterior acoustic artifacts. *AJR Am J Roentgenol* 2014;203:1310-1316
 58. Popowicz B, Klencki M, Lewiński A, Słowińska-Klencka D. The usefulness of sonographic features in selection of thyroid nodules for biopsy in relation to the nodule's size. *Eur J Endocrinol* 2009;161:103-111
 59. Lu Z, Mu Y, Zhu H, Luo Y, Kong Q, Dou J, et al. Clinical value of using ultrasound to assess calcification patterns in thyroid nodules. *World J Surg* 2011;35:122-127
 60. Na DG, Kim DS, Kim SJ, Ryoo JW, Jung SL. Thyroid nodules with isolated macrocalcification: malignancy risk and diagnostic efficacy of fine-needle aspiration and core needle biopsy. *Ultrasonography* 2015 Dec 27 [Epub]. <http://dx.doi.org/10.14366/usg.15074>
 61. Kim BM, Kim MJ, Kim EK, Kwak JY, Hong SW, Son EJ, et al. Sonographic differentiation of thyroid nodules with eggshell calcifications. *J Ultrasound Med* 2008;27:1425-1430
 62. Park M, Shin JH, Han BK, Ko EY, Hwang HS, Kang SS, et al. Sonography of thyroid nodules with peripheral calcifications. *J Clin Ultrasound* 2009;37:324-328
 63. Rago T, Vitti P, Chiovato L, Mazzeo S, De Liperi A, Miccoli P, et al. Role of conventional ultrasonography and color flow-doppler sonography in predicting malignancy in 'cold' thyroid nodules. *Eur J Endocrinol* 1998;138:41-46
 64. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules? *J Ultrasound Med* 2003;22:127-131; quiz 132-134
 65. Appetecchia M, Solivetti FM. The association of colour flow Doppler sonography and conventional ultrasonography improves the diagnosis of thyroid carcinoma. *Horm Res* 2006;66:249-256
 66. Ma JJ, Ding H, Xu BH, Xu C, Song LJ, Huang BJ, et al. Diagnostic performances of various gray-scale, color Doppler, and contrast-enhanced ultrasonography findings in predicting malignant thyroid nodules. *Thyroid* 2014;24:355-363
 67. Moon HJ, Kwak JY, Kim MJ, Son EJ, Kim EK. Can vascularity at power Doppler US help predict thyroid malignancy? *Radiology* 2010;255:260-269
 68. Zhou JQ, Zhou C, Zhan WW, Zhou W, Dong YJ. Maximal, minimal, and mean pulsed Doppler parameters: which should be utilized in the diagnosis of thyroid nodules? *Clin Radiol* 2014;69:e477-e484

69. Fukunari N, Nagahama M, Sugino K, Mimura T, Ito K, Ito K. Clinical evaluation of color Doppler imaging for the differential diagnosis of thyroid follicular lesions. *World J Surg* 2004;28:1261-1265
70. Miyakawa M, Onoda N, Etoh M, Fukuda I, Takano K, Okamoto T, et al. Diagnosis of thyroid follicular carcinoma by the vascular pattern and velocimetric parameters using high resolution pulsed and power Doppler ultrasonography. *Endocr J* 2005;52:207-212
71. De Nicola H, Szejnfeld J, Logullo AF, Wolosker AM, Souza LR, Chiferi V Jr. Flow pattern and vascular resistive index as predictors of malignancy risk in thyroid follicular neoplasms. *J Ultrasound Med* 2005;24:897-904
72. Iared W, Shigueoka DC, Cristófoli JC, Andriolo R, Atallah AN, Ajzen SA, et al. Use of color Doppler ultrasonography for the prediction of malignancy in follicular thyroid neoplasms: systematic review and meta-analysis. *J Ultrasound Med* 2010;29:419-425
73. Choi YJ, Yun JS, Kim DH. Clinical and ultrasound features of cytology diagnosed follicular neoplasm. *Endocr J* 2009;56:383-389
74. Trimboli P, Sorrenti S. Low value of color flow-doppler in predicting malignancy of thyroid follicular neoplasms. *Diagn Cytopathol* 2009;37:391-392
75. Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: basic principles and terminology. *Ultrasound Med Biol* 2015;41:1126-1147
76. Kwak JY, Kim EK. Ultrasound elastography for thyroid nodules: recent advances. *Ultrasonography* 2014;33:75-82
77. Rago T, Santini F, Scutari M, Pinchera A, Vitti P. Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. *J Clin Endocrinol Metab* 2007;92:2917-2922
78. Asteria C, Giovanardi A, Pizzocaro A, Cozzaglio L, Morabito A, Somalvico F, et al. US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Thyroid* 2008;18:523-531
