



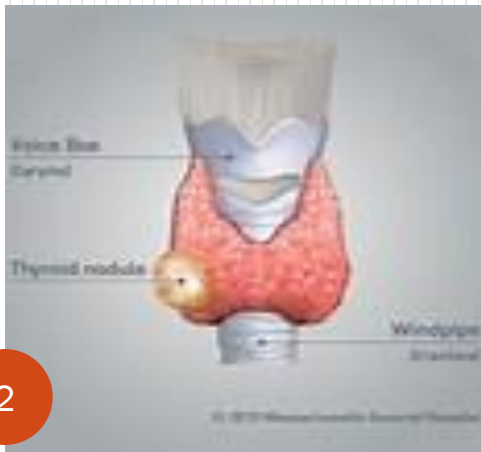
Clinical Approach to Thyroid Nodule

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Agenda

- Definition
- Epidemiology
- Clinical Importance
- Approach to thyroid nodule



Definition

- *Historically:* palpable lump in the thyroid gland
- *Now:* discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma.
- *Incidentaloma:*
 - Nonpalpable nodules detected on US or other anatomic imaging studies are termed incidentally discovered nodules

Prevalence

- Thyroid nodules are a common clinical problem.
- *Prevalence :*
 - *Studies based on inspection and palpation reported a 3 to 7%*
 - *Clinically inapparent thyroid nodules have been detected by US in 20% to as many as 76% of the general population a prevalence similar to that in autopsy data.*

Prevalence

- Palpable thyroid nodules in iodine-sufficient area :
 - 5% in women and 1% in men
- *Thyroid nodules are more common in:*
 - *Elderly persons,*
 - *Females,*
 - *Subjects from iodine-deficient geographic areas,*
 - *Those with a history of radiation exposure*
- Widespread use of imaging techniques has generated an epidemic of nonpalpable thyroid nodules

Initial

- Thyroid nodules come to clinical attention
- Noted by the patient
- By a clinician during routine physical examination
- During a radiologic procedure:
- Carotid ultrasonography
- Neck or chest computed tomography (CT)
- magnetic resonance imaging (MRI)
- Positron emission tomography (PET) scanning

Clinical Importance

- Both benign and malignant disorders can cause thyroid nodules
- The clinical importance of a newly diagnosed thyroid nodule is primarily the exclusion of malignancy .
- Thyroid cancer occurs in 7%–15% of thyroid nodules(4 to 6.5% of all thyroid nodules in nonsurgical series)
- depending on:
 - Age(Children,Adults less than 30 years of age)
 - Sex
 - Patients with a history of head and neck irradiation
 - Patients with a family history of thyroid cancer.....

Clinical Importance

- Nonpalpable nodules(incidentalomas) have the same risk of malignancy as palpable nodules of the same size.
- DTC (differentiated thyroid cancers):
 - >90% of all thyroid cancers
 - Including :
 - Papillary
 - Follicular
- Recent population-based study reported:
 - Doubling of thyroid cancer incidence from 2000 to 2012 compared to the prior decade
 - Arch Surg 2005; 140:981
 - Clin Endocrinol (Oxf)2004; 60:21

Approach to thyroid nodules

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

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Thyroid 2016, 26: 1-133

**AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS,
AMERICAN COLLEGE OF ENDOCRINOLOGY, AND
ASSOCIAZIONE MEDICI ENDOCRINOLOGI MEDICAL GUIDELINES FOR
CLINICAL PRACTICE FOR THE DIAGNOSIS AND MANAGEMENT OF
THYROID NODULES – 2016 UPDATE**

APPENDIX



ENDOCRINE PRACTICE Vol 22 (Suppl 1) May 2016 1

Management of thyroid Nodule

- *The basis of thyroid nodule management:*

Clinical findings with:

- History and physical examination
- Sensitive thyrotropin (TSH) assay
- High-resolution ultrasonography (US)
- Fine-needle aspiration (FNA) biopsy

Clinical findings :

- *History:*
 - Age
 - Family history of thyroid cancer, or thyroid cancer syndromes (eg, multiple endocrine neoplasia type 2 [MEN2, familial adenomatous polyposis])
 - Childhood head and neck irradiation
 - Total body irradiation for bone marrow transplantation
 - History of rapid growth of a neck mass
 - Anterior neck pain
 - Dysphonia, dysphagia, or dyspnea
 - Use of iodine-containing drugs or supplements

Growth rate

- *The sudden appearance of a lump with pain:*
 - Hemorrhage in a cystic nodule (more commonly)
 - Anaplastic thyroid carcinoma
 - Rare forms of chronic thyroiditis (Riedel disease)
 - Primary lymphoma of the thyroid

History

- Symptoms such as :
 - Usually NONE
 - Choking sensations
 - Vague cervical tenderness or pain
 - Dysphagia or
 - Hoarseness
-
- The symptoms and signs of tracheal compression (cough and dysphonia) may suggest the risk of an underlying malignant lesion.

