Thyroid Incidentalomas
Practice Considerations for Radiologists in the Age of Incidental Findings

Xuan V. Nguyen, MD, PhD[a,*], Joici Job, MD[a], Lauren E. Fiorillo, MD[b], Jennifer Sipos, MD[c]

KEYWORDS

• Thyroid • Incidentaloma • Nodule • ACR TI-RADS • Thyroid cancer

KEY POINTS

- Thyroid incidentalomas are very common and can be initially detected on computed tomography, MR, ultrasound, PET, or other modalities.
- Most thyroid nodules are benign, and most malignant nodules are papillary carcinomas with a favorable prognosis.
- Appropriateness of dedicated sonographic evaluation of incidental thyroid nodules depends on nodule size, presence of aggressive imaging features, patient age, and absence of comorbidities that limit life expectancy.
- Thyroid ultrasound permits stratification of malignancy risk of thyroid incidentalomas and can guide decisions for biopsy or follow-up with imaging.

INTRODUCTION

In routine clinical practice, radiologists are very likely to encounter incidental thyroid abnormalities during interpretation of imaging studies of the neck, chest, or spine. Occasionally, a diffuse thyroid abnormality, such as goiter, may be incidentally encountered (**Fig. 1**), particularly in areas with iodine deficiency, but this article will primarily discuss recent literature relevant to the thyroid incidentaloma or incidental thyroid nodule (ITN), a term that refers to an asymptomatic thyroid nodule identified on imaging studies not specifically intended for assessment of thyroid pathologic conditions. Although incidental detection of an ITN often leads to further evaluation to exclude or diagnose malignancy, fortunately, most ITNs are benign,[1] and most thyroid cancers are papillary thyroid carcinomas, which generally have an excellent prognosis.[2] Familiarity with existing guidelines and evidence-based recommendations regarding ITNs will enable radiologists to more effectively and appropriately communicate the significance of incidentally detected abnormalities to patients and referring providers.

PREVALENCE OF THYROID INCIDENTALOMAS

A familiarity with ITNs is crucial because they are exceedingly common in clinical and radiology practice, with reported prevalence varying by the examined population and assessment

[a] Division of Neuroradiology, Department of Radiology, The Ohio State University Wexner Medical Center, 395 West 12th Avenue, Columbus, OH 43210, USA; [b] Division of Abdominal Imaging, Department of Radiology, The Ohio State University Wexner Medical Center, 395 West 12th Avenue, Columbus, OH 43210, USA; [c] Division of Endocrinology, Diabetes, and Metabolism, The Ohio State University Wexner Medical Center, 1581 Dodd Drive, McCampbell Hall, Columbus, OH 43210, USA
* Corresponding author.
E-mail address: Xuan.Nguyen@osumc.edu

Radiol Clin N Am 58 (2020) 1019–1031
https://doi.org/10.1016/j.rcl.2020.06.005

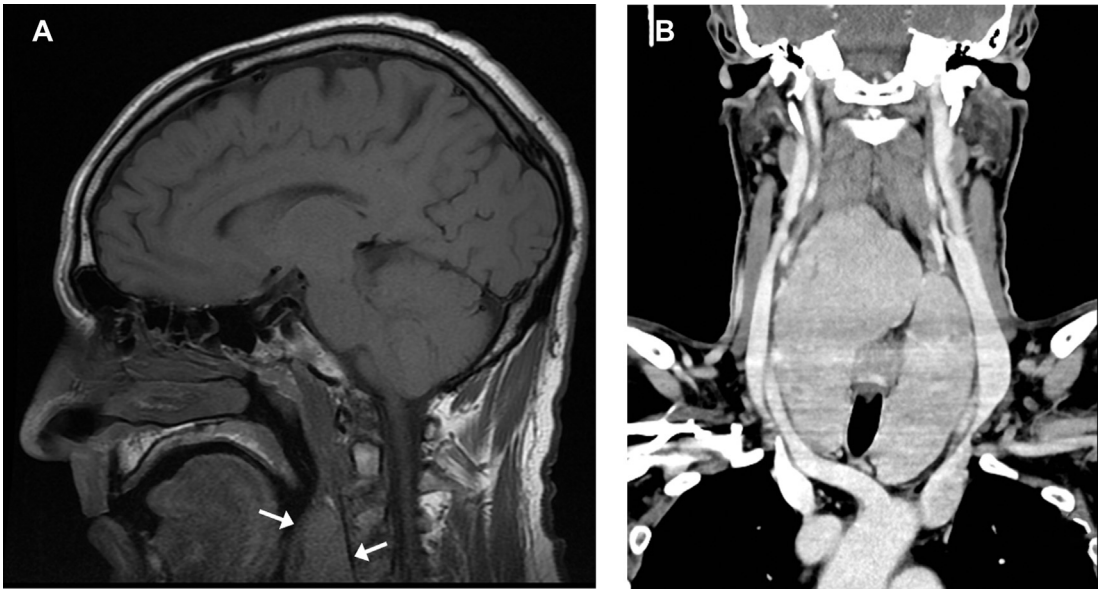

Fig. 1. An incidental retropharyngeal mass (*arrows*) detected on an emergent brain MR performed for headache (*A*) was confirmed to represent goiter on a subsequent neck CT (*B*). This case illustrates the extent to which thyroid abnormalities can be detected on imaging unrelated to thyroid pathologic conditions.

technique. Based on postmortem examinations of thyroid glands of asymptomatic subjects, thyroid nodules are present in approximately half the population.[3] In contrast, thyroid palpation detects nodules in roughly a fifth of asymptomatic subjects.[4] In general, thyroid nodule prevalence varies somewhat linearly with age and shows a strong female predominance.[4,5] Incidentalomas on imaging are reported at frequencies between that of autopsy and palpation, although one should keep in mind that imaging utilization, which varies with age and gender,[6] can have confounding effects on the prevalence and malignancy risk of ITNs.

On neck computed tomography (CT) examinations, ITNs have a prevalence of 16% to 18% based on retrospective investigations,[7,8] but they are described in clinical radiology reports at a lower rate of 6%.[7] About 1 in 4 contrast-enhanced chest CT examinations have an ITN,[9] and lung cancer screening chest CTs can potentially contribute to incidental detection of thyroid abnormalities.[10] CT represents a very common modality on which ITNs or incidental thyroid cancers are initially detected.[11–14] Prevalence of ITNs on MR imaging (**Fig. 2**A, B) is similar to that of CT.[7] However, MR imaging represents a much smaller contribution to incidentaloma detection than CT.[11,12,14]

Ultrasound (US) is generally the modality of choice for characterizing ITNs, but US studies performed for unrelated indications, such as assessing neck vasculature or in a screening context, can result in incidental detection of nodules. US-detected thyroid nodules represent a sizable component of ITNs.[11,12,14] Sonography in randomly selected individuals in a Finnish study detected ITNs in 21% and diffuse abnormalities in 6%.[15] An Italian study examining US examinations in individuals without thyroid disease reported an ITN prevalence of 33%,[16] similar to findings from a large Korean study showing prevalence of thyroid nodules or cysts to be 34% among subjects undergoing thyroid US during routine health evaluations.[17] Prevalence of ITNs as high as 67% on US has been reported.[4]

Focal thyroid gland uptake on fluorodeoxyglucose (FDG)-PET (**Fig. 3**) is detected in only 2% to 3% of oncologic PET studies.[18,19] Nonetheless, PET-detected ITNs comprise a substantial portion of imaging-detected incidentalomas[12,14] and account for a quarter of thyroid cancers initially detected on imaging.[12] Other modalities may detect incidental thyroid cancers and nodules, such as other nuclear medicine studies (octreotide scans), chest radiography, and echocardiography,[11,12] but incidentalomas detected on these modalities are much less common.

