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Ultrasonography Efficiency in detection of thyroid malignant nodules

[1]Mashael Abdulelah Al-zaylae'e, [2]Munira Mohammed Aldakheel,
[3]Saja Omar Bakhshwain, [4]Shaima Mohammed Alghuraybi, [5]Jumana khalid alansari,
[6]Juhaina Mohammed Shames Aldeen, [7]Ghady khaled al-sadiq, [8]Rahik azzam alshawaf

Abstract: **In this reviews we provide the most recent information about diagnosis of thyroid nodules and discuss the efficiency of ultrasonography diagnosis, which is the first line test. We searched multiple electronic databases using a search strategy to find relevant studies related to our topic from inception to July 2018. Eligible studies included ultrasonography diagnosis thyroid nodules. Thyroid ultrasound need to be carried out in all patients with a presumed thyroid nodule or nodular goiter on physical exam or with nodules incidentally kept in mind on various other imaging research studies (carotid ultrasound, CT, MRI, or FDG-PET scan). Diagnosis and also therapy of thyroid nodules is extremely determinate by very early assessment, medical criteria applying US and also FNA as initial test. They should be practical, reliable and cost-effective.**

Keywords: **ultrasonography diagnosis, Thyroid ultrasound, carotid ultrasound, CT, MRI, FDG-PET scan).**

1. INTRODUCTION

Nodules in the thyroid gland, whether solitary or several, are typical in clinical practice. Thyroid nodules are spotted in roughly 5-7% of a grown-up population after physical examination. Given that modern ultrasound (US) techniques could spot small nodules, the regularity of thyroid nodules has been reported as high as 67% in unselected subjects [1].In addition, thyroid nodules continuously be detected with good frequency, probably because of extensive use of various imaging methods (computed tomography (CT) scan, magnetic resonance imaging (MRI), positron emission tomography (PET), and so on) that identify thyroid nodules "incidentally" [2].Thyroid nodules are medically important because they can stands for thyroid cancer, which happens approximately 10-15% of nodules [3].Other factor to consider are the risk of thyroid dysfunction (autonomous adenoma and also harmful multinodular goiter), compressive symptoms and some aesthetic issue. The main worry of patients and doctors is to detected the suspected cancers as rapidly and also cost effectively as possible and decrease unnecessary thyroid surgery [4].

Thyroid nodules are often discovered. Although they are mostly palpable, many are discovered incidentally throughout unrelated radiographic reports. 10 to 15% of thyroid nodules stands for thyroid malignancy. In this reviews we provide the most recent information about diagnosis of thyroid nodules and discuss the efficiency of ultrasonography diagnosis, which is the first line test.

2. METHODOLOGY

We searched multiple electronic databases using a search strategy to find relevant studies related to our topic from inception to July 2018. Eligible studies included ultrasonography diagnosis thyroid nodules. We furthermore searched the references list of included studies to have more evidence for our review. Restriction of search to published English language studies with human subjects.

3. DISCUSSION

- **Etiology of thyroid nodules:**

As defined by the ATA's task force on the management of thyroid nodules and distinguished thyroid cancer, [5] a thyroid nodule can have specified as a distinct lesion within the thyroid gland that is radiologically specific from the bordering parenchyma. It might be solitary, multiple, cystic, or solid, and also might or otherwise be functional; accordingly, the

specific morphological features, thyroid functional standing and pathological evaluation need to be assessed [6].A simple way to classify thyroid nodules is to define them as non-neoplastic and neoplastic. Neoplastic thyroid nodules can be benign or malignant [7]. The differential diagnosis of the thyroid nodule are detailed in Table 1.

Table 1: Clinical and pathological classification of thyroid nodules[5-7].

Non-neoplastic nodules	**Benign neoplasms**	**Malignant neoplasms**
Hyperplastic	***Non-functioning (cold nodules)***	***Primary carcinoma***
- Spontaneous	- Solid (or mixed): adenoma - Cystic	- Papillary carcinoma
- Compensatory after partial thyroidectomy	***Functioning (hot nodules)***	- Follicular carcinoma
Inflammatory	- Adenoma	- Anaplastic carcinoma
- Acute bacterial thyroiditis		- Medullary carcinoma
- Subacute thyroiditis		***Thyroid lymphoma***
- Lymphocytic (Hashimoto's) thyroiditis		***Thyroid metastasis from other primaries***

- **Thyroid nodules evaluation:**

Thyroid nodules concern clinical attention as an incidental finding throughout routine physical exam, or when noted by the patient, or during a radiologic process, such as carotid ultrasonography, neck computed tomography (CT), or positron emission tomography (PET) scanning. Several different conditions could create thyroid nodules (table 2). Their medical value is mostly related to the need to omit thyroid cancer, which accounts for 4.0 to 6.5 percent of all thyroid nodules in non-surgical set [7-11].