79. Moon HJ, Sung JM, Kim EK, Yoon JH, Youk JH, Kwak JY. Diagnostic performance of gray-scale US and elastography in solid thyroid nodules. *Radiology* 2012;262:1002-1013
80. Cappelli C, Pirola I, Gandossi E, Agosti B, Cimino E, Casella C, et al. Real-time elastography: a useful tool for predicting malignancy in thyroid nodules with nondiagnostic cytologic findings. *J Ultrasound Med* 2012;31:1777-1782
81. Nell S, Kist JW, Debray TP, de Keizer B, van Oostenbrugge TJ, Borel Rinkes IH, et al. Qualitative elastography can replace thyroid nodule fine-needle aspiration in patients with soft thyroid nodules. A systematic review and meta-analysis. *Eur J Radiol* 2015;84:652-661
82. Rago T, Scutari M, Santini F, Loiacono V, Piaggi P, Di Coscio G, et al. Real-time elastosonography: useful tool for refining the presurgical diagnosis in thyroid nodules with indeterminate or nondiagnostic cytology. *J Clin Endocrinol Metab* 2010;95:5274-5280
83. Choi WJ, Park JS, Koo HR, Kim SY, Chung MS, Tae K. Ultrasound elastography using carotid artery pulsation in the differential diagnosis of sonographically indeterminate thyroid nodules. *AJR Am J Roentgenol* 2015;204:396-401
84. Samir AE, Dhyani M, Anvari A, Prescott J, Halpern EF, Faquin WC, et al. Shear-wave elastography for the preoperative risk stratification of follicular-patterned lesions of the thyroid: diagnostic accuracy and optimal measurement plane. *Radiology* 2015;277:565-573
85. Campanella P, Ianni F, Rota CA, Corsello SM, Pontecorvi A. Quantification of cancer risk of each clinical and ultrasonographic suspicious feature of thyroid nodules: a systematic review and meta-analysis. *Eur J Endocrinol* 2014;170:R203-R211
86. Horvath E, Majlis S, Rossi R, Franco C, Niedmann JP, Castro A, et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. *J Clin Endocrinol Metab* 2009;94:1748-1751
87. Russ G, Royer B, Bigorgne C, Rouxel A, Bienvenu-Perrard M, Leenhardt L. Prospective evaluation of thyroid imaging reporting and data system on 4550 nodules with and without elastography. *Eur J Endocrinol* 2013;168:649-655
88. Park JY, Lee HJ, Jang HW, Kim HK, Yi JH, Lee W, et al. A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma. *Thyroid* 2009;19:1257-1264
89. Kim DW, Lee EJ, In HS, Kim SJ. Sonographic differentiation of partially cystic thyroid nodules: a prospective study. *AJNR Am J Neuroradiol* 2010;31:1961-1966
90. Park JM, Choi Y, Kwag HJ. Partially cystic thyroid nodules: ultrasound findings of malignancy. *Korean J Radiol* 2012;13:530-535
91. Vera MI, Meroño T, Urrutia MA, Parisi C, Morosan Y, Rosmarin M, et al. Differential profile of ultrasound findings associated with malignancy in mixed and solid thyroid nodules in an elderly female population. *J Thyroid Res* 2014;2014:761653
92. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedüs L, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. *Endocr Pract* 2010;16 Suppl 1:1-43
93. Wémeau JL, Sadoul JL, d'Herbomez M, Monpeyssen H, Tramalloni J, Leteurtre E, et al. Guidelines of the French society of endocrinology for the management of thyroid nodules. *Ann Endocrinol (Paris)* 2011;72:251-281
94. Perros P, Boelaert K, Colley S, Evans C, Evans RM, Gerrard BA G, et al. Guidelines for the management of thyroid cancer. *Clin Endocrinol (Oxf)* 2014;81 Suppl 1:1-122
95. National Comprehensive Cancer Network. 2014 Practice Guidelines in Oncology-Thyroid Carcinoma v.2. Web site. <http://www.nccn.org/>. Accessed May 18, 2015
96. Andersen PE, Kinsella J, Loree TR, Shaha AR, Shah JP. Differentiated carcinoma of the thyroid with extrathyroidal

- extension. *Am J Surg* 1995;170:467-470
97. Ito Y, Tomoda C, Urano T, Takamura Y, Miya A, Kobayashi K, et al. Prognostic significance of extrathyroid extension of papillary thyroid carcinoma: massive but not minimal extension affects the relapse-free survival. *World J Surg* 2006;30:780-786