Clinical findings :

- *Physical Examination:*
- Careful, focused examination of the thyroid gland and cervical lymph nodes:
 - Thyroid volume and consistency
 - Location, consistency, size, and number of nodule(s)
 - Neck tenderness or pain
 - Cervical adenopathy

Clinical findings :

- Most nodules are asymptomatic and benign, but the **absence of symptoms** does *not rule out* malignancy [BEL 2, GRADE A].
- The risk of cancer is not substantially different in patients with a *solitary nodule* versus patients with a *multinodular goiter (MNG)* [BEL 2, GRADE B].

Features suggesting Increased Risk of Malignant Potential

Table 3. Features Suggesting Increased Risk of Malignant Potential

- | |
|--|
| • History of head and neck irradiation |
| • Family history of medullary thyroid carcinoma, multiple endocrine neoplasia type 2, or papillary thyroid carcinoma |
| • Age <14 or >70 years |
| • Male sex |
| • Growth of the nodule |
| • Firm or hard nodule consistency |
| • Cervical adenopathy |
| • Fixed nodule |
| • Persistent dysphonia, dysphagia, or dyspnea |

Sensitive TSH assay

- *Serum thyrotropin (TSH) should be measured during the initial evaluation of a patient with a thyroid nodule.*

(Strong recommendation, Moderate-quality evidence)

- *If the serum TSH is subnormal, a radionuclide (preferably ¹²³I) thyroid scan should be performed.*

(Strong recommendation, Moderate-quality evidence)

- *If the serum TSH is normal or elevated, a radionuclide scan should not be performed as the initial imaging evaluation.*

(Strong recommendation, Moderate-quality evidence)

Sensitive TSH assay

- Since hyperfunctioning nodules rarely harbor malignancy, no cytologic evaluation is necessary
- Higher serum TSH level (even within the upper part of the reference range) is associated with increased risk of malignancy in a thyroid nodule, as well as more advanced stage thyroid cancer

Serum Thyroglobulin

- Routine measurement of serum Tg for initial evaluation of thyroid nodules is not recommended.

(Strong recommendation, Moderate-quality evidence)

Serum calcitonin

- *The panel cannot recommend either for or against routine measurement of serum calcitonin in patients with thyroid nodules.*

(No recommendation, Insufficient evidence)

- May be considered in the subgroup of patients in whom an elevated calcitonin may change the diagnostic or surgical approach:
 - Patients considered for less than total thyroidectomy
 - Patients with suspicious cytology not consistent with PTC
- Unstimulated serum calcitonin level >50 – 100 pg/mL:
 - Diagnosis of MTC is common

Thyroid Imaging

- *Thyroid sonography with survey of the cervical LN should be performed in all patients with known or suspected thyroid nodules.*

(Strong recommendation, High-quality evidence)

- *Ultrasound should evaluate the following:*
 - Thyroid parenchyma (homogeneous or heterogeneous)
 - Thyroid gland size
 - Nodules size
 - Location
 - Sonographic characteristics of any nodule(s)
 - Nodules incidentally noted on other imaging studies (carotid ultrasound, CT, MRI, or fludeoxyglucose [FDG]-PET scan)
- *Ultrasound for FNA decision-making*

Thyroid Ultrasonography:

- *When to Perform Thyroid Ultrasound:*
- US evaluation is **recommended** for:
 - Patients who are at risk for thyroid malignancy
 - Have palpable thyroid nodules or goiter
 - Have neck lymphadenopathy suggestive of a malignant lesion [BEL 2, GRADE A].
- US evaluation is **not recommended** :
 - As a screening test for the general population or patients with a normal thyroid on palpation and a low clinical risk of thyroid disease [BEL 4, GRADEC].

Thyroid Ultrasonography:

- *How to Describe US Findings:*
 - Focus the US report on stratification for risk of malignancy
 - Describe position, size, shape, margins, content, echogenic pattern, and vascular features of the nodule(s)
 - For multiple nodules, detail the nodule(s) bearing the US characteristics associated with malignancy rather than describing the largest (dominant) nodule.
 - For suspicious regional neck lymph nodes, describe the cervical compartment, number, shape, size, margins, content, echogenic pattern, presence of hilum, and vascular features [BEL 2, GRADE A].

Comparison of the 2016 AACE/ACE-AME, 2015 ATA, and 2014 BTA Thyroid Nodule Ultrasound Classification Systems

AACE/ACE-AME	ATA	BTA
		Normal
Low Risk thyroid lesion	Benign Very low suspicion Low suspicion	Benign
Intermediate Risk thyroid lesion	Intermediate suspicion	Intermediate/ equivocal
High Risk thyroid lesion	High suspicion	Suspicious
		Malignant

the American Thyroid Association (ATA) , British **Thyroid** Association (BTA)
 American College of Endocrinology (ACE)
 Associazione Medici Endocrinologi (AME)
 American Association of Clinical Endocrinologists (AACE)

Us features of thyroid nodule

<i>US patterns</i>	<i>US features</i>
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with <i>one or more</i> of the following features: • Irregular margins (infiltrative, microlobulated), • Microcalcifications, • Taller than wide shape, • Rim calcifications with small extrusive soft tissue component, • Evidence of ETE
Intermediate suspicion	Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape
Low suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETE, or taller than wide shape
Very low suspicion	Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns
Benign	Purely cystic nodules (no solid component)

