

## Diagnostic Approach for Thyroid Nodules

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### **ABSTRAK**

*Nodul tiroid merupakan masalah kesehatan yang sering dijumpai dalam praktik sehari-hari, sehingga diperlukan panduan klinis. Pedoman ini dibuat oleh tim multidisiplin, dan diharapkan dapat dijadikan panduan dalam melakukan pendekatan diagnosis nodul tiroid yang komprehensif dalam praktek klinis sehari-hari.*

**Kata kunci:** nodul tiroid, pengelolaan nodul tiroid.

### **ABSTRACT**

*Thyroid nodule is a health problem which commonly found in daily practice, therefore clinical guidance is needed. This guideline was compiled by a multidisciplinary team and expected to be a guideline in diagnosing thyroid nodules on daily clinical practice.*

**Keywords:** thyroid nodules, management of thyroid nodules.

## INTRODUCTION

Thyroid nodule are common health problems in clinical practice.<sup>1,2</sup> Furthermore, with the advancement on the use of radiologic imaging, incidental findings of thyroid nodule are increasing. This will also urge the patients to seek medical advice to clinicians. Of all the 7.384 outpatient thyroid cases in RSUPN Dr.CiptoMangunkusumo, a tertiary care and a national referral hospital in Indonesia, dating from 2012 to 2016, about 68,7% of them were thyroid nodule cases. Among those thyroid nodule cases, 3-7% were incidental findings through physical examination or by the patient, while 67% were found on radiological examination (67% through USG examination, 15% through cervical CT scan/ MRI, 1-2% through FDG-PET (fluorodeoxyglucose positron emission tomography).<sup>3</sup> It is also important to note that even several studies have reported that around 20-76% population have at least one thyroid nodule.<sup>4</sup>

## DIAGNOSIS

Evaluation in patients with thyroid nodules includes a detailed and relevant history, physical examination, laboratory test, radiologic imaging and, if needed, fine needle aspiration (FNA) biopsy

### History

A detailed, structured, and relevant history taking needs to be conducted. This should include the searching for: pain at the front part of the neck, acute pain, severe pain, progressive enlargement (rapid growth is associated with high risk for malignancy, anaplastic carcinoma develops within 6 months, while papillar/follicular carcinoma develops very slowly), dyspnea, suffocating sensation, cervical pain, dysphagia, hoarse voice, and symptoms of hyper- or hypo-thyroidism.<sup>1</sup> It should also include disease history of thyroid disease, malignancy, whole body radiation, and childhood thyroid nodule. The presence of thyroid nodule in first degree family (parents, older siblings, younger siblings, or children) is a risk factor for thyroid nodule. Most of the nodules which do not show symptoms are benign. However, the lack of

findings of malignancy symptoms does not rule out the chances of malignancy.<sup>5</sup>

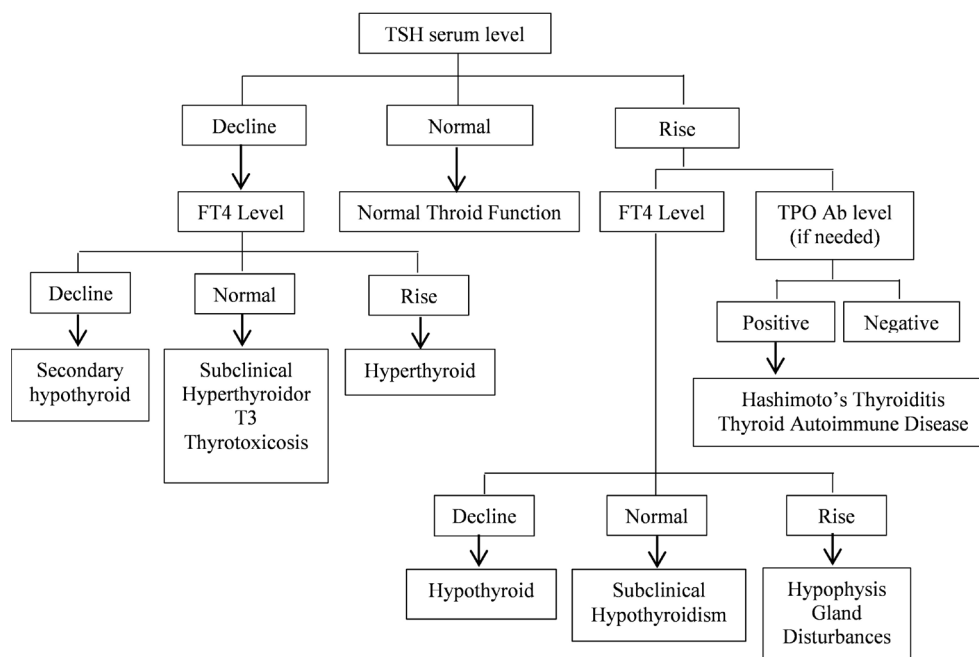
Acute pain can be found on cystic nodule and thyroid infection. Severe pain and progressive growth may be a sign of anaplastic carcinoma or primary lymphoma. Suffocating sensation, cervical pain, dysphagia, and hoarse voice (dysphonia) may be caused by thyroid abnormalities, but are usually caused by diseases other than thyroid. Hoarse voice, vocal cord paralysis, tracheal compression symptoms (dysphoria, cough) may lead to suspicion of malignancy. The existence of fever, dysphagia, and malaise with thyroid pain may lead to a suspicion of subacute thyroiditis.<sup>1</sup>