 98. Riemann B, Krämer JA, Schmid KW, Dralle H, Dietlein M, Schicha H, et al. Risk stratification of patients with locally aggressive differentiated thyroid cancer. Results of the MSDS trial. *Nuklearmedizin* 2010;49:79-84
 99. Radowsky JS, Howard RS, Burch HB, Stojadinovic A. Impact of degree of extrathyroidal extension of disease on papillary thyroid cancer outcome. *Thyroid* 2014;24:241-244
 100. Lee CY, Kim SJ, Ko KR, Chung KW, Lee JH. Predictive factors for extrathyroidal extension of papillary thyroid carcinoma based on preoperative sonography. *J Ultrasound Med* 2014;33:231-238
 101. Kwak JY, Kim EK, Youk JH, Kim MJ, Son EJ, Choi SH, et al. Extrathyroid extension of well-differentiated papillary thyroid microcarcinoma on US. *Thyroid* 2008;18:609-614
 102. Shimamoto K, Satake H, Sawaki A, Ishigaki T, Funahashi H, Imai T. Preoperative staging of thyroid papillary carcinoma with ultrasonography. *Eur J Radiol* 1998;29:4-10
 103. Choi JS, Chung WY, Kwak JY, Moon HJ, Kim MJ, Kim EK. Staging of papillary thyroid carcinoma with ultrasonography: performance in a large series. *Ann Surg Oncol* 2011;18:3572-3578
 104. 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
 105. Moon SJ, Kim DW, Kim SJ, Ha TK, Park HK, Jung SJ. Ultrasound assessment of degrees of extrathyroidal extension in papillary thyroid microcarcinoma. *Endocr Pract* 2014;20:1037-1043
 106. Kim SS, Lee BJ, Lee JC, Kim SJ, Lee SH, Jeon YK, et al. Preoperative ultrasonographic tumor characteristics as a predictive factor of tumor stage in papillary thyroid carcinoma. *Head Neck* 2011;33:1719-1726
 107. Ito Y, Miyauchi A, Oda H, Kobayashi K, Kihara M, Miya A. Revisiting low-risk thyroid papillary microcarcinomas resected without observation: was immediate surgery necessary? *World J Surg* 2016;40:523-528
 108. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994;97:418-428
 109. Machens A, Holzhausen HJ, Dralle H. The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma. *Cancer* 2005;103:2269-2273
 110. Koo JH, Shin JH, Han BK, Ko EY, Kang SS. Cystic thyroid nodules after aspiration mimicking malignancy: sonographic characteristics. *J Ultrasound Med* 2010;29:1415-1421
 111. Park NH, Kim DW, Park HJ, Lee EJ, Park JS, Park SI, et al. Thyroid cysts treated with ethanol ablation can mimic malignancy during sonographic follow-up. *J Clin Ultrasound* 2011;39:441-446
 112. Zacharia TT, Perumpallichira JJ, Sindhvani V, Chavhan G. Gray-scale and color Doppler sonographic findings in a case of subacute granulomatous thyroiditis mimicking thyroid carcinoma. *J Clin Ultrasound* 2002;30:442-444
 113. Ito Y, Miyauchi A, Inoue H, Fukushima M, Kihara M, Higashiyama T, et al. An observational trial for papillary thyroid microcarcinoma in Japanese patients. *World J Surg* 2010;34:28-35
 114. Ito Y, Miyauchi A, Kihara M, Higashiyama T, Kobayashi K, Miya A. Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation. *Thyroid* 2014;24:27-34
 115. Pacini F. Management of papillary thyroid microcarcinoma: primum non nocere! *J Clin Endocrinol Metab* 2013;98:1391-1393
 116. Takami H, Ito Y, Okamoto T, Onoda N, Noguchi H, Yoshida A. Revisiting the guidelines issued by the Japanese Society of Thyroid Surgeons and Japan Association of Endocrine Surgeons: a gradual move towards consensus between Japanese and western practice in the management of thyroid carcinoma. *World J Surg* 2014;38:2002-2010
 117. Oda H, Miyauchi A, Ito Y, Yoshioka K, Nakayama A, Sasai H, et al. Incidences of unfavorable events in the management of low-risk papillary microcarcinoma of the thyroid by active surveillance versus immediate surgery. *Thyroid* 2016;26:150-155