AN ERA OF INCIDENTAL FINDINGS?

According to the Surveillance, Epidemiology, and End Results (SEER) Program, thyroid cancer incidence is 15.8/100,000 per year, with a mortality

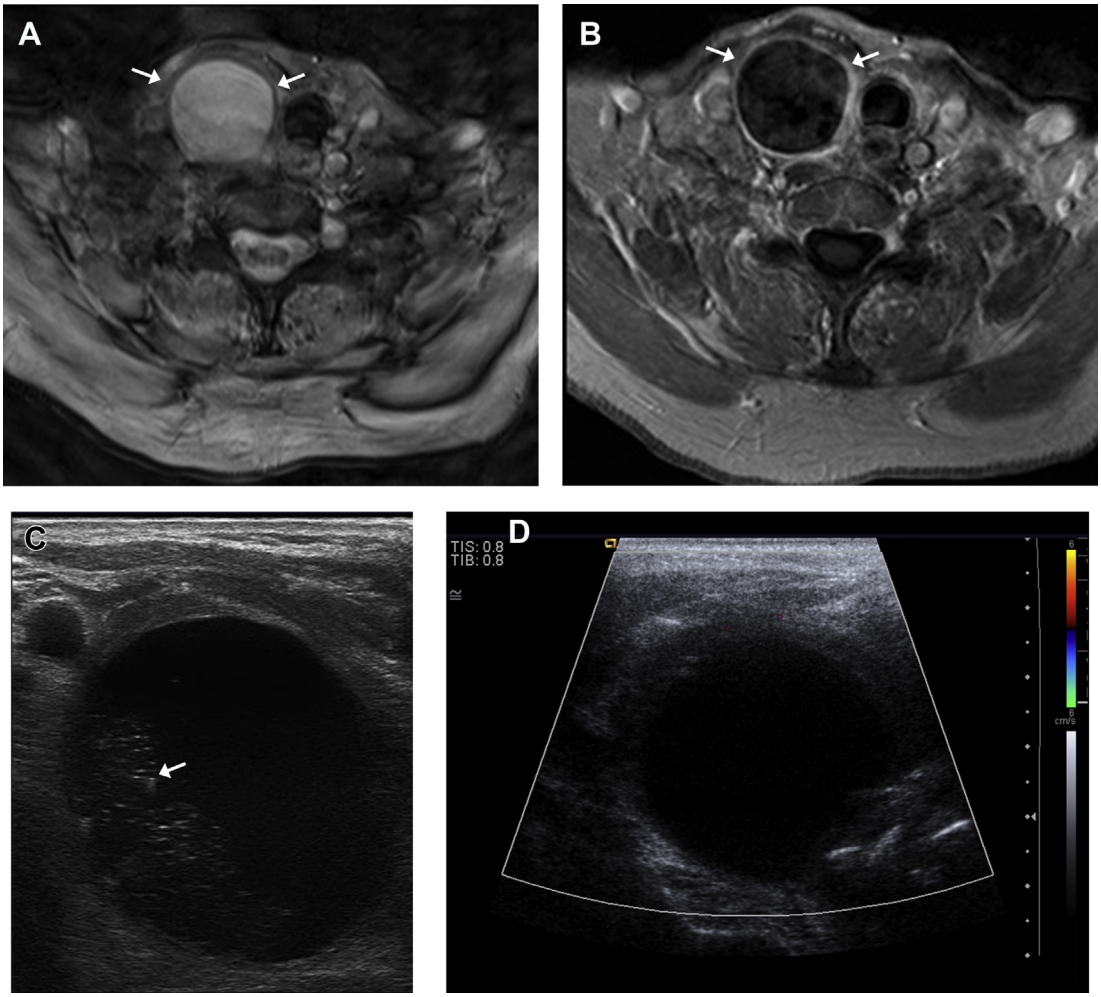

Fig. 2. Axial T2-weighted (*A*) and postcontrast T1-weighted (*B*) MR images show a rounded nonenhancing T2-hyperintense lesion (*arrows*) in the right thyroid lobe. Grayscale (*C*) and color Doppler (*D*) US images show an anechoic cyst lacking vascular flow and containing echogenic foci that have comet-tail artifacts (*arrow*) and likely represent colloid inclusions. This is considered benign by both ATA and ACR TI-RADS criteria.

of 0.5/100,000 per year[2] Much has been written about the seemingly alarming increase in thyroid cancer incidence of approximately 3-fold over the past 4 decades.[20,21] Most of the increased incidence is attributable to more frequent detection of subcentimeter papillary thyroid carcinomas.[20] However, because overall mortality from thyroid cancer has remained relatively stable,[21] several investigators have described this phenomenon as a problem of overdiagnosis.[21–23] One mechanistic explanation underlying the observed increase in thyroid cancer incidence is the presence of a large reservoir of asymptomatic, indolent thyroid cancers that may never reach clinical attention. The near-ubiquity of clinically occult thyroid cancers is demonstrated in 1 study that found foci of papillary carcinoma, most of which were less than 1 cm, in 36% of consecutive autopsies,[24] indicating a high prevalence of small foci meeting histologic criteria for carcinoma that may never manifest as a clinically apparent cancer.

There are other factors that may contribute to increased detection of incidental findings. Increasing utilization of cross-sectional imaging modalities, including a 10% per year growth in CT imaging use over a similar time period[25] and increased use of point-of-care sonography,[26] because of higher quality and lower cost of US equipment, is thought to contribute to a large portion of the observed increase in thyroid cancer diagnoses. In addition, incidental cancers may also be detected at a greater rate because of rising rates of fine-needle aspiration (FNA) and thyroid