US pattern of Thyroid Nodule (ATA)

US-Patterns	Estimated risk of malignancy (%)
High suspicion	>70-90
Intermediate suspicion	10-20
Low suspicion	5-10
Very low suspicion	<3
Benign	<1

Thyroid imaging reporting and data system (TI-RADS)

- **Category definitions**
- **TI-RADS 1:** normal thyroid gland
- **TI-RADS 2:** benign conditions (0% risk of malignancy)
- **TI-RADS 3:** probably benign nodules (<5% malignancy)
- **TI-RADS 4:** suspicious nodules (5-80% malignancy)
 - **TI-RADS 4a:** undetermined (5-10% malignancy)
 - **TI-RADS 4b:** suspicious (10-80% malignancy)
- **TI-RADS 5:** probably malignant nodules (>80% malignancy)
- **TI-RADS 6:** biopsy proven malignancy

ACR TI-RADS

COMPOSITION (Choose 1)	ECHOGENICITY (Choose 1)	SHAPE (Choose 1)	MARGIN (Choose 1)	ECHOGENIC FOCI (Choose All That Apply)
Cystic or almost completely cystic 0 points	Anechoic 0 points	Wider-than-tall 0 points	Smooth 0 points	None or large comet-tail artifacts 0 points
Spongiform 0 points	Hyperechoic or isoechoic 1 point	Taller-than-wide 3 points	Ill-defined 0 points	Macrocalcifications 1 point
Mixed cystic and solid 1 point	Hypoechoic 2 points		Lobulated or irregular 2 points	Peripheral (rim) calcifications 2 points
Solid or almost completely solid 2 points	Very hypoechoic 3 points		Extra-thyroidal extension 3 points	Punctate echogenic foci 3 points

Add Points From All Categories to Determine TI-RADS Level



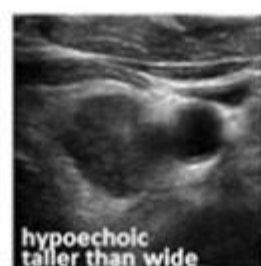
COMPOSITION	ECHOGENICITY	SHAPE	MARGIN	ECHOGENIC FOCI
Spongiform: Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories. Mixed cystic and solid: Assign points for predominant solid component. Assign 2 points if composition cannot be determined because of calcification.	Anechoic: Applies to cystic or almost completely cystic nodules. Hyperechoic/isoechoic/hypoechoic: Compared to adjacent parenchyma. Very hypoechoic: More hypoechoic than strap muscles. Assign 1 point if echogenicity cannot be determined.	Taller-than-wide: Should be assessed on a transverse image with measurements parallel to sound beam for height and perpendicular to sound beam for width. This can usually be assessed by visual inspection.	Lobulated: Protrusions into adjacent tissue. Irregular: Jagged, spiculated, or sharp angles. Extra-thyroidal extension: Obvious invasion = malignancy. Assign 0 points if margin cannot be determined.	Large comet-tail artifacts: V-shaped, >1 mm, in cystic components. Macrocalcifications: Cause acoustic shadowing. Peripheral: Complete or incomplete along margin. Punctate echogenic foci: May have small comet-tail artifacts.

*Refer to discussion of papillary microcarcinomas for 5-9 mm TR5 nodules.

Thyroid imaging reporting and data system (TI-RADS)

- A meta-analysis of 12 comparative studies found that ACR-TIRADS performed better than the ATA and Korean-TIRADS at identifying malignant nodules .

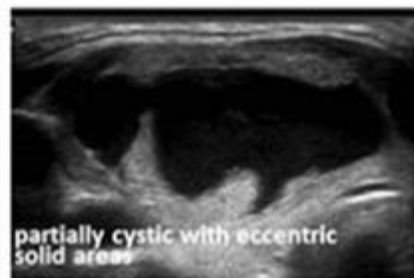
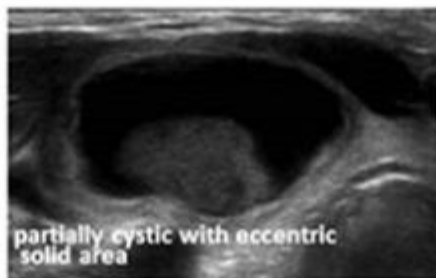
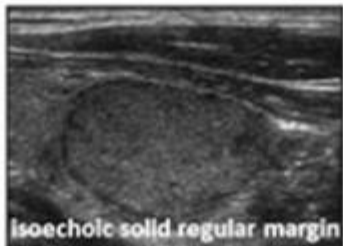
High
Suspicion
>70-90%



Intermediate
Suspicion
10-20%



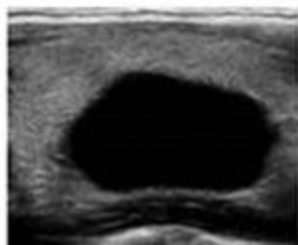
Low
Suspicion
5-10%



Very low
Suspicion
<3%



Benign



Ultrasound Features of Lymph Nodes Predictive of Malignant Involvement

<i>Sign</i>	<i>Reported sensitivity, %</i>	<i>Reported specificity, %</i>
Microcalcifications	5–69	93–100
Cystic aspect	10–34	91–100
Peripheral vascularity	40–86	57–93
Hyperechogenicity	30–87	43–95
Round shape	37	70