 118. Brito JP, Ito Y, Miyauchi A, Tuttle RM. A clinical framework to facilitate risk stratification when considering an active surveillance alternative to immediate biopsy and surgery in papillary microcarcinoma. *Thyroid* 2016;26:144-149
 119. Ghossein R, Ganly I, Biagini A, Robenshtok E, Rivera M, Tuttle RM. Prognostic factors in papillary microcarcinoma with emphasis on histologic subtyping: a clinicopathologic study of 148 cases. *Thyroid* 2014;24:245-253
 120. Lecumberri B, Alvarez-Escolá C, Martín-Vaquero P, Nistal M, Martín V, Riesco-Eizaguirre G, et al. Solitary hemorrhagic cerebellar metastasis from occult papillary thyroid microcarcinoma. *Thyroid* 2010;20:563-567
 121. Jeon MJ, Kim WG, Choi YM, Kwon H, Lee YM, Sung TY, et al. Features predictive of distant metastasis in papillary thyroid microcarcinomas. *Thyroid* 2016;26:161-168
 122. Noguchi S, Yamashita H, Uchino S, Watanabe S. Papillary microcarcinoma. *World J Surg* 2008;32:747-753
 123. Roti E, Rossi R, Trasforini G, Bertelli F, Ambrosio MR, Busutti L, et al. Clinical and histological characteristics of papillary thyroid microcarcinoma: results of a retrospective study in 243 patients. *J Clin Endocrinol Metab* 2006;91:2171-2178
 124. Mercante G, Frasoldati A, Pedroni C, Formisano D, Renna L, Piana S, et al. Prognostic factors affecting neck lymph node recurrence and distant metastasis in papillary microcarcinoma of the thyroid: results of a study in 445 patients. *Thyroid* 2009;19:707-716
 125. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. *Thyroid* 2009;19:1159-1165

126. Moon HJ, Kim EK, Yoon JH, Kwak JY. Malignancy risk stratification in thyroid nodules with nondiagnostic results at cytologic examination: combination of thyroid imaging reporting and data system and the Bethesda System. *Radiology* 2015;274:287-295
127. Kim SY, Han KH, Moon HJ, Kwak JY, Chung WY, Kim EK. Thyroid nodules with benign findings at cytologic examination: results of long-term follow-up with US. *Radiology* 2014;271:272-281
128. Rosario PW. Thyroid nodules with atypia or follicular lesions of undetermined significance (Bethesda Category III): importance of ultrasonography and cytological subcategory. *Thyroid* 2014;24:1115-1120
129. Bongiovanni M, Spitale A, Faquin WC, Mazzucchelli L, Baloch ZW. The Bethesda System for Reporting Thyroid Cytopathology: a meta-analysis. *Acta Cytol* 2012;56:333-339
130. Singh RS, Wang HH. Timing of repeat thyroid fine-needle aspiration in the management of thyroid nodules. *Acta Cytol* 2011;55:544-548
131. Lubitz CC, Nagarkatti SS, Faquin WC, Samir AE, Hassan MC, Barbesino G, et al. Diagnostic yield of nondiagnostic thyroid nodules is not altered by timing of repeat biopsy. *Thyroid* 2012;22:590-594
132. Yeon JS, Baek JH, Lim HK, Ha EJ, Kim JK, Song DE, et al. Thyroid nodules with initially nondiagnostic cytologic results: the role of core-needle biopsy. *Radiology* 2013;268:274-280
133. Samir AE, Vij A, Seale MK, Desai G, Halpern E, Faquin WC, et al. Ultrasound-guided percutaneous thyroid nodule core biopsy: clinical utility in patients with prior nondiagnostic fine-needle aspirate. *Thyroid* 2012;22:461-467
134. Na DG, Kim JH, Sung JY, Baek JH, Jung KC, Lee H, et al. Core-needle biopsy is more useful than repeat fine-needle aspiration in thyroid nodules read as nondiagnostic or atypia of undetermined significance by the Bethesda system for reporting thyroid cytopathology. *Thyroid* 2012;22:468-475
135. Choi SH, Baek JH, Lee JH, Choi YJ, Hong MJ, Song DE, et al. Thyroid nodules with initially non-diagnostic, fine-needle aspiration results: comparison of core-needle biopsy and repeated fine-needle aspiration. *Eur Radiol* 2014;24:2819-2826
136. Ha EJ, Baek JH, Lee JH, Song DE, Kim JK, Shong YK, et al. Sonographically suspicious thyroid nodules with initially benign cytologic results: the role of a core needle biopsy. *Thyroid* 2013;23:703-708