Table 2: Causes of thyroid nodules

Benign	Malignant
Multinodular (sporadic) goiter ("colloid adenoma")	Papillary carcinoma
Hashimoto's (chronic lymphocytic) thyroiditis	Follicular carcinoma
Cysts: colloid, simple, or hemorrhagic	Minimally or widely invasive
Follicular adenomas	Oxyphilic (Hurthle-cell) type
Macrofollicular adenomas	Medullary carcinoma
Microfollicular or cellular adenomas	Anaplastic carcinoma
Hurthle-cell (oxyphil-cell) adenomas	Primary thyroid lymphoma
Macro- or microfollicular patterns	Metastatic carcinoma (Breast, renal cell, others)

Nonpalpable nodules (incidentalomas) have the very same danger of malignancy as palpable nodules [12-15].Therefore, the initial assessment in all patients with a thyroid nodule (uncovered either by palpation or incidentally indicated on a radiologic processes, such as carotid ultrasonography, neck CT, MRI, or PET) consists of a history, checkup, and measurement of serum thyroid stimulating hormone (TSH). Ultrasound is additionally advised for all patients to verify the presence of nodularity, evaluate sonographic features, and to assess for the existence of additional nodules and also lymphadenopathy. Fine needle aspiration (FNA) biopsy is the most precise method for evaluating thyroid nodules and also recognizing patients who need surgical resection [16].If a serum TSH is typical or elevated, the following action in the assessment of a thyroid nodule is a palpation or ultrasound-guided fine needle aspiration biopsy. If the nodule is complicated or posterior, ultrasound guidance is strongly advised to avoid nondiagnostic or incorrect cytology outcomes. Over the last decade, the use of thyroid scintigraphy to examine thyroid nodules has actually become much less usual [16].Although scintigraphy stays the only way to establish the functional status of a nodule, high-resolution thyroid ultrasonography supplies anatomic definition superior to thyroid scintigraphy. Scintigraphy serves in patients with a low serum TSH concentration. It may be useful in patients with numerous thyroid nodules to choose those that are hypofunctional and for that reason may need FNA [10-15].

- **Thyroid Ultrasonography:**

Sonography is the primary device utilized for initial cancer threat stratification of thyroid nodules and also ultimately determining whether to purchase a fine-needle aspiration biopsy. Due to the fact that the thyroid is superficially situated in the neck, with its posterior border usually situated less than 4 cm from the skin, high-resolution (12 MHz) probes provide excellent image description [17].Ultrasound is indicated when either the thyroid gland is palpably uncommon or a thyroid

nodule is incidentally discovered on one more radiological study. Nonspecific signs or abnormal lab examination outcomes (such as exhaustion, raised serum thyrotropin degrees, or autoimmune thyroiditis) are not indications for sonography. However, ultrasound is required to differentiate in between asymmetric involvement of the thyroid gland by lymphocytic thyroiditis vs a superimposed thyroid nodule, for which more examination might be required. A diagnostic ultrasound record should consist of description of the background thyroid parenchyma, nodule locality, sizing (in 3 dimensions), sonographic features (Table 3), and also survey of the cervical lymph nodes [17].

US assessment is extremely precise and vulnerable in reviewing thyroid nodules [5], [19],[20].US exam was able to find thyroid incidentaloma which could not be gotten by checkup. Thyroid US is the first choice of imaging researches for thyroid gland evaluation. Indication of US evaluation on thyroid nodules are: a) all types of thyroid nodules, b) thyroid nodules with the background of neck radiation, as well as c) thyroid nodules with the background of familial thyroid cancer, multiple endocrine neoplasia (MEN) type 2, even if the gland shows up normal by palpation [5].Several ultrasound findings have actually been located to be connected with malignancy amongst patients brought to surgical procedure after FNA. A solid nodule, microcalcifications, hypoechogenicity, subcapsular localization, irregular shapes, invasive growth, multifocal sore, boosted nodule blood flow on Doppler (when TSH is normal) and suspicious regional lymphadenopathy on US show malignancy [15].A ratio of the anteroposterior size of the nodule to the transverse diameter (AP/T) > 1 showed malignancy [18].Nodules that are cystic, isoechoic, have regular borders, do not have calcification and show no invasive growth usually taken into consideration benign [20].