### Physical Examination

Physical examination through inspection and palpation need to be done thoroughly and should focus on thyroid gland and cervical lymphs. Take note on the volume, location, consistency, size, number, and tenderness of the nodule(s), as well as, if present, cervical adenopathy. Voice evaluation needs to be done for pre-operation purpose.<sup>1</sup>

### Laboratory Examination

Laboratory examination is the initial step that needs to be done for all cases of thyroid nodule. Thyroid examination begins with examining Thyroid Stimulating Hormone (TSH) levels.<sup>1</sup> (**Figure 1**) If the result is normal, no further examination of free thyroid hormone is needed. On the other hand, if TSH levels is abnormal, free thyroxin levels (FT4) should be tested. Low TSH and high FT4 confirms the presence of hyperthyroidism, while low TSH and normal FT4 might show the presence of subclinical hyperthyroidism or T3 toxicosis. Low TSH and low FT4 suggests the presence of central hypothyroidism. High TSH and high FT4 suggests central hyperthyroidism. While high TSH and low FT4 suggest the presence of primary hypothyroidism, high TSH and normal FT4 suggest the presence of subclinical hypothyroidism. If the TSH levels is high, the presence of thyroiditis should be considered and evaluated. Positive thyroid peroxidase antibody (TPO Ab) finding may lead to suspicion of thyroid autoimmune disease and Hashimoto's Thyroiditis.



**Figure 1.** Laboratory examination algorithm in thyroid nodule diagnosis

## Radiology

Radiological examination of thyroid nodule is conducted to support the physical findings and laboratory results to ensure suitable and optimal classification of the thyroid nodule(s) and guide the treatment. High-resolution ultrasonography (USG) examination is considered the most sensitive method. It enables clinicians to characterize palpable or non-palpable thyroid nodule and cervical lymphadenopathy, thus providing a valid malignancy risk stratification.<sup>1</sup> USG examination is not recommended as a screening test for low-risk patients with normally palpable thyroid. Newer USG technology has enabled clinicians to assess the vasculature of the thyroid, as well as performing elastography. Diagnosis of thyroid nodule(s) is established based on USG findings and, if necessary, the results from FNA (fine needle aspiration) biopsy (**Table 1**), which will be discussed in the next section.

The use of neck MRI and CT-scan may be considered to evaluate the size, respiratory passage compression, substernal extension, or pathological lymphatic nodes on cervical region that is not visible through USG examination.<sup>5</sup> Whereas in thyroid nodule(s) with intermediate cytology finding, the use of PET/ CT-scan may

provide additional information on the risk of malignancy, the lack of diagnostic accuracy, high cost, and limited access precludes its use as a routine diagnostic procedure for thyroid nodule. PET and CT-scan may be considered for pre-operative malignant nodule with aggressive presentation.<sup>1</sup>

Thyroid scintigraphy is the only technique to evaluate functionality of thyroid nodule. Thyroid scintigraphy is indicated for low levels of TSH, ectopic thyroid suspicion, retrosternal struma (multinodal struma that extend to intra-thoracic region), iodine deficiency. Thyroid scintigraphy can also be performed to evaluate the existence of hot nodule when TSH levels is low (0.5 – 1.0 mIU/ L), and to evaluate feasibility for ablation therapy with radioactive iodine. Whole body scan with radioactive iodine (NaI-131) is performed to evaluate thyroid tissue residue and thyroid malignancy metastasis after total thyroidectomy.