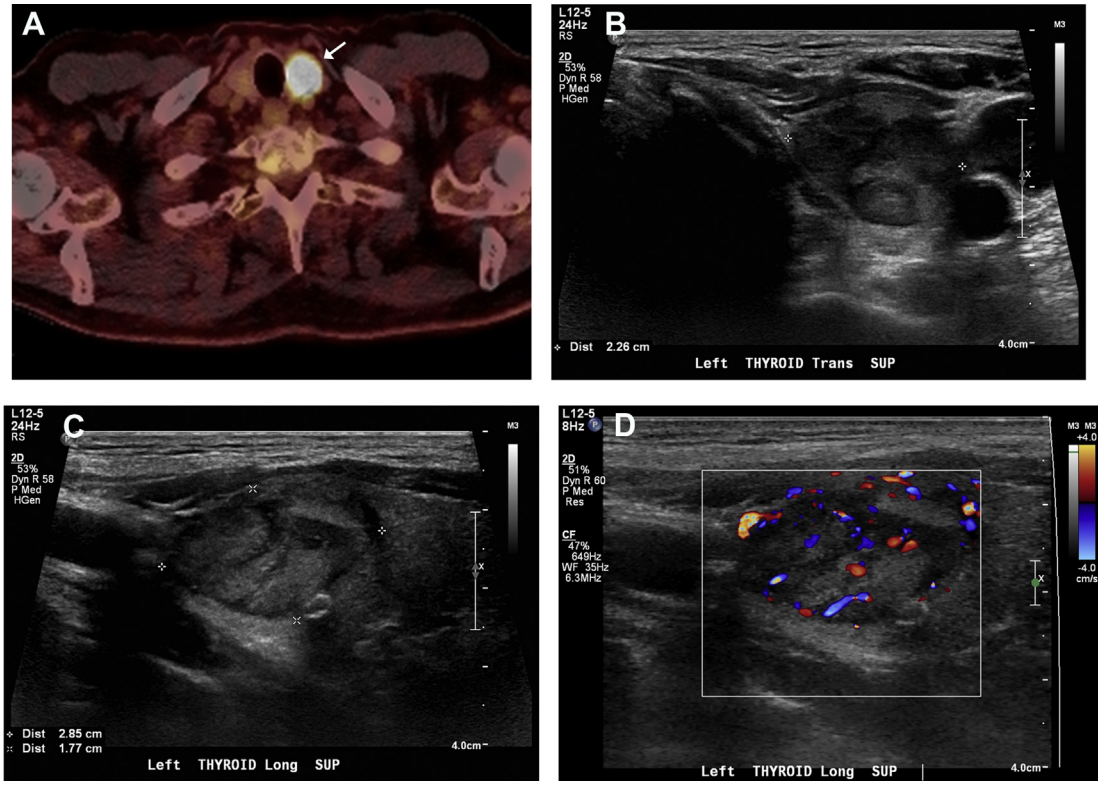

Fig. 3. Staging PET-CT (*A*) for lung cancer shows a hypermetabolic thyroid nodule (*arrow*). Grayscale US (*B*, *C*) shows a 2.9-cm solid isoechoic-to-hypoechoic nodule (*calipers*) with a smooth regular margin, wider-than-tall shape, and absence of echogenic foci. Doppler US (*D*) demonstrates vascular flow within the nodule. FNA results were suspicious for a follicular neoplasm.

surgeries. One study of claims databases from 2006 to 2011 demonstrated annual increases of 16% for thyroid FNAs and 12% for total thyroidectomies in the United States.[27] Therefore, increased imaging detection or increased diagnostic scrutiny could potentially result in higher thyroid cancer incidences over time.

However, some investigators have reported a small yearly change in incidence-based thyroid cancer mortality on the order of 1% per year,[28] raising the possibility of a relatively small superimposed increase in true cancer risk in addition to effects of increased detection. Incidence of clinically symptomatic or palpable cancers has also increased,[29] suggesting that there may be other factors contributing to these thyroid cancer incidence trends. Regardless of the cause of the observed growth in thyroid cancer diagnoses, the relatively indolent course of most incidental thyroid malignancies has led to a growing interest in the radiology community to refine and standardize radiology reporting and management recommendations for this very common incidental finding.

CANCER RISK IN THYROID INCIDENTALOMAS

Thyroid Nodule Epidemiology

Most ITNs are benign. Malignancy risks among ITNs have been reported at approximately 12% in patients undergoing US-guided FNA.[30] Estimates of malignancy risk among CT-detected ITNs are similar at 11%.[31] FNA and surgical series tend to overestimate malignancy risk for ITNs because of ascertainment bias, because many low-risk nodules will not undergo FNA or surgery, and therefore, would be underrepresented in the cytopathologic or histopathologic data. A population-based study estimating cancer risk among thousands of patients who underwent US evaluation of ITNs found a malignancy risk of 1.6% for thyroid nodules at least 5 mm.[1] Although this malignancy risk estimate is lower than that obtained in FNA or surgical series, the linking of a cohort of more than 8000 patients with cancer registry data allowed that study to capture cancers detected as late as 6 years after the US evaluation. Therefore, it likely yields a more reliable and unbiased estimate of malignancy risk for

incidentalomas, irrespective of decisions to perform FNA at the time of imaging.

What Patient Factors Affect Malignancy Risk and/or Prognosis?

One of the early studies examining ITNs in both CT and US detected an increased malignancy risk for thyroid incidentalomas in patients less than 35 years of age.[31] One later study showed better prediction of malignancy when dichotomizing at an age threshold of 52 years.[32] From age 20 to 60, relative risk of malignancy decreases 2.2% per year.[33] However, the effects of age are complicated by the observation that despite the lower risk of malignancy among elderly patients, thyroid cancers identified in older patients are more likely to demonstrate higher-risk histologies.[33] Nonetheless, existing literature offers some justification for a less aggressive management approach for elderly patients. In 1 study of patients at least 70 years of age who had undergone US and FNA for thyroid nodules, the likelihood of death from thyroid cancer, as assessed during follow-up intervals averaging 4 years, was very low (<1%),[34] and 94% of deaths in this cohort were due to causes unrelated to thyroid disease. Of those who did die from thyroid cancer, all had significant-risk thyroid cancers that were not subtle on imaging and/or cytology and were easily discerned at the time of thyroid nodule evaluation. Other potential factors that may increase risk of malignancy in ITNs include male gender,[32,35] radiation exposure in childhood,[36,37] and family history of thyroid cancer.[38]

What Nodule Imaging Characteristics Affect Malignancy Risk and/or Prognosis?

Imaging findings for most ITNs on CT or MR imaging do not permit reliable determination of benignity or malignancy,[31] but the presence of some highly suspicious findings, such as aggressive local invasion, suspicious lymphadenopathy, or systemic metastatic disease, can be used to assign higher risk to nodules seen on CT or MR imaging[8] (**Fig. 4**). Most of the literature quantifying malignancy risk in ITNs is based on ultrasonographic features, but size is 1 property that can be assessed on different modalities. The relationship between nodule size and malignancy risk in the literature is variable, ranging from absent[35] to a modest positive correlation.[32,39] A study using population-based SEER data to predict thyroid cancer outcomes as a function of tumor and patient variables using a proportional hazards model found that tumor size only increased mortality when size exceeded 2.5 cm.[40] Another population-based study following all patients who had thyroid nodules examined under US found size greater than 2 cm to be one of 3 sonographic findings significantly associated with cancer risk.[1]

The other 2 sonographic determinants of cancer risk in the above population-based study were microcalcifications and an entirely solid composition.[1] Microcalcifications in a solitary solid thyroid nodule confer a 48% chance of malignancy based on regression analysis of FNA data in 1 study.[35] In a separate multi-institutional series, thyroid nodules with solid composition had a malignancy risk of 13% compared with 4% for mixed solid and cystic nodules.[41] In addition to nodule composition and calcifications, other imaging features in the sonographic literature that affect risk of malignancy in thyroid nodules include echogenicity, shape, and margins.[35,42–44] Sonographic determinants of malignancy have been reviewed in further detail in recent publications.[45,46]

PUBLISHED GUIDELINES FOR REPORTING AND EVALUATING INCIDENTAL THYROID LESIONS

Overview of Existing Guidelines

Before efforts by the American College of Radiology (ACR) to adopt a standardized reporting system, there had been high variability among radiologists regarding the reporting of ITNs[47,48] and subsequent workup of reported incidentalomas.[49] Reduction in ITN workup can be achieved with minimal risk of missing aggressive cancers by applying varying size thresholds for different levels of estimated malignancy risk.[8,11,14,50,51] Several approaches to stratifying malignancy risk on sonography have been proposed, including pattern-based categorization systems proposed by the American Thyroid Association (ATA)[52] and other organizations.[53,54] In 2017, the ACR finalized a feature-based grading system, designated ACR Thyroid Imaging Reporting and Data System (ACR TI-RADS), loosely modeled after the Breast Imaging Reporting and Data System for mammography reporting.[46] Most of the discussion in the following subsections focuses primarily on recommendations from the ACR and ATA.