Table 3: Standardized Sonographic Scoring Systems Proposed or Endorsed by Practice Guidelines for Risk-Based Fine-Needle Aspiration Biopsy Guidance for Thyroid Nodules

AACE, ACE, and AME, 2016 [22]	ATA, 2015[5]	EU-TIRADS, 2017 [21]	ACR TIRADS, 2017 [20]
Low-Risk and Benign Thyroid Nodules			
Low-risk definition Risk of malignancy, 1% FNAB >20 mm (selective)[a]	**Benign definition** Risk of malignancy,<1% FNAB is not indicated	**Benign (EU-TIRADS 2) definition** Risk of malignancy, ≈0% FNAB is not indicated	**Benign (TR1) definition** Risk of malignancy, 2% FNAB is not indicated
Sonographic pattern Cysts (fluid component >80%) Mostly cystic nodules with reverberating artifacts and not associated with suspicious ultrasound signs Isoechoic spongiform nodules, either confluent or with regular halo	**Sonographic pattern** Purely cystic nodules (no solid component)	**Sonographic pattern** Pure, anechoic cysts; Entirely spongiform nodules	**Sonographic pattern** Spongiform Pure cyst
Intermediate or Moderately Suspicious Thyroid Nodules			
Intermediate-risk definition Risk of malignancy, 5%-15% FNAB >20 mm	**Intermediate-suspicion definition** Risk of malignancy, 10%-20% FNAB ≥10 mm	**Intermediate-risk (EU-TIRADS 4) definition** Risk of malignancy, 6%-17% FNAB >15 mm	**Moderately suspicious (TR4) definition** Risk of malignancy, 5%-20% FNAB >15 mm
Sonographic pattern Slightly hypoechoic (vs thyroid tissue) or isoechoic nodules, with ovoid-to-round shape, smooth or ill-defined margins May be present Intranodular vascularization Elevated stiffness at elastography Macro or continuous rim calcifications Indeterminate hyperechoic spots	**Sonographic pattern** Hypoechoic solid nodule with smooth margins without microcalcifications, extrathyroidal extension or taller than wide shape	**Sonographic pattern** Oval shape, smooth margins, mildly hypoechoic, without any feature of high risk	**Sonographic patterns** Hypoechoic solid noncalcified nodules with oval shape and either smooth or irregular or lobulated margins Isoechoic solid or mixed noncalcified nodules with either nonparallel orientation (taller than wide), lobulated or irregular margins, or punctate echogenic foci

High-Risk or Suspicious Thyroid Nodules			
High-risk definition Risk of malignancy, 50%-90%[b] FNAB ≥10 mm (5 mm, selective)[c]	**High-suspicion definiton** Risk of malignancy, >70%-90% FNAB ≥10 mm	**High-risk (EU-TIRADS 5) definition** Risk of malignancy, 26%-87% FNAB >10 mm	**Suspicious (TR5) definition** Risk of malignancy, ≥20% FNAB >10 mm
Sonographic patterns Nodules with ≥ 1 of the following: Marked hypoechogenicity (vs prethyroid muscles) Spiculated or lobulated margins Microcalcifications Taller-than-wide shape Extrathyroidal growth Pathologic adenopathy	**Sonographic pattern** Solid hypoechoic nodule or solid hypoechoic component of partially cystic nodule with ≥1 of the following: Irregular margins (infiltrative, microlobulated) Microcalcifications Taller than wide shape Rim calcifications with small extrusive soft tissue Extrathyroidal extension	**Sonographic pattern** Nodules with ≥ 1 of the following: Nonoval shape Irregular margins Microcalcifications Marked hypoechogenicity	**Sonographic pattern** Hypoechoic solid nodule with any of the following Nonparallel orientation (taller than wide) Extrathyroidal extension Punctate echogenic foci Isoechoic solid nodule with irregular or lobulated margins and either peripheral rim calcifications or punctate echogenic foci

Abbreviations. AACE/ACE/AME, American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi; ACR, American College of Radiologists; ATA, American Thyroid Association; EU-TIRADS, European Thyroid Imaging Reporting and Data System; FNAB, fine-needle aspiration biopsy; TR, American College of Radiologists Thyroid Imaging Reporting and Data System.

[a] Growing nodule, high-risk history, before surgery or local therapies.

[b] In accordance with the presence of 1 or more suspicious findings.

