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

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Abstract

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 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 Korean Society of Thyroid Radiology 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.

Keywords: Thyroid nodule; Thyroid neoplasm; Lymph nodes; Ultrasonography; Multidetector Computed Tomography; Ablation Techniques

Abbreviations

Ultrasonography (US)

Fine-needle aspiration (FNA)

Core needle biopsy (CNB)

Papillary thyroid carcinoma (PTC)

Korean Society of Thyroid Radiology (KSThR)

Korean Thyroid Imaging Reporting and Data System (K-TIRADS)

Extrathyroidal extension (ETE)

Atypia (follicular lesion) of undetermined significance (AUS/FLUS)

Follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN)

Lymph node (LN)

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, 2, 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 fine-needle aspiration (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. 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 lymph node, 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 (≤ 50% of the cystic portion), predominantly cystic (> 50% of the cystic portion), and cystic (no obvious solid content) (Fig. 1, online only). 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 components in more than 50% of the isoechoic partially cystic nodule (Fig. 2, online only). 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) (Fig. 3. online only). 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 (Fig. 4. online only). 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 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 (Fig. 5, online only). 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 (Fig. 6, online only). 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) (Fig. 7, online only). 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). 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 (PI) 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

US 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 (K-TIRADS)

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 (25) (Fig. 8). 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) (Fig. 9–12). 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 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 (Fig. 13, online only). 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 x 100%) (101, 103) or the diameter ratio (abutting diameter/whole tumor diameter x 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 (Fig. 13 and 14, online only).

INDICATIONS FOR US-GUIDED FINE-NEEDLE ASPIRATION

Fine-needle aspiration has been established as a safe, 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 benign category and has a very low malignancy risk (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, history of childhood radiation therapy, familiar thyroid cancer, increased level of calcitonin, and incidentalomas with FDG (^{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 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 (125-128) (Table 3).

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 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 select cases, in order to supplement the findings of malignancy risk assessment (170, 171).

Follicular Neoplasm or Suspicious for a Follicular Neoplasm (FN/SFN) Cytology

Diagnostic surgery is generally recommended for the nodules with 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). Ultrasonography 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 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) (Fig. 15–18). 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 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 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 lymph nodes.

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 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.

Acknowledgments: None

Disclosure Statement

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

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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 ≤ 50%	
	Predominantly cystic	Cystic portion > 50%	
	Cystic	No solid portion	Pure cyst
Echogenicity			
	Marked hypoechogenicity	Hypoechoic relative to the adjacent anterior neck muscle	
	Mild hypoechogenicity	Hypoechoic relative to the thyroid parenchyma	
	Isoechogenicity	Same echogenicity as that of the thyroid parenchyma	
	Hyperechogenicity	Hyperechoic relative to the thyroid parenchyma	
Shape			
	Round to oval	Round or oval regardless of the orientation	
	Irregular	Neither round nor oval	
Orientation			
	Parallel	Anteroposterior diameter shorter or equal to the transverse or longitudinal diameter	
	Nonparallel	Anteroposterior diameter longer than the transverse or longitudinal diameter on the transverse or longitudinal image	Taller-than-wide shape
Margin	Smooth	Obviously discernible smooth edge	Regular, Circumscribed
	Spiculated/microlobulated	Obviously discernible, but a non-smooth edge showing spiculation, microlobulation, or jagged appearance	Irregular, infiltrative, non-smooth,
	Ill-defined	Poorly demarcated margin which cannot be obviously differentiated from the adjacent thyroid tissue	Indistinct
Calcification			
	Microcalcification	Echogenic foci of 1 mm or less with or without posterior acoustic shadowing within the 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 the nodule	
Spongiform			
	Present or absent	Isoechoic nodule with microcystic	Honeycomb

		change greater than 50% of a nodule
Colloid (comet-tail artifact)		
	Present or absent	Echogenic foci with reverberation artifacts within the cystic component
Vascularity		
	Type 1 (none)	Absence of intranodular or perinodular vascularity
	Type 2 (perinodular vascularity)	Presence of circumferential vascularity at the margin of the 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%)

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

Category	US feature	Malignancy risk (%)	Calculated malignancy risk (%) Overall (LV, HV)	Calculated Sensitivity for malignancy (%) Overall (LV, HV)	FNA[d]
5 High suspicion	Solid hypoechoic nodule with any of 3 suspicious US features[a]	> 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[a] or 2) Partially cystic or isohyperechoic nodule with any of 3 suspicious US features[a]	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[a]	3~15	7.8 (6, 10.3)[b]	19.2 (34.2, 13.9)	≥ 1.5 cm
2 Benign[c]	Spongiform	< 3	0	0	≥ 2 cm
	Pure cyst Partially cystic nodule with comet tail artifact	< 1	0	0	NA
1 No nodule	-	-	-	-	NA

Note.— LV and HV indicate low and high cancer volume data, respectively. Solid hypoechoic nodules include solid nodules with marked or mild hypoechogenicity. NA- not applicable for FNA. [a]Microcalcification, nonparallel orientation (taller-than-wide), spiculated/microlobulated margin. [b]Malignancy risk calculated from nodules

excluding spongiform or partially cystic nodules with comet tail artifacts. [c]K-TIRADS 2 (benign category) includes partially cystic nodules with spongiform appearance or comet tail artifacts which do not have any suspicious US feature. [d]FNA is indicated regardless of the size and US feature of a nodule in the 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 the published data (25).

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[a] within 3-6 months[b]
	Intermediate or low suspicion	Repeat FNA or CNB[a] within 6-12 months[b]
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[c]
FN/SFN	All nodules	Diagnostic surgery (lobectomy)[d]
Suspicious malignancy	High or intermediate suspicion	Surgery
	Low suspicion	Repeat FNA or Surgery
		Active surveillance[e]
Malignant	All nodules	Surgery
		Active surveillance[e]

[a]CNB may be considered instead of a repeat FNA if an experienced operator is available.