Other Diagnostic Imaging Studies:

- *Radionuclide Scanning*
- *When to Perform Thyroid Scintigraphy:*
 - In a thyroid nodule or MNG, when *the TSH level is below the lower limit of the reference range*, or when *ectopic thyroid tissue or a retrosternal goiter* is suspected [BEL 2, GRADE A]
 - In iodine-deficient regions, to exclude autonomy of a thyroid nodule or MNG even when the TSH level is low-normal (e.g., 0.5-1.0 mIU/L). [BEL 3, GRADE B]

Other Diagnostic Imaging Studies:

- Thyroid lesions discovered on CT or MRI performed for other reasons have an uncertain risk of malignancy and **should undergo US evaluation** before considering FNA biopsy
- Nodules detected by ***18FDG PET*** have a high risk of malignancy when thyroid uptake is focal .
 - Such lesions should undergo a preliminary thyroid US evaluation because the presence of diffuse thyroid uptake may be linked to inflammatory conditions.
 - After confirmation of a true nodular lesion, FNA should be performed.
- Focal lesions detected by ^{99m}Tc MIBI scans have a high risk of malignancy and should be evaluated carefully.
- When MIBI is positive, the risk of malignancy in nodules is around 27%.

FNA

- *FNA is the procedure of choice in the evaluation of thyroid nodules, when clinically indicated.*

(Strong recommendation, High-quality evidence)

- FNA:
 - Palpation-guide
 - US-guide

Palpation or US guide FNA

- US-guided FNA is preferred for nodules with higher likelihood of :
 - Nondiagnostic cytology ($>25\%$ — 50% cystic component)
 - Sampling error (difficult to palpate or posteriorly located nodules)
- If the diagnostic US confirms the presence of a predominantly ***solid nodule*** corresponding to what is palpated, the FNA may be performed using palpation or US guidance.

Indication of diagnostic FNA (ATA)

<i>US pattern of thyroid nodule</i>	<i>FNA size cut off indication (largest dimension)</i>
<i>High suspicion</i>	<i>Recommend FNA at ≥ 1 cm</i>
<i>Intermediate suspicion</i>	<i>Recommend FNA at ≥ 1 cm</i>
<i>Low suspicion</i>	<i>Recommend FNA at ≥ 1.5 cm</i>
<i>Very low suspicion</i>	<i>Consider FNA at ≥ 2 cm Observation without FNA is also a reasonable option</i>
<i>Benign</i>	<i>No biopsy</i>

Lymph Node Evaluation

- *Sonographic evaluation of the anterior cervical lymph node compartments (central and lateral) should be performed* when thyroid nodules are detected .
- FNA of the suspicious lymph node (for cytology and washout for Tg measurement) :
 - In US detects cervical lymph nodes that are sonographically suspicious for thyroid cancer

AACE/ACE Indication of FNA:

- FNA is *recommended* for the following:
 - High US risk thyroid lesions ≥ 10 mm
 - Intermediate US risk thyroid lesions > 20 mm
 - Low US risk thyroid lesions only when > 20 mm and increasing in size or associated with a risk history and before thyroid surgery or minimally invasive ablation therapy [BEL 2, GRADE A]
- FNA is *not recommended* for nodules that are:
 - Functional on scintigraphy [BEL 2, GRADE B].

FNA of thyroid incidentalomas

- Manage thyroid incidentalomas according to the previously described criteria for nodule diagnosis [BEL 2, GRADE A].
- Perform US evaluation of incidentalomas detected by **CT** or **MRI** before consideration of FNA biopsy [BEL 2, GRADE A].
- We recommend that thyroid incidentalomas detected by **PET** with 18F-fluorodeoxyglucose (focal uptake, in particular) should undergo US evaluation and FNA because of the high risk of malignancy [BEL 2, GRADE A].