## FNA (Fine Needle Aspiration) Biopsy

The FNA biopsy should be done on thyroid lesion with the following findings on USG examination (**Table 1**): high risk of malignancy with size  $\leq 10$  mm,<sup>6-8</sup> intermediate risk of malignancy with size  $> 20$  mm, and low risk of malignancy with size  $> 20$  mm and progressively

**Table 1.** Ultrasonography, risk of malignancy, and fine-needle aspiration guidance for thyroid nodules.<sup>1</sup>

Sonographic pattern	Ultrasonography features	Risk of Malignancy, %	FNA size cutoff (largest dimension)
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features:	>70-90*	Recommend FNA at ≥1 cm
	irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE		Recommend FNA at ≥1 cm
Intermediate suspicion	Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape	10-20	Recommend FNA at ≥1.5 cm
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.	5-10	Consider FNA at ≥2 cm. Observation without FNA
Very low suspicion	Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns	<3	is also a reasonable option
Benign	Purely cystic nodules (no solid component)	<1	No biopsy <sup>b</sup>

<sup>a</sup> The estimate is derived from high volume centers, the overall risk of malignancy may be lower given the interobserver variability in sonography.

<sup>b</sup> Aspiration of the cyst may be considered for symptomatic or cosmetic drainage. ETE, extrathyroidal extension.

Adapted from 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.

**Table 2.** Malignancy risk and clinical treatment based on Bethesda criteria.<sup>12</sup>

Diagnostic criteria	Risk of malignancy (%)	General treatment
Non-diagnostic or unsatisfactory (ND/UNS)	1-4	Repeat FNAB with ultrasonography
Benign	0-3	Clinical follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)	~5-15	Repeat FNAB
Follicular neoplasm/ suspicious for a follicular neoplasm (FN/SFN)	15-30	Surgical lobectomy
Suspicious of malignancy (SUSP)	60-75	Near-total thyroidectomy or surgical lobectomy
Malignant	97-99	Near-total thyroidectomy

Adapted from The Bethesda system for reporting thyroid cytopathology, 2009

grows in size or has risk based on history and before thyroid operation or minimal invasive ablation therapy,<sup>9-11</sup> nodule with USG finding that shows extra-capsular extension or cervical lymphatic nodes metastasis, nodules on patients with radiation history during childhood/ teenage years; family history<sup>11</sup> with PTC, MTC, or MEN 2 in the first degree family; thyroid surgery history; and increase levels of calcitonin with unrelated factors.

However, in several conditions FNA biopsy is not warranted. Low risk of malignancy with clinical presentation of nodule sizing <5

mm is best observed than biopsy regardless of the thyroid USG finding, while high risk of malignancy on USG findings with nodule sizing 5-10 mm also does not call for FNA biopsy. Guided FNAB examination is considered more accurate for non-palpable thyroid nodule or lymph node, subcapsular or paratracheal lesion, suspicious lymph nodes, previous history or family history of thyroid cancer, and clinical findings such as dysphonia. FNA biopsy is less accurate on pediatric population, thus aggressive surgical excision is preferred. Several types of nodules, such as functional nodules on

scintigraphy, functional nodules on toxic Grave's disease, and supposedly non-malignant nodules are not indicated for FNAB.

FNA biopsy result is reported based on the Bethesda System for Reporting Thyroid Cytopathology criteria.<sup>9</sup> (Table 2) Malignancy risk of every category is then associated with rational clinical treatment guideline. The weakness of Bethesda criteria is its inability to show the exact number, only the depiction of quantity (many or few).

## CONCLUSION

The optimal management of thyroid nodule calls for clinicians' skilled handling on conducting the comprehensive diagnostic approach. This comprehensive approach should include structured history taking, physical examination, laboratory examination, radiology and, if needed, fine needle aspiration biopsy.

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