[b]The optimal timing of the repeat FNA or CNB should be determined by a clinical decision based on the consideration of the nodule size, presence of poor prognostic factors such as a suspected nodal metastasis or gross extrathyroidal extension, and clinical factors as well as the US features.

[c]A close follow-up may be considered depending on the clinical risk factors, US features, patient preference, and, when possible, results of the molecular studies. If the repeat FNA cytology findings are inconclusive, a close follow-up or diagnostic surgery can be considered.

[d]A close follow-up instead of an immediate surgery may be considered in some selected patients based on the consideration of the clinical factors, nodule size, US features, and, when possible, results of the molecular study.

[e]Active surveillance with close follow-up instead of an immediate surgery may be considered in adult patients with a probable or proven low-risk papillary microcarcinoma.

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

Category	US	CT
Suspicious[a]	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[b]	Loss of central hilar echo and absence of central hilar vascularity	Loss of central hilar fat and absence of central hilar vessel enhancement
Benign[c]	Central hilar echo Central hilar vascularity	Central hilar fat Central hilar vessel enhancement

[a]Lymph nodes with any imaging feature for suspicious lymph nodes are included for this category regardless of the presence of any imaging feature for benign or indeterminate lymph nodes.

[b]Lymph nodes not included in the suspicious or benign categories.

[c]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.

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

• Indication of US-FNA : Preoperative evaluation[a]
1) Suspicious lymph node: size > 3–5 mm (short diameter on the US and CT images).
2) Indeterminate lymph node: size > 5 mm (short diameter on the US and CT images)
• Indication of the US-FNA: Postoperative surveillance[a]
Suspicious or indeterminate lymph node: Size > 8–10 mm (short diameter on the US and CT images) [b]

[a]The measurement of the tissue-washout thyroglobulin is recommended for the lymph nodes in the lateral neck and selectively in the central neck.

[b]When the lymph node is close to the vital organ or the non-surgical treatment including image-guided ablation (ethanol or radiofrequency) is taken into account, FNA could be performed even for the smaller lymph nodes.

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

- To reduce the volume of the 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 the compressive symptoms and cosmetic concerns.
- Thermal ablation (radiofrequency or laser) shows high efficacy and safety in the treatment of the benign solid thyroid nodules, and may be considered as a valid alternative to surgery.

FIGURES

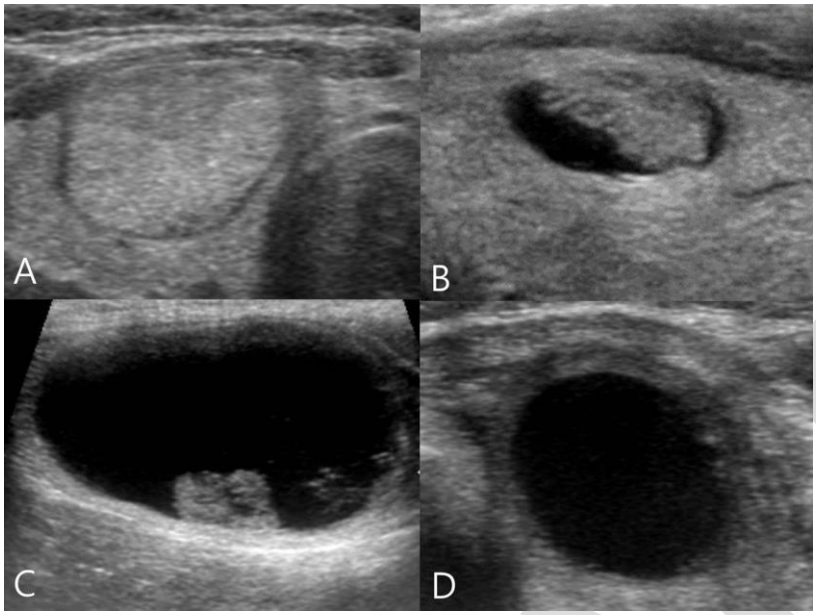

Figure 1. Internal content. A, Solid nodule. B, Predominantly solid nodule. C, Predominantly cystic nodule. D, Cystic nodule. Diagnosis: Benign follicular nodules (A, B, C, D).

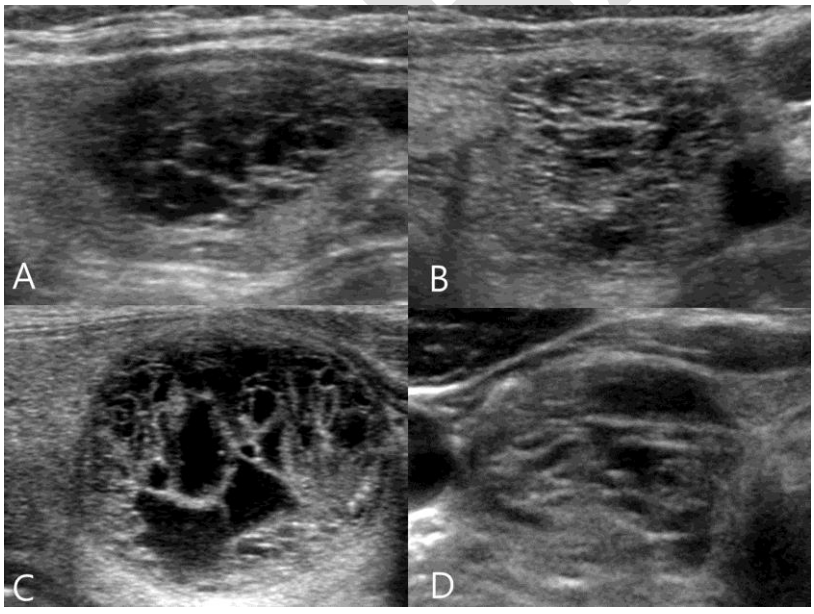

Figure 2. Spongiform appearance. Four partially cystic isoechoic nodules showing typical spongiform appearance. Diagnosis: Benign follicular nodules (A, B, C, D).