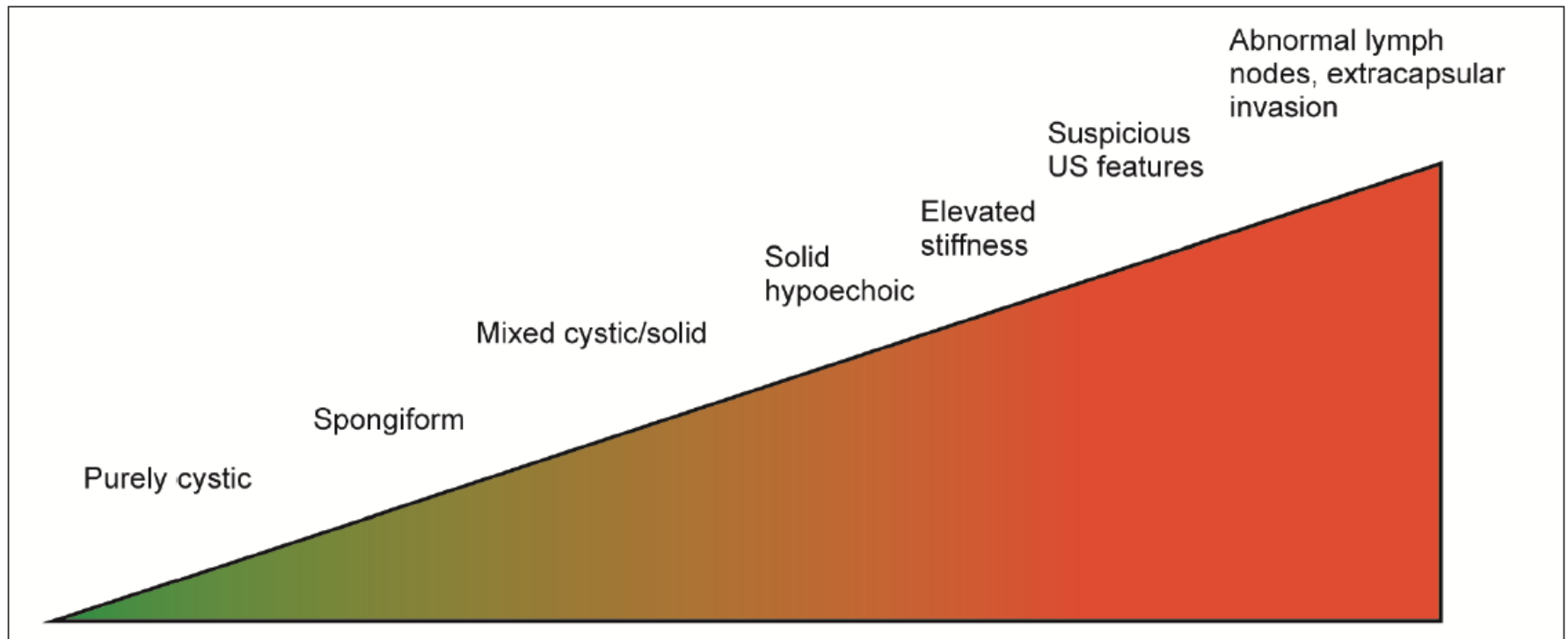
FNA of MNG and lymph nodes

- We do **not recommend** the biopsy of more than 2 nodules in the same patient when the nodules are selected on the basis of the previously described criteria [BEL 3, GRADE C].
- If a radioisotope scan is available, we recommend **not biopsying hot areas** [BEL 2, GRADE B].
- In the presence of suspicious cervical lymphadenopathy, we recommend FNA for cytologic assessment of **both the lymph node and the suspicious nodule(s)** [BEL 2, GRADE A].
- We recommend the determination of thyroglobulin (**Tg**) or **calcitonin, according to clinical indications, on FNA washout of suspicious lymph nodes** [BEL 2, GRADE A].

FNA of complex thyroid nodule(s)

- We recommend **sampling the solid component** of the lesion through FNA biopsy[BEL 3, GRADE B].
- Preferentially sample the **vascularized areas** of complex lesions [BEL 4, GRADE C].
- Submit both the FNA specimen and the drained fluid for cytologic examination [BEL2, GRADE A].

Indication of FNA according to US finding



FNA interpretation

- *Thyroid nodule FNA cytology should be reported using diagnostic groups outlined in the **Bethesda System** for Reporting Thyroid Cytopathology.*

(Strong recommendation, Moderate-quality evidence)

FNA reports:

- *Criteria for cytologic adequacy :*
- Presence of *at least six groups* of well-visualized follicular cells, *each group containing at least 10 well-preserved epithelial cells*, preferably on a single slide)

Nondiagnostic cytology

- *For initial nondiagnostic cytology result, repeat FNA with US guidance and, if available, on-site cytologic evaluation*

(Strong recommendation, Moderate-quality evidence)

- *Repeatedly nondiagnostic nodules without a high suspicion sonographic pattern require:*
 - Close observation or
 - Surgical excision for histopathologic diagnosis

(Weak recommendation, Low-quality evidence)

Nondiagnostic cytology

- *Surgery should be considered for histopathologic diagnosis if:*
 - The cytologically nondiagnostic nodule has a high suspicion sonographic pattern
 - Growth of the nodule ($>20\%$ in two dimensions) is detected during US surveillance
 - Clinical risk factors for malignancy are present

(Weak recommendation, Low-quality evidence)

When repeat FNA

- Repeat FNA should be performed **no sooner than 3 months** after the initial FNA to *prevent false-positive interpretation* due to biopsy-induced reactive/reparative changes (?)
- A 3-month waiting period after a nondiagnostic biopsy is likely not necessary.
- If clinical and US features are suspicious for malignancy, a shorter waiting period may be appropriate.
- *Repeat FNA with US guidance* will yield a diagnostic cytology specimen in 60%–80% of nodules, particularly when the cystic component is <50%

Benign cytology

- *If the nodule is benign on cytology, further immediate diagnostic studies or treatment are not required*

(Strong recommendation, High-quality evidence)

- Based on the evidence, it is still unclear thyroid nodules ≥ 4 cm and benign cytology carry a higher risk of malignancy and should be managed differently than those with smaller nodules

Malignant cytology

- *If a cytology result is diagnostic for primary thyroid malignancy, surgery is generally recommended.*

(Strong recommendation, Moderate-quality evidence)

Malignant cytology

- *Alternative active surveillance management in:*
 - Very low risk tumors (MPTC without clinically evident metastases or local invasion, and no convincing cytologic evidence of aggressive disease)
 - High surgical risk because of comorbid conditions
 - Relatively short remaining life span (serious cardiopulmonary disease, other malignancies, very advanced age)
 - Concurrent medical or surgical issues that need to be addressed prior to thyroid surgery.