Decision to Pursue Dedicated Thyroid Ultrasonography

ITNs are frequently detected on CT, MR imaging, or PET as nonspecific nodular findings. In general, ultrasonography allows more definitive characterization of these nodules, but the need to detect potential thyroid malignancy must be weighed against the potential harms of pursuing definitive

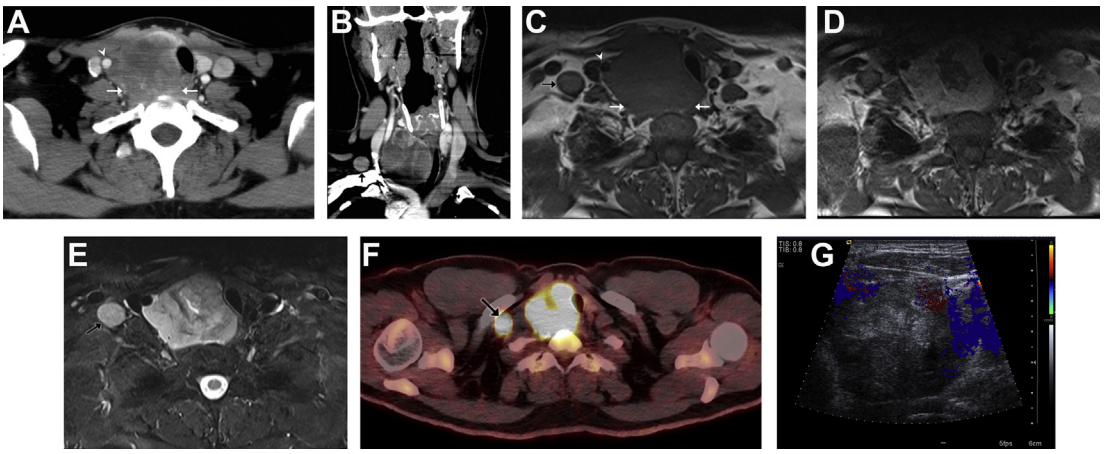

Fig. 4. Axial (*A*) and coronal (*B*) contrast-enhanced CT images and axial precontrast T1-weighted (*C*), postcontrast T1-weighted (*D*), and short tau inversion recovery (*E*) MR images show a large abnormality in the right thyroid lobe with highly suspicious findings, including extrathyroidal extension with loss of adjacent fat planes (*white arrows*) and encasement of the right common carotid artery (*arrowhead*). There is an enlarged, rounded right supraclavicular lymph node (*black arrow* in *B*, *C*, and *E*). PET-CT (*F*) shows FDG avidity in both the thyroid lesion and the right supraclavicular lymph node (*black arrow*). US (*G*) shows a solid hypoechoic mass. Histopathology was anaplastic carcinoma.

evaluation and treatment of a predominantly indolent and asymptomatic incidental finding.[23] A radionuclide thyroid scan is unnecessary in most patients and is only helpful in the setting of low serum thyroid-stimulating hormone.[52] Often, before pursuing further evaluation, review of prior available imaging may be helpful to determine the presence or absence of the nodule on a prior imaging study, even if not explicitly mentioned in the imaging report, and interval change can provide critical information regarding the malignancy risk of the nodule. For instance, a nodule with long-term stability is unlikely to represent a malignancy, whereas a nodule not present on a scan a year ago or having doubled in size over a short time interval raises concern.

A diagnostic thyroid US examination typically involves a high-resolution sonographic evaluation of the neck in hyperextension with imaging performed in longitudinal and transverse planes and includes assessment of the thyroid gland and cervical lymph nodes.[55] Sonographic findings determine the need for FNA or sonographic follow-up or may reassure against the need for further nodule evaluation, but not all ITNs require dedicated evaluation with sonography. The 2015 ATA guidelines[52] state that dedicated thyroid sonography "should be performed in all patients with a suspected thyroid nodule, nodular goiter, or radiographic abnormality suggesting a thyroid nodule incidentally detected on another imaging study," but also include a general statement that evaluation with FNA should only be performed in nodules greater than 1 cm along with an acknowledgment that subcentimeter nodules may occasionally warrant workup because of symptoms or lymphadenopathy. The general practice of avoiding workup of most subcentimeter nodules is supported by data showing subcentimeter thyroid carcinomas have a favorable prognosis amenable to nonsurgical management using imaging surveillance.[56]

An ACR white paper published in 2015 provides evidence-based recommendations for communicating workup recommendations for ITNs incidentally detected on radiologic imaging.[57] According to these recommendations, dedicated ultrasonography should be performed on all ITNs that are accompanied by suspicious imaging features, such as evidence of local invasion or lymphadenopathy, regardless of nodule size or patient age. For this purpose, focal radiotracer uptake on a nuclear medicine study is considered a suspicious imaging feature, because focal ITN uptake on PET confers a relatively high risk of malignancy (as high as 50%–60%).[18,19,58,59]

In otherwise healthy patients without suspicious imaging features, the ACR recommends US for nodules meeting a minimum size threshold of 1 cm in patients younger than 35 years and 1.5 cm in patients 35 years and older.[57] Pursuing sonographic evaluation may not necessarily be warranted in patients with comorbidities that limit life expectancy or increase treatment risks. For patients with such comorbidities, the ACR white paper recommends against further evaluation in the

absence of suspicious imaging features, even if nodules exceed the aforementioned size thresholds. For example, in most patients with stage IV lung cancer incidentally noted to have an ITN on staging scans, further workup of the ITN is generally not indicated. Treatment of the more aggressive malignancy is preferable to interrupting therapy to investigate a much less concerning thyroid neoplasm. In an elderly cohort of patients with ITNs undergoing US and FNA described above, close to half had a comorbidity, such as coronary artery disease, or another primary malignancy at the time of nodule evaluation that more than doubles the risk of all-cause mortality,[34] suggesting that even if workup yields a malignant cytologic diagnosis, there may be relatively little benefit on overall survival.