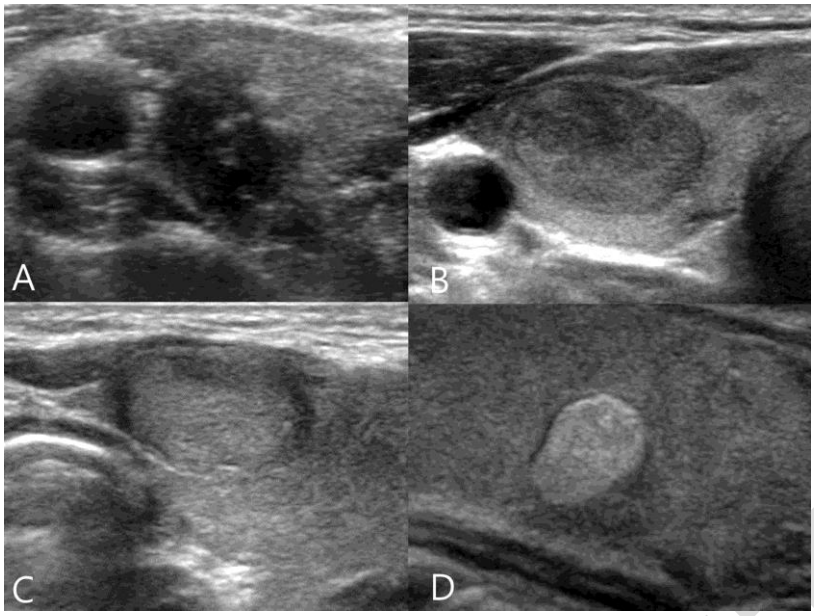

Figure 3. Echogenicity. A, Marked hypoechogenicity. Diagnosis: Papillary carcinoma. B, Mild hypoechogenicity. Diagnosis: Follicular variant papillary carcinoma. C, Isoechogenicity. Diagnosis: Follicular carcinoma (minimally invasive). D, Hyperechogenicity. Diagnosis: Benign follicular nodule.

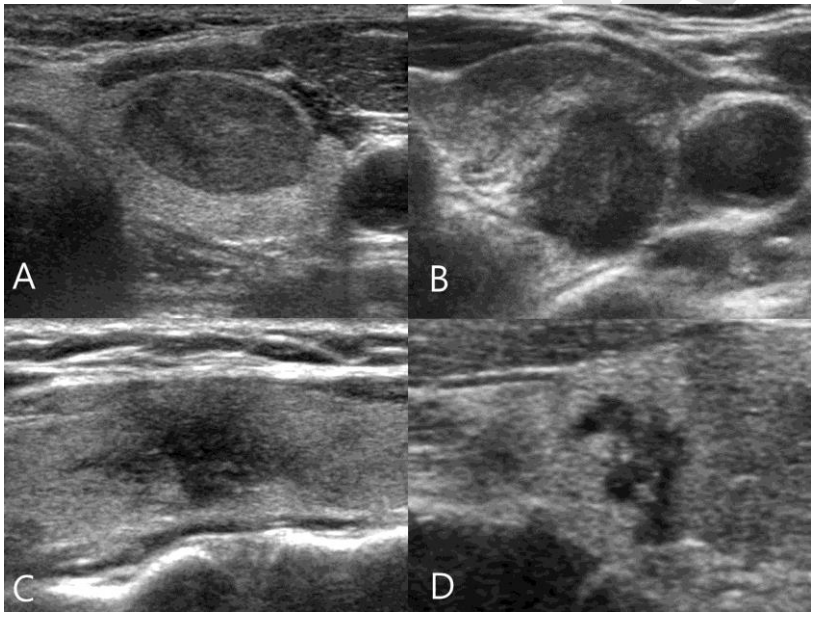

Figure 4. Nodule shape and orientation. A, Ovoid shape and parallel orientation. Diagnosis: Follicular adenoma. B, Ovoid shape and non-parallel orientation. Diagnosis: Papillary carcinoma. C, Irregular shape and parallel orientation. Diagnosis: Subacute granulomatous thyroiditis. D, Irregular shape and non-parallel orientation. Diagnosis: Papillary carcinoma.