137. Kwak JY, Kim EK, Kim HJ, Kim MJ, Son EJ, Moon HJ. How to combine ultrasound and cytological information in decision making about thyroid nodules. *Eur Radiol* 2009;19:1923-1931
138. Kwak JY, Koo H, Youk JH, Kim MJ, Moon HJ, Son EJ, et al. Value of US correlation of a thyroid nodule with initially benign cytologic results. *Radiology* 2010;254:292-300
139. Chernyavsky VS, Shanker BA, Davidov T, Crystal JS, Eng O, Ibrahim K, et al. Is one benign fine needle aspiration enough? *Ann Surg Oncol* 2012;19:1472-1476
140. Shin JH, Han BK, Ko K, Choe YH, Oh YL. Value of repeat ultrasound-guided fine-needle aspiration in nodules with benign cytological diagnosis. *Acta Radiol* 2006;47:469-473
141. Hwang SH, Sung JM, Kim EK, Moon HJ, Kwak JY. Imaging-cytology correlation of thyroid nodules with initially benign cytology. *Int J Endocrinol* 2014;2014:491508
142. Moon HJ, Kim EK, Kwak JY. Malignancy risk stratification in thyroid nodules with benign results on cytology: combination of thyroid imaging reporting and data system and Bethesda system. *Ann Surg Oncol* 2014;21:1898-1903
143. Rosário PW, Calsolari MR. What is the best criterion for repetition of fine-needle aspiration in thyroid nodules with initially benign cytology? *Thyroid* 2015;25:1115-1120
144. Chehade JM, Silverberg AB, Kim J, Case C, Mooradian AD. Role of repeated fine-needle aspiration of thyroid nodules with benign cytologic features. *Endocr Pract* 2001;7:237-243
145. Orlandi A, Puscar A, Capriata E, Fideleff H. Repeated fine-needle aspiration of the thyroid in benign nodular thyroid disease: critical evaluation of long-term follow-up. *Thyroid* 2005;15:274-278
146. Pinchot SN, Al-Wagih H, Schaefer S, Sippel R, Chen H. Accuracy of fine-needle aspiration biopsy for predicting neoplasm or carcinoma in thyroid nodules 4 cm or larger. *Arch Surg* 2009;144:649-655
147. Carrillo JF, Frias-Mendivil M, Ochoa-Carrillo FJ, Ibarra M. Accuracy of fine-needle aspiration biopsy of the thyroid combined with an evaluation of clinical and radiologic factors. *Otolaryngol Head Neck Surg* 2000;122:917-921
148. Albuja-Cruz MB, Goldfarb M, Gondek SS, Allan BJ, Lew JJ. Reliability of fine-needle aspiration for thyroid nodules greater than or equal to 4 cm. *J Surg Res* 2013;181:6-10
149. Porterfield JR Jr, Grant CS, Dean DS, Thompson GB, Farley DR, Richards ML, et al. Reliability of benign fine needle aspiration cytology of large thyroid nodules. *Surgery* 2008;144:963-968; discussion 968-969
150. Kuru B, Gulcelik NE, Gulcelik MA, Dincer H. The false-negative rate of fine-needle aspiration cytology for diagnosing thyroid carcinoma in thyroid nodules. *Langenbecks Arch Surg* 2010;395:127-132
151. Yoon JH, Kwak JY, Moon HJ, Kim MJ, Kim EK. The diagnostic accuracy of ultrasound-guided fine-needle aspiration biopsy and the sonographic differences between benign and malignant thyroid nodules 3 cm or larger. *Thyroid* 2011;21:993-1000
152. Nou E, Kwong N, Alexander LK, Cibas ES, Marqusee E, Alexander EK. Determination of the optimal time interval for repeat evaluation after a benign thyroid nodule aspiration. *J Clin Endocrinol Metab* 2014;99:510-516
153. Nakamura H, Hirokawa M, Ota H, Kihara M, Miya A, Miyauchi A. Is an increase in thyroid nodule volume a risk factor for malignancy? *Thyroid* 2015;25:804-811
154. Ho AS, Sarti EE, Jain KS, Wang H, Nixon IJ, Shaha AR, et al. Malignancy rate in thyroid nodules classified as Bethesda category III (AUS/FLUS). *Thyroid* 2014;24:832-839
155. Faquin WC, Baloch ZW. Fine-needle aspiration of follicular patterned lesions of the thyroid: Diagnosis, management,

- and follow-up according to National Cancer Institute (NCI) recommendations. *Diagn Cytopathol* 2010;38:731-739
156. Kim DW, Lee EJ, Jung SJ, Ryu JH, Kim YM. Role of sonographic diagnosis in managing Bethesda class III nodules. *AJNR Am J Neuroradiol* 2011;32:2136-2141
 157. Gweon HM, Son EJ, Youk JH, Kim JA. Thyroid nodules with Bethesda system III cytology: can ultrasonography guide the next step? *Ann Surg Oncol* 2013;20:3083-3088