Indeterminate cytology

(AUS/FLUS, FN, SUSP)

- *Molecular Markers :*
 - Diagnostic
 - Prognostic (predictive purpose)
- The principal proposed use of molecular markers in indeterminate thyroid FNA specimens is:
 - Diagnostic (ruling out or in the presence of malignancy), with the implication of a companion use to inform decision-making on primary surgical treatment

Molecular marker testing

- Seven-gene panel of genetic mutations and rearrangements(BRAF, RAS, RET/PTC, PAX8/PPARc)
- Gene expression classifier (167 GEC; mRNA expression of 167 genes)
- Galectin-3 immunohistochemistry(cell blocks)

Molecular marker testing

- Long term outcome data on companion use of molecular marker status to guide therapeutic decision-making *is currently lacking*
- Significant overall benefit in health outcomes in patients with thyroid nodules from implementation of molecular marker use in routine clinical practice *is not clear*

Molecular marker testing

- The pretest probability of malignancy (based on clinical risk factors, cytology, US findings), feasibility considerations, and patient preferences are some additional factors that need to be considered in decision-making related to molecular marker testing of FNA specimens.

Molecular marker testing

- If molecular testing is being considered, patients should be counseled regarding the **potential benefits and limitations** of testing and about the **possible uncertainties** in the therapeutic and long-term clinical implications of results.

(Strong recommendation, Low-quality evidence)

AUS/FLUS cytology

- For AUS/FLUS cytology, after consideration of worrisome clinical and sonographic features:
 - *Repeat FNA* or
 - *Molecular testing*
- To supplement malignancy risk assessment in lieu of proceeding directly with a strategy of either *surveillance* or *diagnostic surgery*.
- Informed *patient preference* and *feasibility* should be considered in clinical decision-making.

(Weak recommendation, Moderate-quality evidence)

AUS/FLUS cytology

- If repeat FNA cytology, molecular testing, or both are *not performed or inconclusive*:
- Either *surveillance* or *diagnostic surgical excision* may be performed depending on :
 - Clinical risk factors
 - Sonographic pattern
 - Patient preference.

(Strong recommendation, Low-quality evidence)

Follicular neoplasm/suspicious for follicular neoplasm cytology

- **Diagnostic surgical excision** is the long-established standard of care for the management of FN/SFN cytology nodules.
- However after consideration of clinical and sonographic features, **molecular testing may be used** to supplement malignancy risk assessment data in lieu of proceeding directly with surgery. Informed patient preference and feasibility should be considered in clinical decision-making.

(Weak recommendation, Moderate-quality evidence)

Follicular neoplasm/suspicious for follicular neoplasm cytology

- If molecular testing is either not performed or inconclusive, surgical excision may be considered for removal and definitive diagnosis of an FN/SFN thyroid nodule.

(Strong recommendation, Low-quality evidence)

Suspicious for malignancy cytology

- If the cytology is reported as suspicious for PTC (SUSP), surgical management should be similar to that of malignant cytology, depending on clinical risk factors, sonographic features, patient preference, and possibly results of mutational testing (if performed).

(Strong recommendation, Low-quality evidence)

Suspicious for malignancy cytology

- After consideration of clinical and sonographic features, mutational testing for BRAF or the seven-gene mutation marker panel (BRAF, RAS, RET/PTC, PAX8/ PPAR δ) **may be considered** in nodules with SUSP cytology if such data would be expected to alter surgical decision making.

(Weak recommendation, Moderate-quality evidence)

Type of surgery

- When surgery is considered for patients with a **solitary, cytologically indeterminate nodule**, **thyroid lobectomy** is the recommended initial surgical approach. This approach may be modified based on clinical or sonographic characteristics, patient preference, and/or molecular testing when performed

(Strong recommendation, Moderate-quality evidence)

Type of surgery

- Because of increased risk for malignancy, *total thyroidectomy* may be preferred in patients with indeterminate nodules that are:
 - Cytologically suspicious for malignancy,
 - Positive for known mutations specific for carcinoma
 - Sonographically suspicious
 - Large (>4 cm)
 - In patients with familial thyroid carcinoma
 - History of radiation exposure
- If completion thyroidectomy would be recommended based on the indeterminate nodule being malignant following lobectomy.
(Strong recommendation, Moderate-quality evidence)

Type of surgery

- Patients with indeterminate nodules who have :
 - Bilateral nodular disease
 - Those with significant medical comorbidities,
 - Those who prefer to undergo bilateral thyroidectomy to avoid the possibility of requiring a future surgery on the contralateral lobe, may undergo total or near-total thyroidectomy, assuming completion thyroidectomy would be recommended if the indeterminate nodule proved malignant following lobectomy.