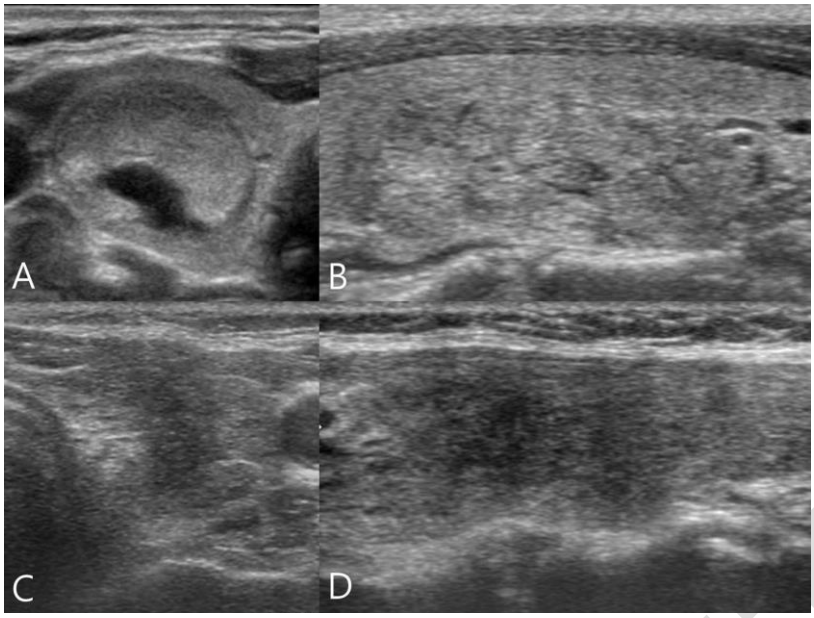

Figure 5. Margin (smooth and ill-defined). A, Smooth margin and a hypoechoic halo. Diagnosis: Benign follicular nodule. B, Ill-defined margin of an isoechoic nodule. Diagnosis: Benign follicular nodule. C, Ill-defined margin of a hypoechoic nodule with nonparallel orientation. Diagnosis: Papillary carcinoma. D, Ill-defined margin of a hypoechoic nodule. Diagnosis: Subacute granulomatous thyroiditis.

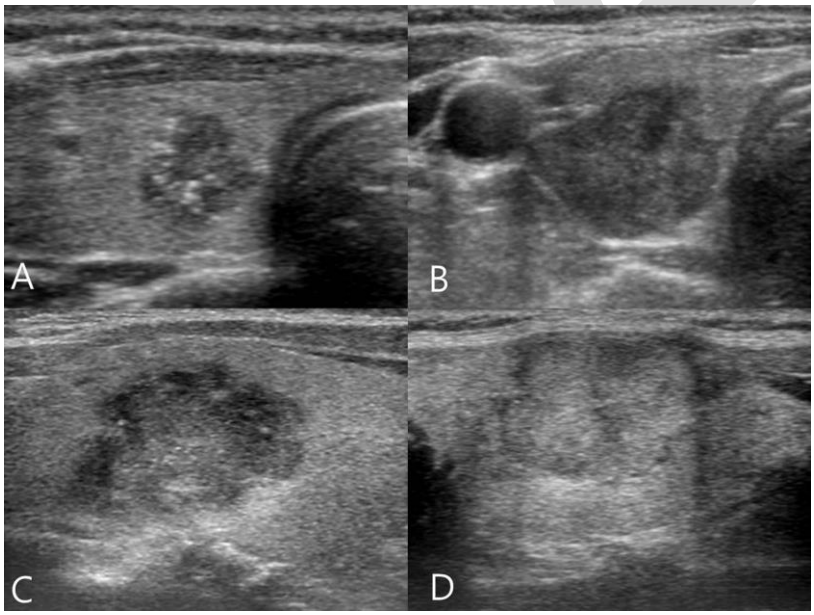

Figure 6. Margin (spiculated/microlobulated). A, Microlobulated margin of a hypoechoic nodule. B, Spiculated margin at the superomedial margin of a hypoechoic nodule. C, Microlobulated margin of a hypoechoic nodule. D, Spiculated and microlobulated margin of an isoechoic nodule. Diagnosis: Papillary carcinoma (A, B, C, D).

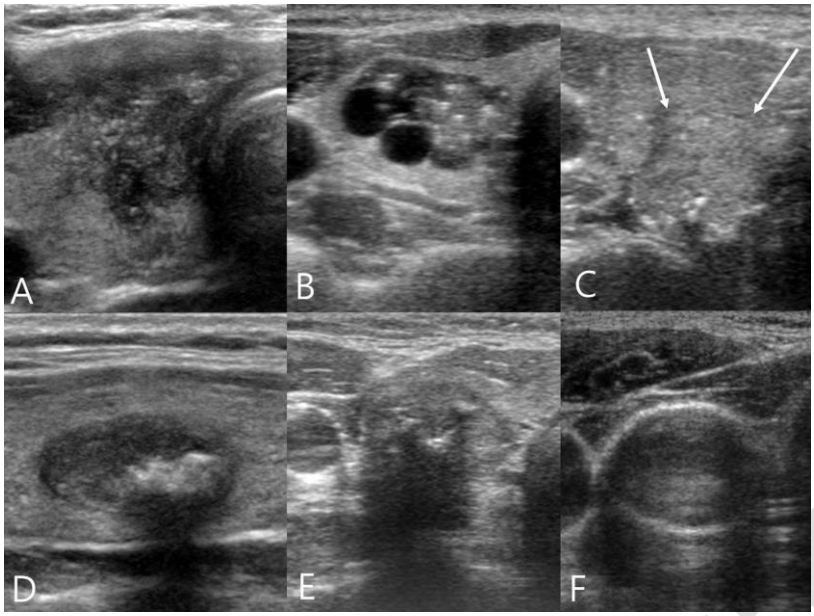

Figure 7. Calcifications. A, Microcalcifications (numerous) in a hypoechoic solid nodule. Diagnosis: Papillary carcinoma. B, Microcalcifications (multiple) in a hypoechoic partially cystic nodule. Diagnosis: Papillary carcinoma. C, Microcalcifications (a few) in an isoechoic solid nodule with ill-defined margin (arrows). Diagnosis: Follicular variant papillary carcinoma. D, Macrocalcification in a hypoechoic solid nodule. Diagnosis: Benign follicular nodule. E, Macrocalcifications in a hypoechoic solid nodule. Diagnosis: Papillary carcinoma. F, Rim calcification. Diagnosis: Follicular carcinoma (minimally invasive).