[c] An FNAB is recommended for smaller nodules that are subcapsular location near the recurrent nerve or trachea; suspicious lymph nodes or extrathyroid spread; personal or family history of thyroid cancer; history of head and neck irradiation; coexistent suspicious clinical findings. An FNAB indicates the size above which a FNAB cytology is recommended.

Particular sonographic features are related to thyroid cancer while others are most likely to show a benign nature. Ultrasound qualities connected with malignancy consist of solid structure, hypoechogenicity (nodule is darker compared to regular thyroid tissue), margins that appear infiltrative or uneven, as well as existence of microcalcifications. Additionally, a nodule bordered by interrupted rim calcifications with proof of soft tissue extrusion is likely to be an infiltrative cancer [25]. Alternatively, pure cysts and also nodules with a "spongiform" uniformity, defined when more than half of nodule volume is made up of microcystic spaces, are unlikely to be malignant (< 2%). Cancer threat is low (< 5% -10%) for solid noncalcified smoothly marginated nodules that are either isoechoic or hyperechoic (same or lighter grey range imaging compared with typical thyroid)[26].

The American Thyroid Association [5] and various other professional teams [20], [22-23] have actually devised similar but not identically tiered systems to categorize nodules by constellations of sonographic features that convey cancer danger and to advise dimension cutoffs for fineneedle aspiration biopsy (Table 3, Figure 1). Guidelines from endocrinology cultures have focused on nodule pattern recognition, [5], [21],[22] accompanied by figures showing these patterns. Guides correlate each pattern to an approximated cancer threat. Just recently, the American College of Radiology [20] advised a point system for systematic assessment of imaging for thyroid nodules (Thyroid Imaging Reporting and Data System); this mirrors the American College of Radiology technique to imaging other organs (eg, the breast). Factors are assigned based upon 5 ultrasound features and the amount figures out the Thyroid Imaging Reporting and Data System category of the nodule, its estimated cancer danger, and also referrals for either fine-needle aspiration biopsy or monitoring. Malignancy risk estimates based upon sonographic appearance are comparable throughout all 4 classification systems; nonetheless, fineneedle aspiration biopsy recommended cutoff sizes vary (Table 1, Figure 1).

Fine-needle aspiration biopsy is not suggested for pure cysts, except if it is for liquid aspiration for symptomatic relief. If fineneedle aspiration biopsy is to be done for spongiform nod Table 3. Standard Sonographic Scoring Systems Proposed or Endorsed by Practice Guidelines for Risk-Based Fine-Needle Aspiration Biopsy Guida ules, the size cutoff is larger

than 2 centimeters, with some guidelines not recommending fine-needle desire biopsy [20],[21].There is wide irregularity in the description of single ultrasonographic features (Cohen κ variety, 0.4-0.6 for the majority of variables); the classification systems may improve interobserver contract (κ array, 0.61-0.82) [24].No evidence is available to guide which system is best. Long-term prospective researches are required.