 158. Yoo WS, Choi HS, Cho SW, Moon JH, Kim KW, Park HJ, et al. The role of ultrasound findings in the management of thyroid nodules with atypia or follicular lesions of undetermined significance. *Clin Endocrinol (Oxf)* 2014;80:735-742
 159. Jeong SH, Hong HS, Lee EH, Cha JG, Park JS, Kwak JJ. Outcome of thyroid nodules characterized as atypia of undetermined significance or follicular lesion of undetermined significance and correlation with Ultrasound features and BRAF(V600E) mutation analysis. *AJR Am J Roentgenol* 2013;201:W854-W860
 160. Bongiovanni M, Krane JF, Cibas ES, Faquin WC. The atypical thyroid fine-needle aspiration: past, present, and future. *Cancer Cytopathol* 2012;120:73-86
 161. Hyeon J, Ahn S, Shin JH, Oh YL. The prediction of malignant risk in the category "atypia of undetermined significance/follicular lesion of undetermined significance" of the Bethesda System for Reporting Thyroid Cytopathology using subcategorization and BRAF mutation results. *Cancer Cytopathol* 2014;122:368-376
 162. Sullivan PS, Hirschowitz SL, Fung PC, Apple SK. The impact of atypia/follicular lesion of undetermined significance and repeat fine-needle aspiration: 5 years before and after implementation of the Bethesda System. *Cancer Cytopathol* 2014;122:866-872
 163. Renshaw AA. Does a repeated benign aspirate change the risk of malignancy after an initial atypical thyroid fine-needle aspiration? *Am J Clin Pathol* 2010;134:788-792
 164. VanderLaan PA, Marqusee E, Krane JF. Clinical outcome for atypia of undetermined significance in thyroid fine-needle aspirations: should repeated fna be the preferred initial approach? *Am J Clin Pathol* 2011;135:770-775
 165. Wu HH, Inman A, Cramer HM. Subclassification of "atypia of undetermined significance" in thyroid fine-needle aspirates. *Diagn Cytopathol* 2014;42:23-29
 166. Park KT, Ahn SH, Mo JH, Park YJ, Park do J, Choi SI, et al. Role of core needle biopsy and ultrasonographic finding in management of indeterminate thyroid nodules. *Head Neck* 2011;33:160-165
 167. Hahn SY, Shin JH, Han BK, Ko EY, Ko ES. Ultrasonography-guided core needle biopsy for the thyroid nodule: does the procedure hold any benefit for the diagnosis when fine-needle aspiration cytology analysis shows inconclusive results? *Br J Radiol* 2013;86:20130007
 168. Lee KH, Shin JH, Oh YL, Hahn SY. Atypia of undetermined significance in thyroid fine-needle aspiration cytology: prediction of malignancy by US and comparison of methods for further management. *Ann Surg Oncol* 2014;21:2326-2331
 169. Na DG, Min HS, Lee H, Won JK, Seo HB, Kim JH. Role of core needle biopsy in the management of atypia/follicular lesion of undetermined significance thyroid nodules: comparison with repeat fine-needle aspiration in subcategory nodules. *Eur Thyroid J* 2015;4:189-196
 170. Bernet V, Hupart KH, Parangi S, Woeber KA. AACE/ACE disease state commentary: molecular diagnostic testing of thyroid nodules with indeterminate cytopathology. *Endocr Pract* 2014;20:360-363
 171. Ferris RL, Baloch Z, Bernet V, Chen A, Fahey TJ 3rd, Ganly I, et al. American thyroid association statement on surgical application of molecular profiling for thyroid nodules: current impact on perioperative decision making. *Thyroid* 2015;25:760-768
 172. Kwak JY, Kim EK, Kim MJ, Hong SW, Choi SH, Son EJ, et al. The role of ultrasound in thyroid nodules with a cytology reading of "suspicious for papillary thyroid carcinoma". *Thyroid* 2008;18:517-522
 173. Mulla M, Schulte KM. Central cervical lymph node metastases in papillary thyroid cancer: a systematic review of imaging-guided and prophylactic removal of the central compartment. *Clin Endocrinol (Oxf)* 2012;76:131-136
 174. Rotstein L. The role of lymphadenectomy in the management of papillary carcinoma of the thyroid. *J Surg Oncol* 2009;99:186-188