Decision to Perform Fine-Needle Aspiration or Surveillance

High-resolution thyroid ultrasonography is the test of choice for determining the need for tissue sampling or imaging surveillance. Nodule size can be reliably assessed on US and has been incorporated into both the ATA guidelines and the ACR TI-RADS management recommendations in the form of size thresholds for FNA or surveillance that vary depending on the risk categorization for a given nodule[52,60,61] (**Table 1**). In ACR TI-RADS, points are assigned based on sonographic determination of composition (cystic/solid characteristics), dominant echogenicity pattern, shape, margins, and echogenic foci,[45,46,60,62] with sonographic features associated with higher malignancy risk, such as taller-than-wide shape or microcalcifications (**Fig. 5**), awarded more points. These points are summed for the nodule of interest to determine placement in one of 5 risk categories (**Table 2**). Validation of the ACR TI-RADS criteria has been performed in a multi-institutional study of more than 3000 nodules that found that the vast majority (86%) of nodules showed empiric malignancy risks within 1% of the specified ACR TI-RADS risk thresholds.[41] One of the main differences between ACR TI-RADS and other systems is that it uses a set of imaging characteristics that can be independently assessed, whereas the ATA and several other systems use a pattern-based approach.[52] Both the ATA and ACR TI-RADS systems recommend against FNA for nodules falling under their most benign risk category (**Fig. 2**C, D). At the highest-risk category, both use a 1-cm threshold for recommending FNA. Between these extremes, ACR TI-RADS and ATA differ slightly in the size threshold used, with ACR TI-RADS using higher size thresholds for FNA. In addition, ACR TI-RADS does not recommend FNA of spongiform nodules (**Fig. 6**), whereas ATA recommends FNA for spongiform nodules above 2 cm.

Compared with ATA, the ACR TI-RADS system results in a greater biopsy yield of malignancy (14% vs 10%) and a lower estimated frequency of biopsy rate among benign nodules (47% vs 78%).[63] Under the ACR TI-RADS system, nodules classified as at least mildly suspicious but not

Table 1
Thyroid nodule management options under American College of Radiology Thyroid Imaging Reporting and Data System and American Thyroid Association

Management Options	ACR TI-RADS Risk Categories	ATA Risk Categories
FNA	TR5: Highly suspicious (if ≥1.0 cm) TR4: Moderately suspicious (if ≥1.5 cm) TR3: Mildly suspicious (if ≥2.5 cm)	High suspicion (if ≥1 cm) Intermediate suspicion (if ≥1 cm) Low suspicion (if ≥1.5 cm) Very low suspicion (if ≥2 cm)
Surveillance if benign cytology on FNA[a]	TR5: Highly suspicious (if ≥0.5 cm) TR4: Moderately suspicious (if ≥1.0 cm) TR3: Mildly suspicious (if ≥1.5 cm)	High suspicion[b] Intermediate suspicion Low suspicion Very low suspicion
No further workup	TR2: Not suspicious TR1: Benign TR3, TR4, and TR5 (if not meeting surveillance size threshold)	Benign

[a] Or, under ACR TI-RADS, if FNA is not indicated, but the nodule meets listed size thresholds for surveillance. Timing of surveillance varies for each risk category and differs between ACR TI-RADS and ATA.
[b] In addition to repeat FNA.
Data from Refs.[46,52]

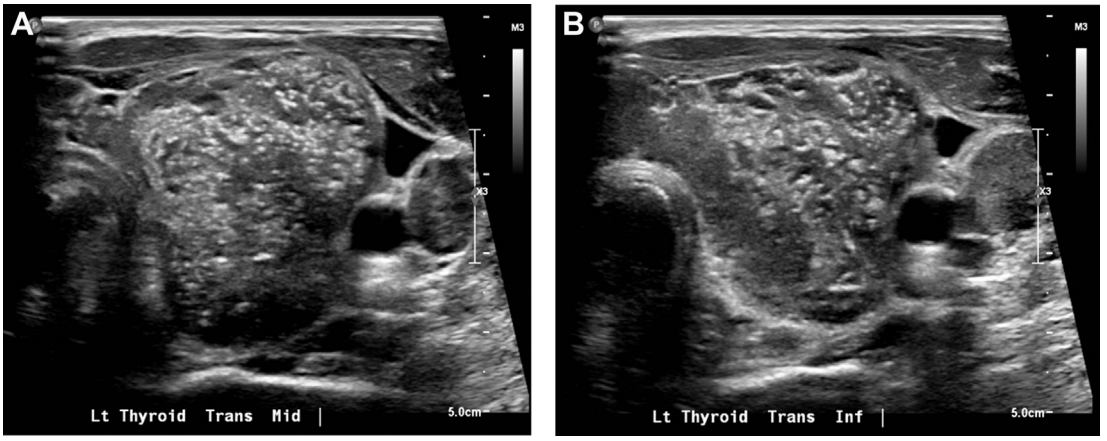

Fig. 5. Axial US images of the left thyroid lobe (*A*, *B*) illustrate microcalcifications and taller-than-wide shape, which are 2 sonographic findings that are assigned the maximum number of points in their respective feature categories in ACR TI-RADS and are also considered high-risk features in ATA.

Table 2
Risk category assignment under American College of Radiology Thyroid Imaging Reporting and Data System and American Thyroid Association

ACR TI-RADS		ATA	
Risk Category	**Description**	**Risk Category**	**Description**
TR5: Highly suspicious	Composition[a] + Echogenicity[b] + Shape[c] + Margin[d] + Echogenic foci[e] = Total score ≥7	High suspicion	Solid hypoechoic nodule or nodular component & ≥1 high-risk feature [f]
TR4: Moderately suspicious	Total score = 4, 5, or 6	Intermediate suspicion	Solid hypoechoic nodule with smooth margins & no high-risk features
TR3: Mildly suspicious	Total score = 3	Low suspicion	Solid hyperechoic or isoechoic nodule OR partially cystic nodule with an eccentric solid component & no high-risk features
TR2: Not suspicious	Total score = 2	Very low suspicion	Spongiform or partially cystic nodules without any of the above sonographic patterns
TR1: Benign	Total score = 0	Benign	Simple cysts

[a] Composition score = {cystic or spongiform = 0; mixed = 1; solid or cannot be determined due to calcification = 2}. If the nodule is spongiform, the scores for all the remaining feature categories are 0. If mixed, scores for the remaining categories are assigned based on the predominant solid component.
[b] Echogenicity score = {anechoic = 0; hyperechoic or isoechoic or cannot be determined = 1; hypoechoic = 2; very hypoechoic = 3}. Echogenicity is assessed relative to adjacent parenchyma.
[c] Shape score = {wider-than-tall = 0; taller-than-wide = 3}.
[d] Margin score = {smooth or ill-defined or cannot be determined = 0; lobulated or irregular = 2; extrathyroidal extension = 3}.
[e] Echogenic foci score = {none or large comet-tail = 0; macrocalcifications = 1; rim calcifications = 2; punctate = 3}.
[f] ATA high-risk features: irregular margins, microcalcifications, taller-than-wide shape, interrupted rim calcifications, extrathyroidal extension.
Data from Refs.[46,52]