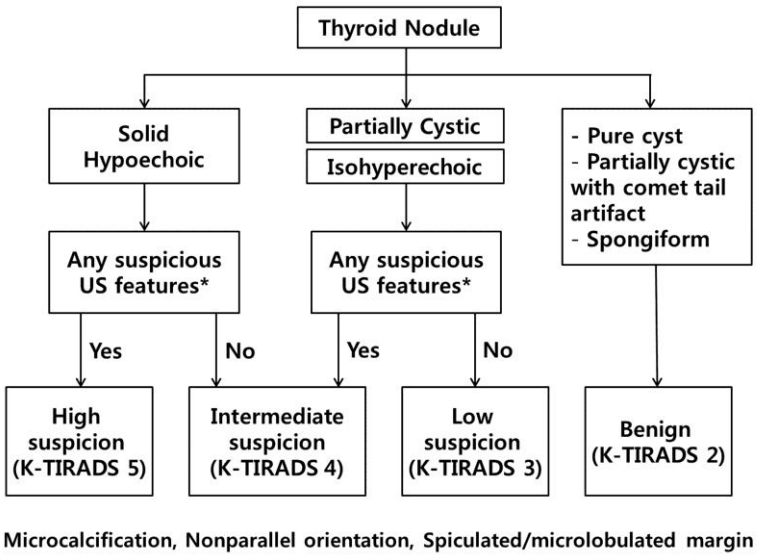

Figure 8. An Algorithm of the K-TIRADS for the malignancy risk stratification based on the solidity and echogenicity of the thyroid nodules. Modified from the published data (25).

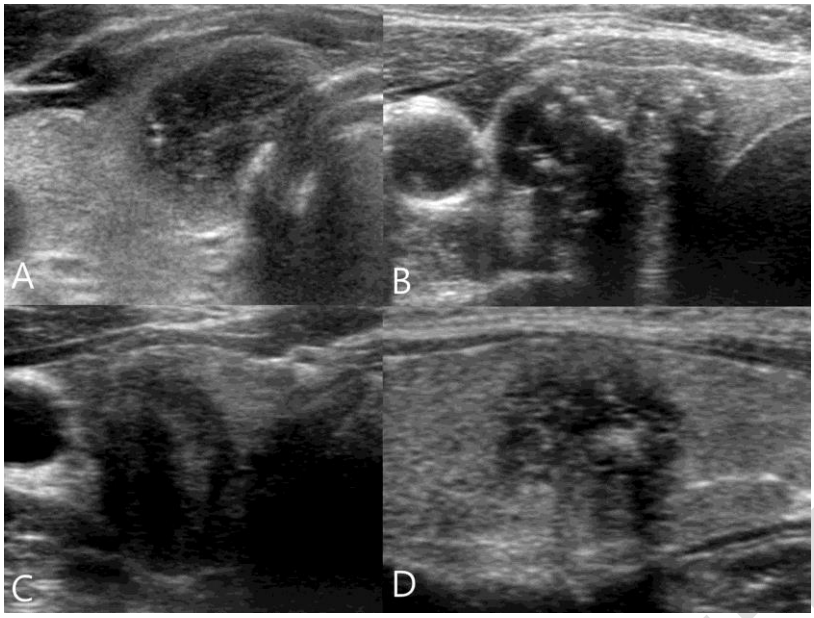

Figure 9. K-TIRADS 5 (high suspicion). A, A solid hypoechoic nodule with microcalcifications. B, A solid hypoechoic nodule with multiple microcalcifications and macrocalcifications. C, A solid hypoechoic nodule with non-parallel orientation. D, A solid hypoechoic nodule with spiculated/microlobulated margin. Diagnosis: Papillary carcinoma (A, B, C, D).

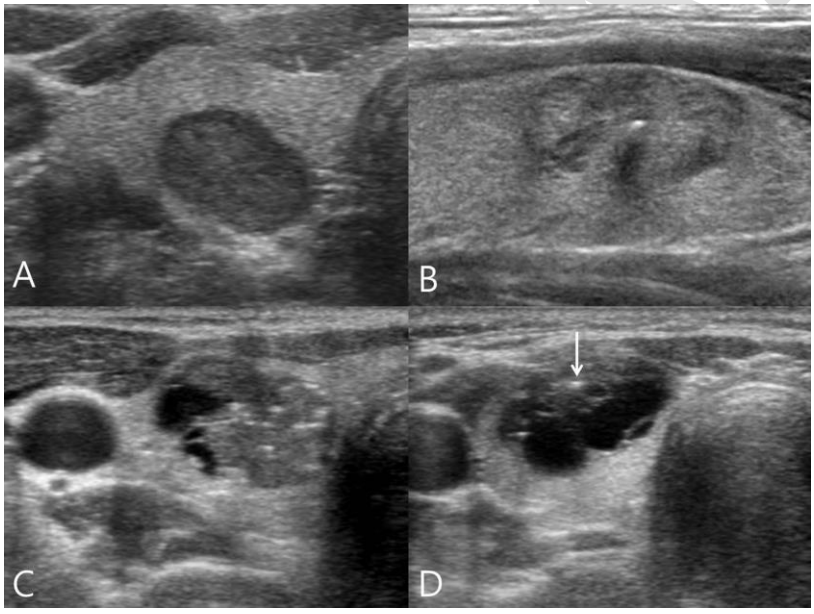

Figure 10. K-TIRADS 4 (intermediate suspicion). A, A solid hypoechoic nodule without suspicious US features. Diagnosis: Benign follicular nodule. B, A solid isoechoic (predominantly isoechoic) nodule with microcalcification. Diagnosis: Benign follicular nodule. C, A predominantly solid hypoechoic nodule with multiple microcalcifications. Diagnosis: Papillary carcinoma. D, A predominantly cystic hypoechoic nodule with a microcalcification (arrow). Diagnosis: Diagnosis: Papillary carcinoma.