 175. Sivanandan R, Soo KC. Pattern of cervical lymph node metastases from papillary carcinoma of the thyroid. *Br J Surg* 2001;88:1241-1244
 176. Randolph GW, Duh QY, Heller KS, LiVolsi VA, Mandel SJ, Steward DL, et al. The prognostic significance of nodal metastases from papillary thyroid carcinoma can be stratified based on the size and number of metastatic lymph nodes, as well as the presence of extranodal extension. *Thyroid* 2012;22:1144-1152
 177. Amdur RJ, Mazzaferri EL. *Essentials of Thyroid Cancer Management*. New York: Springer, 2005:212-215
 178. Spate VL, Morris JS, Nichols TA, Baskett CK, Mason MM, Horsman TL, et al. Longitudinal study of iodine in toenails following IV administration of an iodine containing contrast agent. *J Radioanal Nucl Chem* 1998;236:71-76
 179. Padovani RP, Kasamatsu TS, Nakabashi CC, Camacho CP, Andreoni DM, Malouf EZ, et al. One month is sufficient for urinary iodine to return to its baseline value after the use of water-soluble iodinated contrast agents in post-thyroidectomy patients requiring radioiodine therapy. *Thyroid* 2012;22:926-930
 180. Sohn SY, Choi JH, Kim NK, Joung JY, Cho YY, Park SM, et al. The impact of iodinated contrast agent administered during preoperative computed tomography scan on body iodine pool in patients with differentiated thyroid cancer preparing for radioactive iodine treatment. *Thyroid* 2014;24:872-877
 181. Ho JD, Tsang JF, Scoggan KA, Leslie WD. Urinary iodine clearance following iodinated contrast administration: a comparison of euthyroid and postthyroidectomy subjects. *J Thyroid Res* 2014;2014:580569

182. Mishra A, Pradhan PK, Gambhir S, Sabaretnam M, Gupta A, Babu S. Preoperative contrast-enhanced computerized tomography should not delay radioiodine ablation in differentiated thyroid carcinoma patients. *J Surg Res* 2015;193:731-737
183. Tala Jury HP, Castagna MG, Fioravanti C, Cipri C, Brianzoni E, Pacini F. Lack of association between urinary iodine excretion and successful thyroid ablation in thyroid cancer patients. *J Clin Endocrinol Metab* 2010;95:230-237
184. 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;18:411-418
185. Ahn JE, Lee JH, Yi JS, Shong YK, Hong SJ, Lee DH, et al. Diagnostic accuracy of CT and ultrasonography for evaluating metastatic cervical lymph nodes in patients with thyroid cancer. *World J Surg* 2008;32:1552-1558
186. Lesnik D, Cunnane ME, Zurakowski D, Acar GO, Ecevit C, Mace A, et al. Papillary thyroid carcinoma nodal surgery directed by a preoperative radiographic map utilizing CT scan and ultrasound in all primary and reoperative patients. *Head Neck* 2014;36:191-202
187. Lee DW, Ji YB, Sung ES, Park JS, Lee YJ, Park DW, et al. Roles of ultrasonography and computed tomography in the surgical management of cervical lymph node metastases in papillary thyroid carcinoma. *Eur J Surg Oncol* 2013;39:191-196
188. Yeh MW, Bauer AJ, Bernet VA, Ferris RL, Loevner LA, Mandel SJ, et al. American Thyroid Association statement on preoperative imaging for thyroid cancer surgery. *Thyroid* 2015;25:3-14
189. 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;193:871-878
190. Leenhardt L, Erdogan MF, Hegedus L, Mandel SJ, Paschke R, Rago T, et al. 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. *Eur Thyroid J* 2013;2:147-159
191. 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
192. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, et al. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. *J Clin Endocrinol Metab* 2007;92:3590-3594
193. Ito Y, Jikuzono T, Higashiyama T, Asahi S, Tomoda C, Takamura Y, et al. Clinical significance of lymph node metastasis of thyroid papillary carcinoma located in one lobe. *World J Surg* 2006;30:1821-1828