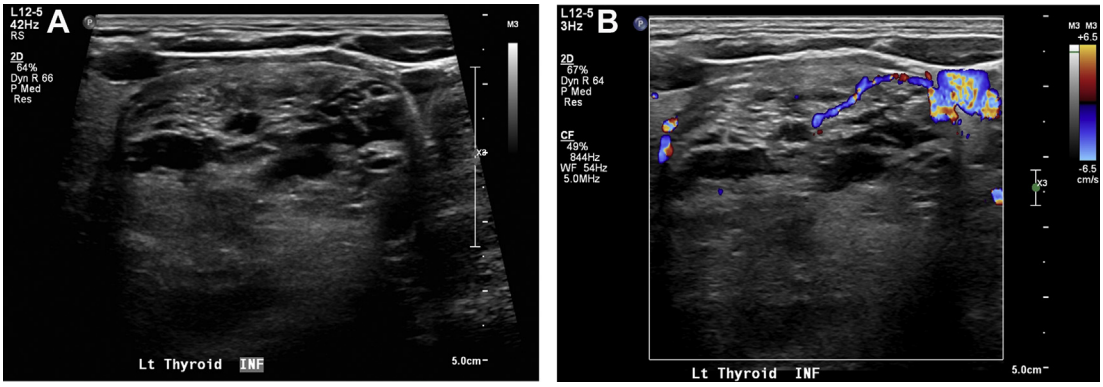

Fig. 6. Grayscale (*A*) US image shows a benign spongiform pattern, considered Very Low Suspicion under ATA and TR1 Benign under ACR TI-RADS. On color Doppler (*B*), there is no abnormal vascularity within the nodule.

meeting size criteria for FNA are followed by US for 5 years in lieu of FNA if they meet size criteria for surveillance. A definitive recommendation against further workup can potentially be made in 32% of nodules under ACR TI-RADS, compared with 1.5% under the ATA guidelines.[63] One advantage of the point-based system used in ACR TI-RADS is that it allows all nodules to be characterized, whereas 3% to 14% of nodules, such as nonhypoechoic nodules with microcalcifications, do not match one of the defined patterns in the ATA system[63,64] (see **Table 2**). Moreover, these unclassifiable nodules have malignancy risks slightly higher than those classified as intermediate risk.[64] The ACR TI-RADS system also has some limitations. Some definitively benign but relatively uncommon sonographic appearances, such as the "giraffe" pattern and "white knight" pattern associated with Hashimoto thyroiditis,[65] would not be categorized as benign under the ACR TI-RADS points system.[46] Another limitation of a points-based system is that the alteration in risk associated with a given finding in 1 feature category theoretically could vary depending on findings in other categories; in other words, simple addition of points from each category may not lead to an accurate risk estimate if the feature categories do not independently and linearly contribute to malignancy risk.

The ATA pattern-based approach may be more efficient among experienced sonographers, whereas the ACR TI-RADS points-based system may be more user-friendly and somewhat easier to implement in clinical practice. Some may find the follow-up guidelines in ACR TI-RADS to be clearer. Until data are available demonstrating superiority of any 1 system in terms of reliability or cost-effectiveness, the risk stratification system used will likely depend on an individual provider's familiarity, comfort, and experience.

FUTURE DIRECTIONS FOR IMPROVING INCIDENTALOMA MANAGEMENT

With better standardization of diagnostic reporting and increasing availability of large-scale clinical and outcomes data, prediction models can be developed to allow more personalized risk assessment and management for individual patients. For instance, 1 group using regression analysis to identify variables predicting malignancy risk made their prediction model accessible in the form of an online calculator (http://thyroidcancerrisk.brighamandwomens.org) that computes risk of malignancy for a thyroid nodule for any combination of selection choices for 5 demographic and US input variables.[32] Although this model requires validation, cancer risk models will continue to evolve in the era of Big Data, and more robust predictions of individualized risk may enable more customized tailoring of management to match each patient's risk tolerance.

Machine learning and other artificial intelligence approaches represent a growing area of interest in the medical arena that could potentially improve prediction of malignancy risk in ITNs. One 2016 study using various machine learning classifier models to predict malignancy risk from a combination of clinical variables and US features performed better than an inexperienced radiologist but not as well as an experienced radiologist.[66] Recently, a machine learning approach was used to tweak point assignments for sonographic features in ACR TI-RADS, producing a simpler set of point assignments with improved specificity.[67] It is likely that new data made available through adoption of standardized reporting practices and ongoing collection of relevant outcomes data will help guide any future adjustments to the various risk stratification systems.

Deep-learning approaches can also be applied to more rapidly assess sonographic images in the context of computer vision. Many studies have applied texture analysis to obtain imaging features from a nodule's sonographic appearance for computer-aided prediction of malignancy.[68] Some studies applied semiautomated or automated techniques to extract texture or morphologic features from US images to serve as input to train machine learning models to predict a nodule's final benign or malignant classification.[69,70] Computer-aided diagnosis (CAD) was recently incorporated into a US workflow in which manual selection of a region of interest yielded an automated real-time prediction of benign or malignant status for a given nodule.[71] In that study, the performance of the CAD system alone was comparable to that of a radiologist, but a radiologist assisted by the CAD showed improved diagnostic sensitivity. Another study reported a detection system for automated thyroid nodule localization on US, feature extraction, and real-time prediction of a nodule's malignant status that performs comparably to experienced radiologists by most metrics, including overall accuracy of 90%, and even shows higher specificity for thyroid malignancy than experienced radiologists.[72] In addition, risk stratification can be extended further to assist in identifying nodules with high-risk genetic profiles; 1 study found that a deep-learning model applied to sonographic images of thyroid nodules can differentiate between high-risk and low-risk genetic mutations with an overall accuracy of 77%.[73] Although many of these artificial intelligence approaches are not currently in widespread clinical use, they likely represent additional future adjunctive mechanisms to facilitate risk stratification of incidentalomas and allow providers to more efficiently prioritize treatment of higher-risk incidentalomas.

WHAT THE REFERRING PHYSICIAN WANTS TO KNOW

- What is the approximate malignancy risk?
- If incidentally detected on a study other than a dedicated thyroid sonogram, is dedicated sonographic evaluation warranted?
- Does the nodule require FNA?
- What is the recommended interval for follow-up imaging?

PEARLS

- ITNs are very common, but most nodules are benign, and most malignant nodules have favorable prognosis.
- Avoid recommending unnecessary tests and review prior imaging studies if available.
- US is the test of choice for stratifying a thyroid nodule's malignancy risk and to guide decisions of whether to biopsy and/or follow-up with imaging.