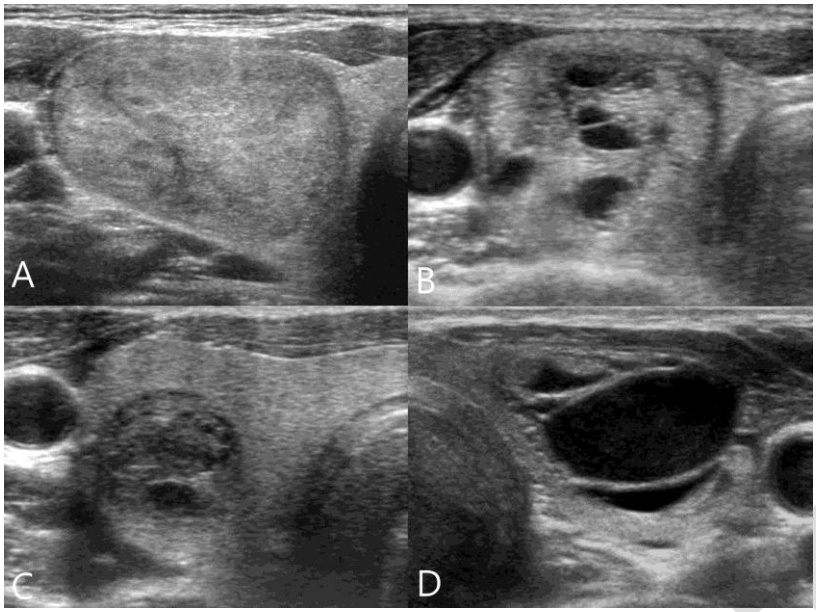

Figure 11. K-TIRADS 3 (low suspicion). None of the nodules have any suspicious US features such as microcalcification, non-parallel orientation, and spiculated/microlobulated margins. A, A solid isoechoic nodule. Diagnosis: Follicular variant papillary carcinoma. B, A predominantly solid and isoechoic nodule. Diagnosis: Benign follicular nodule. C, A predominantly solid and hypoechoic nodule. Diagnosis: Benign follicular nodule. D, A predominantly cystic and isoechoic nodule. Diagnosis: Benign follicular nodule.

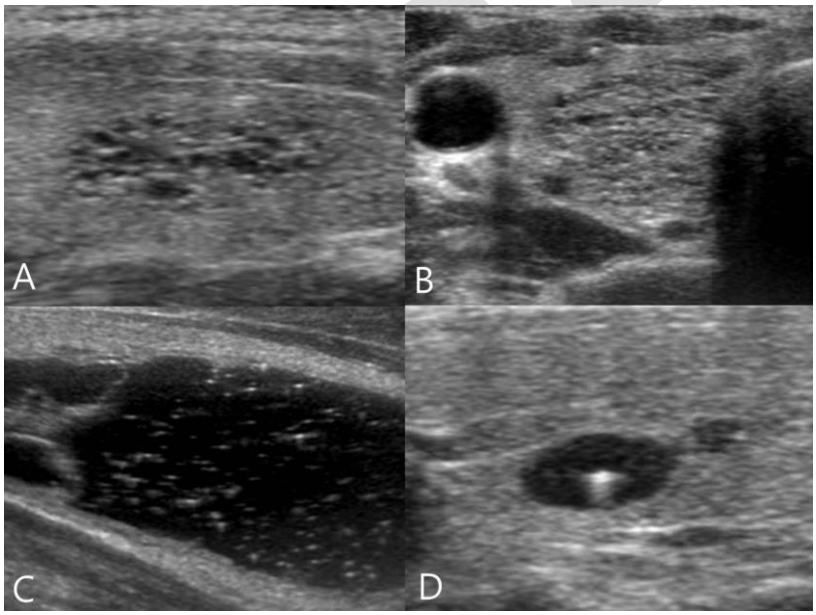

Figure 12. K-TIRADS 2 (Benign). A, A spongiform nodule. Diagnosis: Benign (FNA not performed). B, A spongiform nodule with tiny microcystic changes. Diagnosis: Benign follicular nodule. C, A predominantly cystic nodule with multiple comet tail artifacts. Diagnosis: Benign follicular nodule with a colloid. D, A cyst with a comet-tail artifact. Diagnosis: Benign (colloid

cyst, FNA not performed).

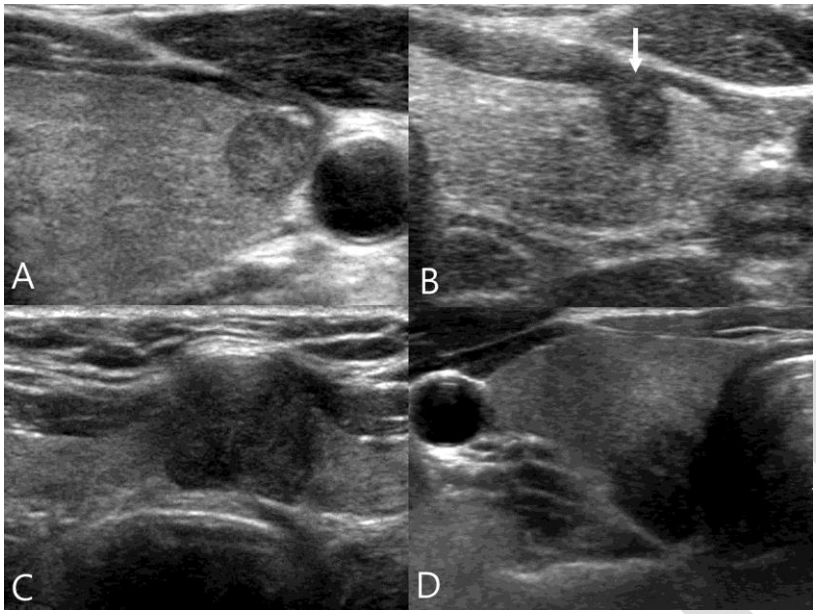

Figure 13. Extrathyroidal extension. A, Capsule abutment. Surgery: Microscopic extrathyroidal extension (pT3). B, Capsular disruption (arrow). Surgery: Microscopic extrathyroidal extension (pT3). C, Capsular protrusion. Surgery: Gross extrathyroidal extension with invasion of anterior strap muscle (pT3). D, Capsular protrusion with loss of intervening normal thyroid parenchyma between the nodule and inferomedial tracheal wall. Surgery: Gross extrathyroidal extension with invasion of the recurrent laryngeal nerve (pT4a). Diagnosis: Papillary carcinoma (A, B, C, D).