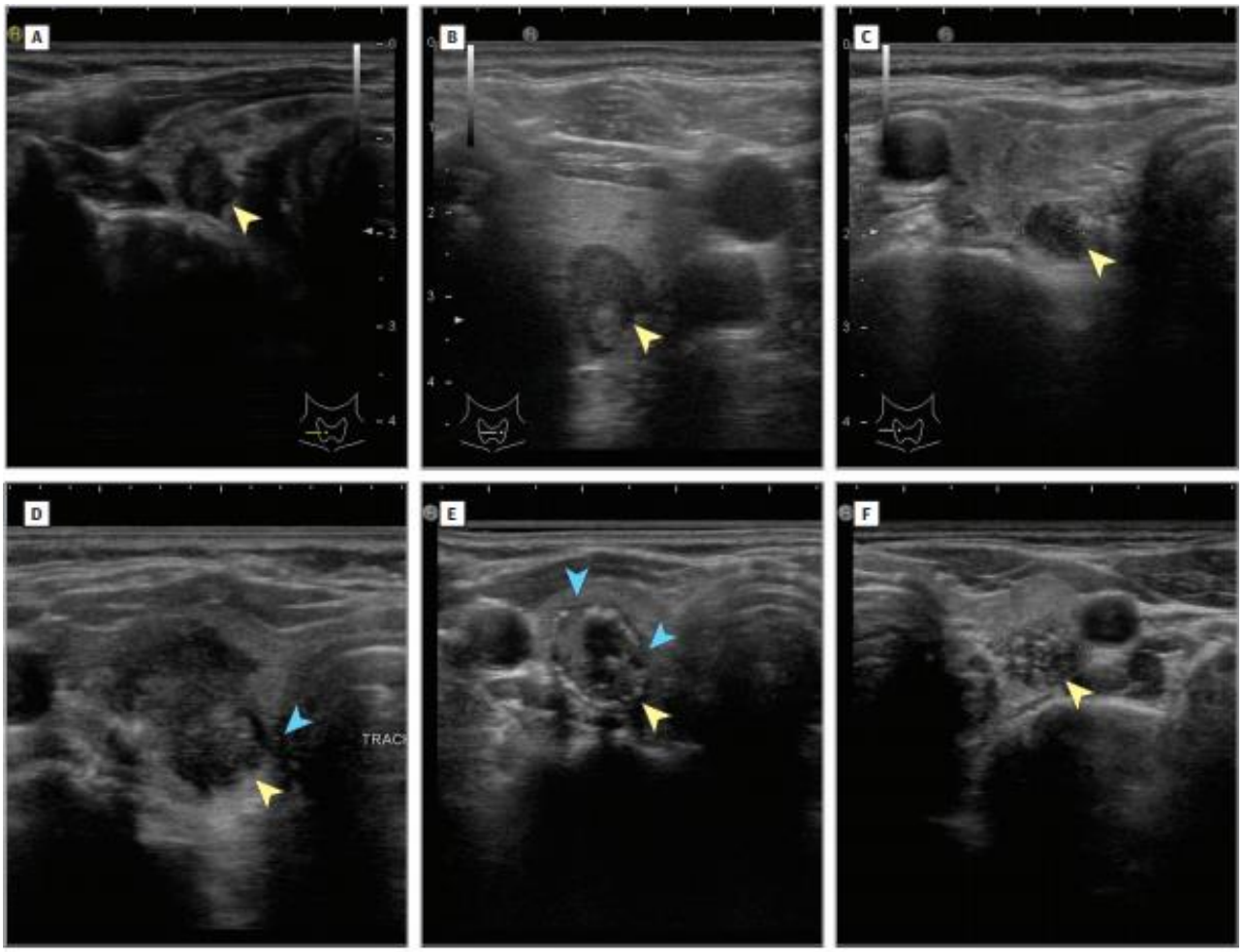

Figure 1. Ultrasonographic Features of Thyroid Nodules Suspicious for Malignancy. A, Markedly hypoechoic nodule (similar echogenicity as the surrounding strap muscles) with irregular margins. B, Taller-than-wide hypoechoic nodule. C, Markedly hypoechoic nodule with regular margins. D, Hypoechoic nodule with infiltrative margins and suspicious extrathyroidal extension (indicated by a blue arrowhead). E, Multiple interruptions in calcific rim with evidence of extrusive tissue (indicated by blue arrowheads). Echogenicity is difficult to interpret because of acoustic shadowing of the calcific rim). F, hypoechoic solid nodule with microcalcifications and irregular margins. The yellow arrowheads indicate the thyroid nodule in each panel.

4. CONCLUSION

The medical significance of the thyroid nodule assessment is mainly associated with the need to exclude thyroid cancer, which exists in 4.0 to 6.5 percent of thyroid nodules. Nonpalpable nodules (incidentalomas) have the very same threat of malignity as palpable nodules. Thyroid ultrasonography is utilized to answer concerns concerning the size and anatomy of the thyroid gland as well as surrounding structures in the neck. It offers substantially more structural detail compared to thyroid scintigraphy,CT,and physical exam .

Sonography is the primary tool used for preliminary cancer threat stratification of thyroid nodules and ultimately deciding whether to purchase a fine-needle aspiration biopsy.There are a number of ultrasonographic findings that are suspicious for thyroid cancer (table 3). The predictive value of these characteristics differs widely, and we do not count on thyroid ultrasound to diagnose cancer or to choose patients for surgery. However, ultrasound results can be utilized to select nodules for FNA biopsy, ultrasound-guided FNA is more efficient.

Thyroid ultrasound need to be carried out in all patients with a presumed thyroid nodule or nodular goiter on physical exam or with nodules incidentally kept in mind on various other imaging research studies (carotid ultrasound, CT, MRI, or FDG-PET scan). Diagnosis and also therapy of thyroid nodules is extremely determinate by very early assessment, medical criteria applying US and also FNA as initial test. They should be practical, reliable and cost-effective.

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