SUMMARY

Because of their high prevalence, ITNs are likely to be encountered in everyday radiology practice on various modalities, including CT, MR, US, and PET. Increased utilization of cross-sectional imaging modalities over the past several decades likely contributes to rising numbers of ITNs detected. Based on ACR recommendations and the predominantly benign prognosis of thyroid nodules, not all ITNs require further evaluation with US, but when indicated, dedicated thyroid sonography is the best imaging test for estimation of a nodule's malignancy risk and can guide decisions for biopsy and/or surveillance. Standardized reporting practices, appropriate application of evidence-based guidelines, and future efforts to improve predictive accuracy for malignancy risk will likely help curtail the number of ITNs subjected to unnecessary biopsies.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Smith-Bindman R, Lebda P, Feldstein VA, et al. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. JAMA Intern Med 2013;173(19):1788–96.
2. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2016, based on November 2018 SEER data submission. Available at: https://seer.cancer.gov/csr/1975_2016/. Accessed January 31, 2020.
3. Mortensen JD, Woolner LB, Bennett WA. Gross and microscopic findings in clinically normal thyroid glands. J Clin Endocrinol Metab 1955;15(10):1270–80.
4. Ezzat S, Sarti DA, Cain DR, et al. Thyroid incidentalomas. Prevalence by palpation and ultrasonography. Arch Intern Med 1994;154(16):1838–40.
5. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993;328(8):553–9.
6. Lang K, Huang H, Lee DW, et al. National trends in advanced outpatient diagnostic imaging utilization: an analysis of the medical expenditure panel survey, 2000-2009. BMC Med Imaging 2013;13:40.
7. Yousem DM, Huang T, Loevner LA, et al. Clinical and economic impact of incidental thyroid lesions found

with CT and MR. AJNR Am J Neuroradiol 1997;18(8):1423–8.
8. Nguyen XV, Choudhury KR, Eastwood JD, et al. Incidental thyroid nodules on CT: evaluation of 2 risk-categorization methods for work-up of nodules. AJNR Am J Neuroradiol 2013;34(9):1812–7.
9. Ahmed S, Horton KM, JR B Jr, et al. Incidental thyroid nodules on chest CT: review of the literature and management suggestions. AJR Am J Roentgenol 2010;195(5):1066–71.
10. Nguyen XV, Davies L, Eastwood JD, et al. Extrapulmonary findings and malignancies in participants screened with chest CT in the national lung screening trial. J Am Coll Radiol 2017;14(3):324–30.
11. Bahl M, Sosa JA, Eastwood JD, et al. Using the 3-tiered system for categorizing workup of incidental thyroid nodules detected on CT, MRI, or PET/CT: how many cancers would be missed? Thyroid 2014;24(12):1772–8.
12. Bahl M, Sosa JA, Nelson RC, et al. Imaging-detected incidental thyroid nodules that undergo surgery: a single-center experience over 1 year. AJNR Am J Neuroradiol 2014;35(11):2176–80.
13. Chaikhoutdinov I, Mitzner R, Goldenberg D. Incidental thyroid nodules: incidence, evaluation, and outcome. Otolaryngol Head Neck Surg 2014;150(6):939–42.
14. Hobbs HA, Bahl M, Nelson RC, et al. Journal Club: incidental thyroid nodules detected at imaging: can diagnostic workup be reduced by use of the Society of Radiologists in Ultrasound recommendations and the three-tiered system? AJR Am J Roentgenol 2014;202(1):18–24.
15. Brander A, Viikinkoski P, Nickels J, et al. Thyroid gland: US screening in a random adult population. Radiology 1991;181(3):683–7.
16. Bartolotta TV, Midiri M, Runza G, et al. Incidentally discovered thyroid nodules: incidence, and grey-scale and colour Doppler pattern in an adult population screened by real-time compound spatial sonography. Radiol Med 2006;111(7):989–98.
17. Moon JH, Hyun MK, Lee JY, et al. Prevalence of thyroid nodules and their associated clinical parameters: a large-scale, multicenter-based health checkup study. Korean J Intern Med 2018;33(4):753–62.
18. Chen W, Parsons M, Torigian DA, et al. Evaluation of thyroid FDG uptake incidentally identified on FDG-PET/CT imaging. Nucl Med Commun 2009;30(3):240–4.
19. Nishimori H, Tabah R, Hickeson M, et al. Incidental thyroid "PETomas": clinical significance and novel description of the self-resolving variant of focal FDG-PET thyroid uptake. Can J Surg 2011;54(2):83–8.
20. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. JAMA 2006;295(18):2164–7.
21. Davies L, Welch HG. Current thyroid cancer trends in the United States. JAMA Otolaryngol Head Neck Surg 2014;140(4):317–22.
22. Hoang JK, Nguyen XV, Davies L. Overdiagnosis of thyroid cancer: answers to five key questions. Acad Radiol 2015;22(8):1024–9.
23. Hoang JK, Nguyen XV. Understanding the risks and harms of management of incidental thyroid nodules: a review. JAMA Otolaryngol Head Neck Surg 2017;143(7):718–24.
24. Harach HR, Franssila KO, Wasenius VM. Occult papillary carcinoma of the thyroid. A "normal" finding in Finland. A systematic autopsy study. Cancer 1985;56(3):531–8.
25. Hoang JK, Roy Choudhury K, Eastwood JD, et al. An exponential growth in incidence of thyroid cancer: trends and impact of CT imaging. AJNR Am J Neuroradiol 2013. https://doi.org/10.3174/ajnr.A3743.
26. Moore CL, Copel JA. Point-of-care ultrasonography. N Engl J Med 2011;364(8):749–57.
27. Sosa JA, Hanna JW, Robinson KA, et al. Increases in thyroid nodule fine-needle aspirations, operations, and diagnoses of thyroid cancer in the United States. Surgery 2013;154(6):1420–6 [discussion: 1426–7].
28. Lim H, Devesa SS, Sosa JA, et al. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. JAMA 2017;317(13):1338–48.
29. Bahl M, Sosa JA, Nelson RC, et al. Trends in incidentally identified thyroid cancers over a decade: a retrospective analysis of 2,090 surgical patients. World J Surg 2014;38(6):1312–7.
30. Nam-Goong IS, Kim HY, Gong G, et al. Ultrasonography-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings. Clin Endocrinol (Oxf) 2004;60(1):21–8.
31. Shetty SK, Maher MM, Hahn PF, et al. Significance of incidental thyroid lesions detected on CT: correlation among CT, sonography, and pathology. AJR Am J Roentgenol 2006;187(5):1349–56.
32. Angell TE, Maurer R, Wang Z, et al. A cohort analysis of clinical and ultrasound variables predicting cancer risk in 20,001 consecutive thyroid nodules. J Clin Endocrinol Metab 2019;104(11):5665–72.
33. Kwong N, Medici M, Angell TE, et al. The influence of patient age on thyroid nodule formation, multinodularity, and thyroid cancer risk. J Clin Endocrinol Metab 2015;100(12):4434–40.
34. Wang Z, Vyas CM, Van Benschoten O, et al. Quantitative analysis of the benefits and risk of thyroid nodule evaluation in patients ≥70 years old. Thyroid 2018;28(4):465–71.
35. Frates MC, Benson CB, Doubilet PM, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. J Clin Endocrinol Metab 2006;91(9):3411–7.