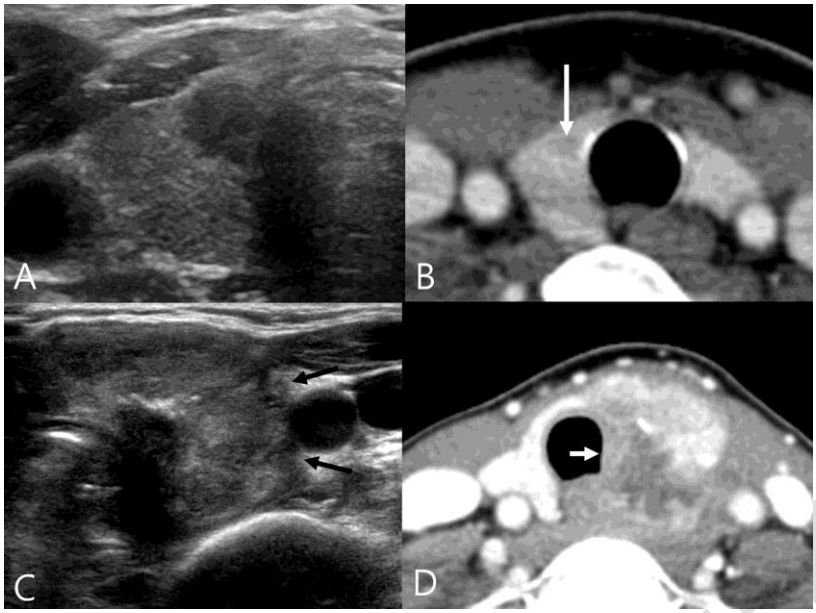

Figure 14. Extrathyroidal extension (tracheal invasion). A, B. Minimal invasion of the peritracheal tissue. The US image shows a nodule abutting the trachea at an obtuse angle (A). The CT image shows no intraluminal tumor invasion (B, arrow). Surgery: Extrathyroidal tumor invasion of the tracheal adventitia (pT4a). Diagnosis: Papillary carcinoma; C, D. Intraluminal tumor invasion of the trachea. The US image shows a large nodule encircling the trachea and a suspicious gross extrathyroidal extension (C, arrows). The CT image reveals an infiltrative large tumor with the intraluminal involvement of the trachea (D, arrow). Surgery: Extensive intraluminal tracheal invasion (pT4a). Diagnosis: Papillary carcinoma.

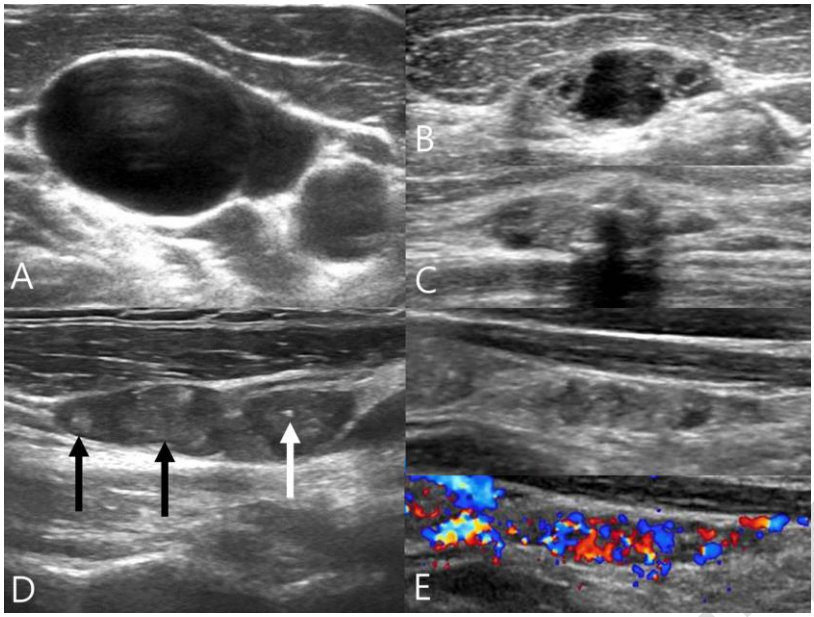

Figure 15. Suspicious lymph nodes (US features). A, A large cystic nodal mass. B, A small focal cystic change and hyperechogenicity in the lymph node. C, Hyperechogenicity and macrocalcifications in the lymph node. D, Multifocal hyperechogenicity (black arrows) and a microcalcification (white arrow) in the lymph node. E, Hyperechogenicity, microcalcification, and abnormal hypervascularity in the lymph node. Diagnosis: Metastatic papillary carcinoma (A, B, C, D, E).