(Weak recommendation, Low-quality evidence)

Long term follow up of thyroid Nodule

- Follow-up of thyroid nodules with *benign cytology diagnoses* should be determined by risk stratification based upon US pattern.
- Nodules with *high suspicion US pattern*: repeat US and US-guided FNA *within 12 months*.

(Strong recommendation, Moderate-quality evidence)

Long term follow up of thyroid Nodule

- Nodules with *low to intermediate suspicion US pattern* repeat US at 12–24 months.
- If *sonographic evidence of growth* (20% increase in at least two nodule dimensions with a minimal increase of 2mm or more than a 50% change in volume) or *development of new suspicious sonographic features*, the FNA could be repeated or observation continued with repeat US, with repeat FNA in case of continued growth.

(Weak recommendation, Low-quality evidence)

Long term follow up of thyroid Nodule

- Nodules with *very low suspicion US pattern* (including spongiform nodules): the utility of surveillance US and assessment of nodule growth as an indicator for repeat FNA to detect a missed malignancy is limited.
- If US is repeated, it should be done at **>24 months.**

(Weak recommendation, Low-quality evidence)

Follow-up of nodules with two benign FNA cytology results

- If a nodule has undergone repeat US-guided FNA with a second benign cytology result:
- **US surveillance** for this nodule for continued risk of malignancy **is no longer indicated**.

(Strong recommendation, Moderate-quality evidence)

Follow-up for nodules that do not meet FNA criteria

- The strategy for sonographic follow-up of nodules that do not meet criteria for FNA at initial imaging should be based upon the nodule's sonographic pattern:
- Nodules with **high suspicion US pattern**: repeat US in **6–12 months**.

(Weak recommendation, Low-quality evidence)

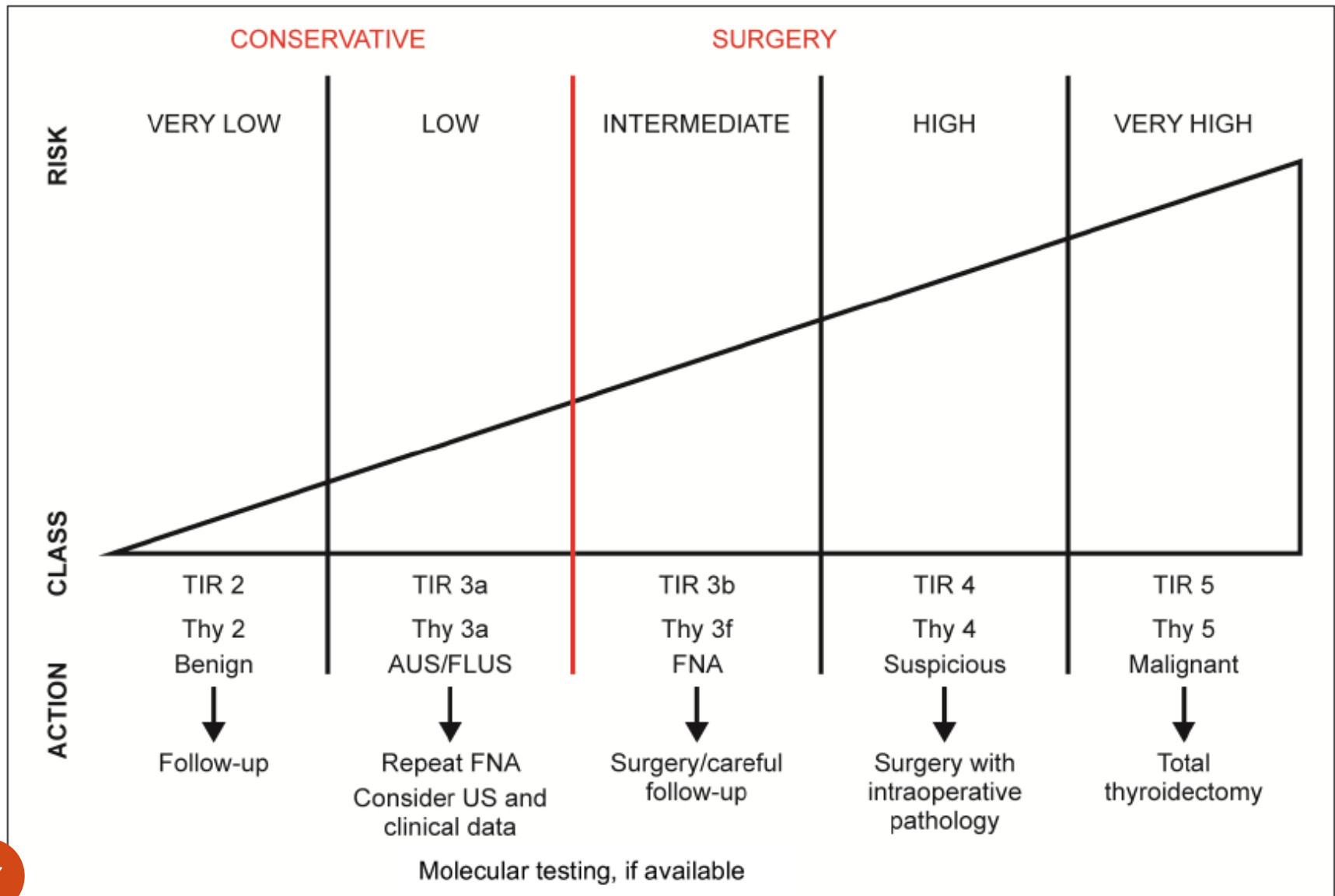
- Nodules with **low to intermediate suspicion US pattern**: consider **repeat US at 12–24 months**.