194. Sywak M, Cornford L, Roach P, Stalberg P, Sidhu S, Delbridge L. Routine ipsilateral level VI lymphadenectomy reduces postoperative thyroglobulin levels in papillary thyroid cancer. *Surgery* 2006;140:1000-1005; discussion 1005-1007
195. Hwang HS, Orloff LA. Efficacy of preoperative neck ultrasound in the detection of cervical lymph node metastasis from thyroid cancer. *Laryngoscope* 2011;121:487-491
196. Gemenjäger E, Perren A, Seifert B, Schüller G, Schweizer I, Heitz PU. Lymph node surgery in papillary thyroid carcinoma. *J Am Coll Surg* 2003;197:182-190
197. Cranshaw IM, Carnaille B. Micrometastases in thyroid cancer. An important finding? *Surg Oncol* 2008;17:253-258
198. Bardet S, Malville E, Rame JP, Babin E, Samama G, De Raucourt D, et al. Macroscopic lymph-node involvement and neck dissection predict lymph-node recurrence in papillary thyroid carcinoma. *Eur J Endocrinol* 2008;158:551-560
199. Ito Y, Tomoda C, Uruno T, Takamura Y, Miya A, Kobayashi K, 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
200. Bardet S, Ciappuccini R, Quak E, Rame JP, Blanchard D, de Raucourt D, et al. Prognostic value of microscopic lymph node involvement in patients with papillary thyroid cancer. *J Clin Endocrinol Metab* 2015;100:132-140
201. Rondeau G, Fish S, Hann LE, Fagin JA, Tuttle RM. Ultrasonographically detected small thyroid bed nodules identified after total thyroidectomy for differentiated thyroid cancer seldom show clinically significant structural progression. *Thyroid* 2011;21:845-853
202. Robenshtok E, Fish S, Bach A, Domínguez JM, Shaha A, Tuttle RM. Suspicious cervical lymph nodes detected after thyroidectomy for papillary thyroid cancer usually remain stable over years in properly selected patients. *J Clin Endocrinol Metab* 2012;97:2706-2713
203. Na DG, Lee JH, Jung SL, Kim JH, Sung JY, Shin JH, et al. Radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: consensus statement and recommendations. *Korean J Radiol* 2012;13:117-125
204. Bennedbaek FN, Nielsen LK, Hegedüs L. Effect of percutaneous ethanol injection therapy versus suppressive doses of L-thyroxine on benign solitary solid cold thyroid nodules: a randomized trial. *J Clin Endocrinol Metab* 1998;83:830-835
205. Sung JY, Baek JH, Kim KS, Lee D, Yoo H, Kim JK, et al. Single-session treatment of benign cystic thyroid nodules with ethanol versus radiofrequency ablation: a prospective randomized study. *Radiology* 2013;269:293-300
206. Sung JY, Kim YS, Choi H, Lee JH, Baek JH. Optimum first-line treatment technique for benign cystic thyroid nodules: ethanol ablation or radiofrequency ablation? *AJR Am J Roentgenol* 2011;196:W210-W214
207. Døssing H, Bennedbæk FN, Hegedüs L. Long-term outcome following interstitial laser photocoagulation of benign cold thyroid nodules. *Eur J Endocrinol* 2011;165:123-128
208. Lim HK, Lee JH, Ha EJ, Sung JY, Kim JK, Baek JH. Radiofrequency ablation of benign non-functioning thyroid

- nodules: 4-year follow-up results for 111 patients. *Eur Radiol* 2013;23:1044-1049
209. Sung JY, Baek JH, Jung SL, Kim JH, Kim KS, Lee D, et al. Radiofrequency ablation for autonomously functioning thyroid nodules: a multicenter study. *Thyroid* 2015;25:112-117
210. Valcavi R, Riganti F, Bertani A, Formisano D, Pacella CM. Percutaneous laser ablation of cold benign thyroid nodules: a 3-year follow-up study in 122 patients. *Thyroid* 2010;20:1253-1261
211. Papini E, Rago T, Gambelunghe G, Valcavi R, Bizzarri G, Vitti P, et al. Long-term efficacy of ultrasound-guided laser ablation for benign solid thyroid nodules. Results of a three-year multicenter prospective randomized trial. *J Clin Endocrinol Metab* 2014;99:3653-3659
212. Ha EJ, Baek JH, Kim KW, Pyo J, Lee JH, Baek SH, et al. Comparative efficacy of radiofrequency and laser ablation for the treatment of benign thyroid nodules: systematic review including traditional pooling and bayesian network meta-analysis. *J Clin Endocrinol Metab* 2015;100:1903-1911