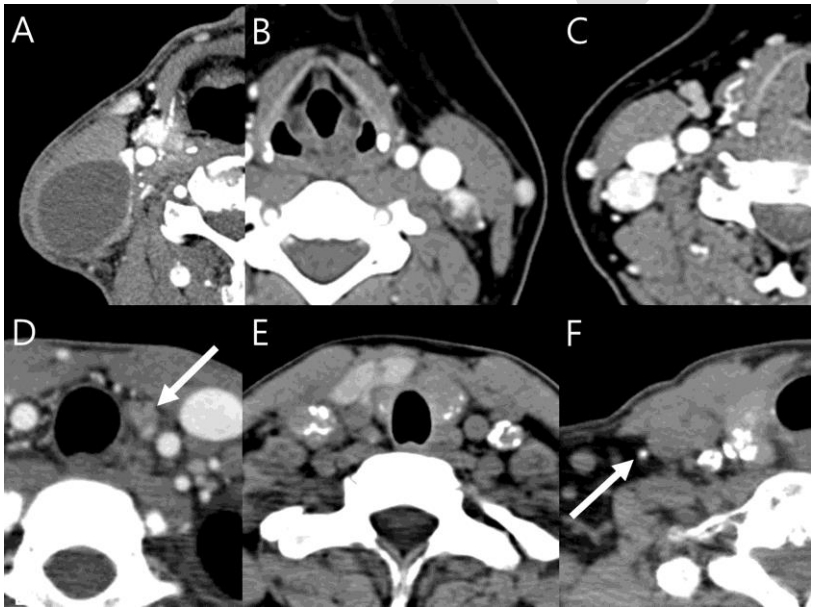

Figure 16. Suspicious lymph nodes (CT features). A, A large nonenhancing cystic nodal mass. B, A small focal cystic change and a strong enhancement in the lymph node. C, A diffuse, strong enhancement in the lymph node. D, A heterogeneous mild enhancement in the lymph node. E, F. Multiple variable-sized nodal calcifications and a tiny nodal calcification (F, arrow) on an

unenhanced CT image. Diagnosis: Metastatic papillary carcinoma (A, B, C, D, E, F).

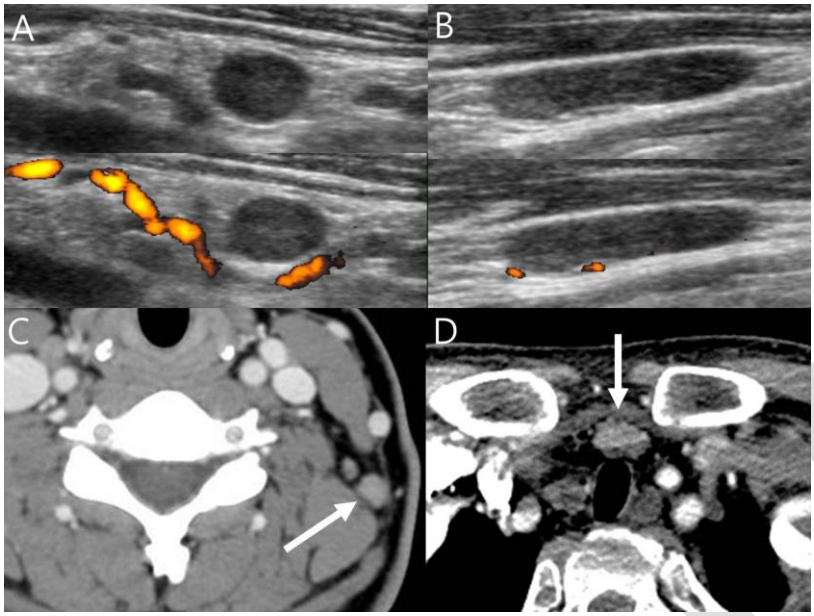

Figure 17. Indeterminate lymph nodes. A, B. The US features of the indeterminate lymph nodes. The US images shows ovoid and elongated lymph nodes which show loss of central echogenic hilum and central hilar vascularity. Note the absence of any suspicious US feature in these nodes. Diagnosis: Probable benign lymph node (FNA not performed). C, D. The CT features of the indeterminate lymph nodes. The CT images show lymph nodes that do not have a central fat hilum and central hilar vessel enhancement. Note the absence of any suspicious CT feature in these nodes. Diagnosis: Probable benign lymph node (C, FNA not performed), metastatic papillary carcinoma (D).

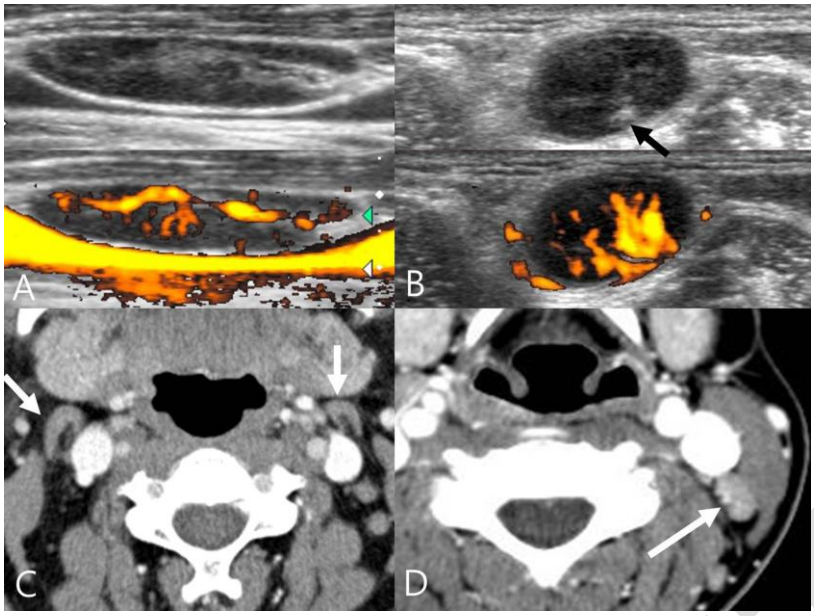

Figure 18. Benign lymph nodes. A, B. The US features of the benign lymph nodes. The US image shows an elongated lymph node with a prominent central echogenic hilum and central hilar vascularity (A). The US image shows an ovoid lymph node with a small deformed echogenic hilum (arrow), however, color-Doppler US shows the prominent typical central hilar vascularity (B). C, D. The CT features of the benign lymph nodes. The CT image shows a lymph node with a central hilar fat (C, arrows) and an enhanced lymph node with central hilar vessel enhancement (D). Diagnosis: Benign lymph node (A, B, C, D, FNA not performed).