36. Sklar C, Whitton J, Mertens A, et al. Abnormalities of the thyroid in survivors of Hodgkin's disease: data from the Childhood Cancer Survivor Study. J Clin Endocrinol Metab 2000;85(9):3227–32.
37. Schneider AB, Ron E, Lubin J, et al. Dose-response relationships for radiation-induced thyroid cancer and thyroid nodules: evidence for the prolonged effects of radiation on the thyroid. J Clin Endocrinol Metab 1993;77(2):362–9.
38. Charkes ND. On the prevalence of familial nonmedullary thyroid cancer in multiply affected kindreds. Thyroid 2006;16(2):181–6.
39. 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(1):263–72.
40. Nguyen XV, Roy Choudhury K, Tessler FN, et al. Effect of tumor size on risk of metastatic disease and survival for thyroid cancer: implications for biopsy guidelines. Thyroid 2018;28(3):295–300.
41. Middleton WD, Teefey SA, Reading CC, et al. Multiinstitutional analysis of thyroid nodule risk stratification using the American College of Radiology thyroid imaging reporting and data system. AJR Am J Roentgenol 2017;208(6):1331–41.
42. Chen SP, Hu YP, Chen B. Taller-than-wide sign for predicting thyroid microcarcinoma: comparison and combination of two ultrasonographic planes. Ultrasound Med Biol 2014;40(9):2004–11.
43. Moon HJ, Kwak JY, Kim EK, et al. A taller-than-wide shape in thyroid nodules in transverse and longitudinal ultrasonographic planes and the prediction of malignancy. Thyroid 2011;21(11):1249–53.
44. Kim EK, Park CS, Chung WY, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. AJR Am J Roentgenol 2002;178(3):687–91.
45. Grant EG, Tessler FN, Hoang JK, et al. Thyroid ultrasound reporting lexicon: white paper of the ACR Thyroid Imaging, Reporting and Data System (TI-RADS) Committee. J Am Coll Radiol 2015;12(12 Pt A):1272–9.
46. Tessler FN, Middleton WD, Grant EG, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): white paper of the ACR TI-RADS Committee. J Am Coll Radiol 2017;14(5):587–95.
47. Grady AT, Sosa JA, Tanpitukpongse TP, et al. Radiology reports for incidental thyroid nodules on CT and MRI: high variability across subspecialties. AJNR Am J Neuroradiol 2015;36(2):397–402.
48. Hoang JK, Riofrio A, Bashir MR, et al. High variability in radiologists' reporting practices for incidental thyroid nodules detected on CT and MRI. AJNR Am J Neuroradiol 2014. https://doi.org/10.3174/ajnr.A3834.
49. Tanpitukpongse TP, Grady AT, Sosa JA, et al. Incidental thyroid nodules on CT or MRI: discordance between what we report and what receives workup. AJR Am J Roentgenol 2015;205(6):1281–7.
50. Bahl M, Sosa JA, Nelson RC, et al. Thyroid cancers incidentally detected at imaging in a 10-year period: how many cancers would be missed with use of the recommendations from the Society of Radiologists in ultrasound? Radiology 2014;271(3):888–94.
51. Hobbs HA, Bahl M, Nelson RC, et al. Applying the Society of Radiologists in Ultrasound recommendations for fine-needle aspiration of thyroid nodules: effect on workup and malignancy detection. AJR Am J Roentgenol 2014;202(3):602–7.
52. Haugen BR, Alexander EK, Bible KC, 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):1–133.
53. Gharib H, Papini E, Valcavi R, et al. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi Medical Guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract 2006;12(1):63–102.
54. Shin JH, Baek JH, Chung J, et al. Ultrasonography diagnosis and imaging-based management of thyroid nodules: revised Korean Society of Thyroid Radiology consensus statement and recommendations. Korean J Radiol 2016;17(3):370–95.
55. American Institute of Ultrasound in Medicine. American College of Radiology, Society for Pediatric Radiology, Society of Radiologists in Ultrasound. AIUM practice guideline for the performance of a thyroid and parathyroid ultrasound examination. J Ultrasound Med 2013;32(7):1319–29.
56. Ito Y, Miyauchi A, Inoue H, et al. An observational trial for papillary thyroid microcarcinoma in Japanese patients. World J Surg 2010;34(1):28–35.
57. Hoang JK, Langer JE, Middleton WD, et al. Managing incidental thyroid nodules detected on imaging: white paper of the ACR Incidental Thyroid Findings Committee. J Am Coll Radiol 2015;12(2):143–50.
58. Soelberg KK, Bonnema SJ, Brix TH, et al. Risk of malignancy in thyroid incidentalomas detected by 18F-fluorodeoxyglucose positron emission tomography: a systematic review. Thyroid 2012;22(9):918–25.
59. Salvatori M, Melis L, Castaldi P, et al. Clinical significance of focal and diffuse thyroid diseases identified by (18)F-fluorodeoxyglucose positron emission tomography. Biomed Pharmacother 2007;61(8):488–93.
60. Tessler FN, Middleton WD, Grant EG. Thyroid imaging reporting and data system (TI-RADS): a user's guide. Radiology 2018;287(1):29–36.
61. Maxwell C, Sipos JA. Clinical diagnostic evaluation of thyroid nodules. Endocrinol Metab Clin North Am 2019;48(1):61–84.

62. Horvath E, Majlis S, Rossi R, et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. J Clin Endocrinol Metab 2009;94(5):1748–51.
63. Middleton WD, Teefey SA, Reading CC, et al. Comparison of performance characteristics of American College of Radiology TI-RADS, Korean Society of Thyroid Radiology TIRADS, and American Thyroid Association Guidelines. AJR Am J Roentgenol 2018;210(5):1148–54.
64. Yoon JH, Lee HS, Kim EK, et al. Malignancy risk stratification of thyroid nodules: comparison between the thyroid imaging reporting and data system and the 2014 American Thyroid Association Management Guidelines. Radiology 2016;278(3):917–24.
65. Virmani V, Hammond I. Sonographic patterns of benign thyroid nodules: verification at our institution. AJR Am J Roentgenol 2011;196(4):891–5.
66. Wu H, Deng Z, Zhang B, et al. Classifier model based on machine learning algorithms: application to differential diagnosis of suspicious thyroid nodules via sonography. AJR Am J Roentgenol 2016;207(4):859–64.
67. Wildman-Tobriner B, Buda M, Hoang JK, et al. Using artificial intelligence to revise ACR TI-RADS risk stratification of thyroid nodules: diagnostic accuracy and utility. Radiology 2019;292(1):112–9.
68. Sollini M, Cozzi L, Chiti A, et al. Texture analysis and machine learning to characterize suspected thyroid nodules and differentiated thyroid cancer: where do we stand? Eur J Radiol 2018;99:1–8.
69. Chi J, Walia E, Babyn P, et al. Thyroid nodule classification in ultrasound images by fine-tuning deep convolutional neural network. J Digit Imaging 2017;30(4):477–86.
70. Yu Q, Jiang T, Zhou A, et al. Computer-aided diagnosis of malignant or benign thyroid nodes based on ultrasound images. Eur Arch Otorhinolaryngol 2017;274(7):2891–7.
71. Yoo YJ, Ha EJ, Cho YJ, et al. Computer-aided diagnosis of thyroid nodules via ultrasonography: initial clinical experience. Korean J Radiol 2018;19(4):665–72.
72. Wang L, Yang S, Yang S, et al. Automatic thyroid nodule recognition and diagnosis in ultrasound imaging with the YOLOv2 neural network. World J Surg Oncol 2019;17(1):12.
73. Daniels K, Gummadi S, Zhu Z, et al. Machine learning by ultrasonography for genetic risk stratification of thyroid nodules. JAMA Otolaryngol Head Neck Surg 2019;1–6. https://doi.org/10.1001/jamaoto.2019.3073.