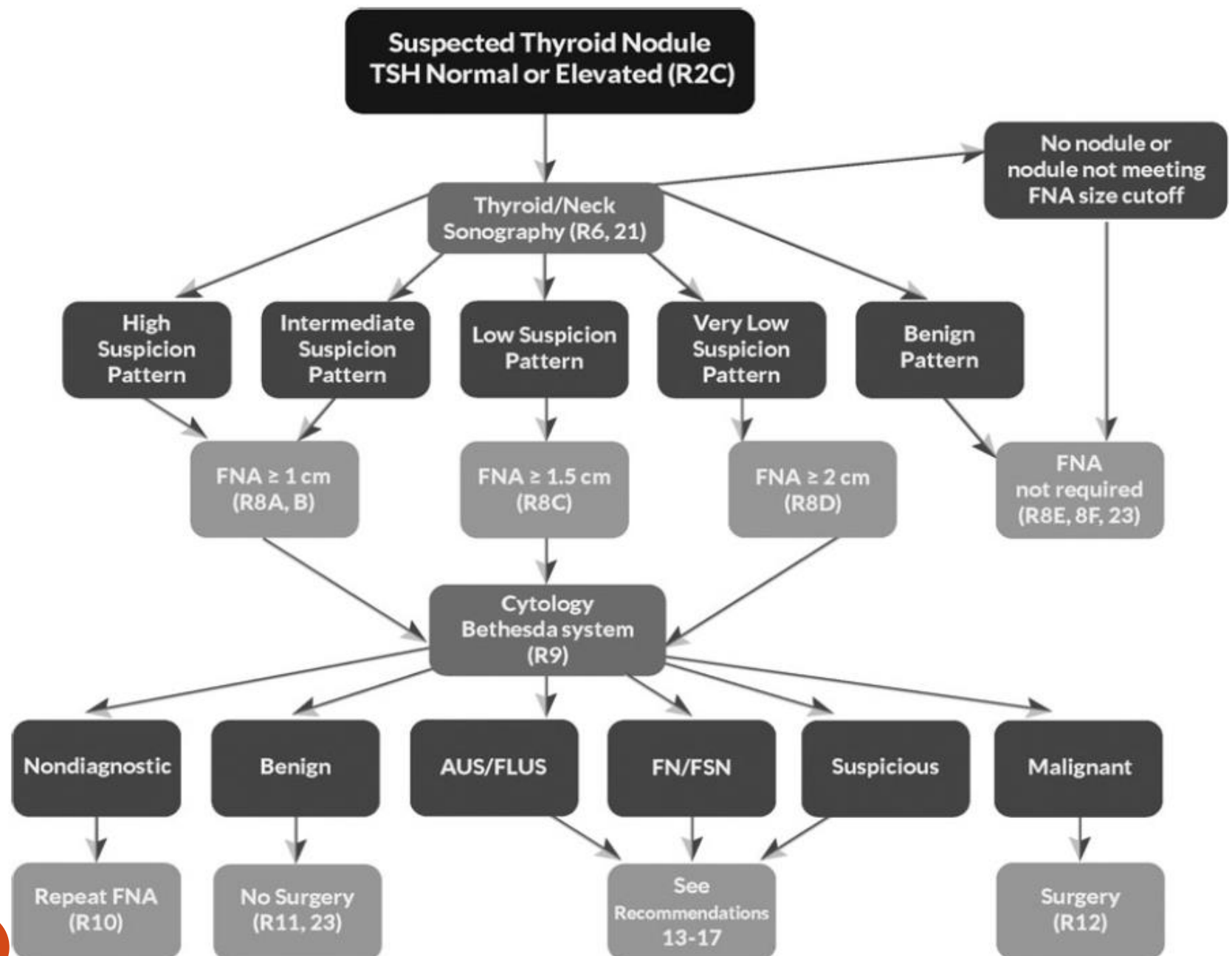
(Weak recommendation, Low-quality evidence)

Follow-up for nodules that do not meet FNA criteria

- Nodules >1 cm with very low suspicion US pattern (including spongiform nodules) and pure cyst: the utility and time interval of surveillance US for risk of malignancy is not known. If US is repeated, it should be **at >24 months**
(No recommendation, Insufficient evidence)
- Nodules <1 cm with very low suspicion US pattern (including spongiform nodules) and pure cysts **do not require routine sonographic follow-up.**
(Weak recommendation, Low-quality evidence)

Cytologic Categories and suggested clinical action





*Thanks For Your
Attention*

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