Thyroid nodules, when to perform a fine needle aspiration

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Learning objectives

- To review general guidelines for fine needle aspiration (FNA) of thyroid nodules and to analyze their similarities and disagreements.
- To describe radiological features of thyroid nodules that raise suspicion for malignancy.

Background

A thyroid nodule is a discrete lesion within the thyroid gland that is sonographically distinguishable from the adjacent parenchyma. Their ultrasound characteristics are the following:

1.- Size

Nodules should be measured with the calipers placed outside of any visible halo. In principle, the size of thyroid nodules should be measured in all three dimensions, nevertheless to provide only the maximal diameter may be acceptable. As nodule size is not useful for distinguishing a malignant nodule from a benign one, FNA is recommended regarding ultrasound suspicious features in conjunction with size.

2.- Nodule growth

Growing is the natural history of both benign and malignant nodules. Nonetheless fast growth of a nodule indicates an increased risk for malignancy. There is no consensus on the definition of substantial growth or how to monitor growth. American Thyroid association (ATA) advocates a 20% increase in the nodule diameter with a minimum increase in two or more dimensions of at least 2 mm, which is roughly a 50% increase in volume.

3.- Internal content (Fig. 1 on page 5)

- cystic
- mixed (solid and cystic)
• solid

A **spongiform nodule** is defined as multiple microcystic spaces separated by thin septae or intervening isoechoic parenchyma in more than 50% of the nodule volume.

4.- **Echogenicity** (Fig. 2 on page 6)

• hyperechoic
• isoechoic
• hypoechoic

The nodule echogenity is compared with the thyroid parenchyma or adjacent muscles. The specificity rises when the nodule is marked hypoechoic (hypoechoic relative to the adjacent muscle).

5.- **Echoestructure** (Fig. 3 on page 6)

• heterogeneous
• homogeneous

This finding is not useful for discrimination between benignity and malignancy.

6.- **Shape** (Fig. 4 on page 7)

A nodule which is taller than wide (anteroposterior diameter longer than transverse one) has high specificity for malignancy. It is thought to be due to centrifugal tumor growth.

7.- **Margins** (Fig. 5 on page 8)

**Irregular margins** are considered when more than 50% of the nodule margins are blur and usually suggest infiltration of the surrounding parenchyma, although benign entities can show this feature.

A **halo** or hypoechoic rim surrounding a nodule is comprised of a pseudocapsule that is caused by fibrous connective tissue, compressed thyroid tissue and chronic inflammatory changes. When uniform and complete suggests benignity (although not pathognomonic).
8.- Calcifications ( Fig. 6 on page 9 )

- Microcalcifications
- Coarse calcifications
- Rim calcifications

Calcifications within a thyroid nodule raises the likelihood of malignancy: approximately threefold increase in cancer risk for microcalcifications and twofold increase for coarse calcifications in a predominantly solid nodule.

**Microcalcifications** depict psammoma bodies, typical of papillary thyroid cancer, although also present in benign entities. They appear as fine punctuate calcifications too small to induce posterior acoustic shadow and are difficult to differentiate from echogenic foci in partially cystic nodules. The key point is that the latter produce comet-tail artifacts.

**Coarse calcifications** are secondary to tissue necrosis and cast a shadow. Frequently involved in multinodular goiter, its presence rises the likelihood of malignancy in solitary nodules.

The meaning of **rim calcifications** is controversial.

9.- Extracapsular invasion ( Fig. 7 on page 10 )

Tumor direct invasion of adjacent tissues is shown as blur thyroid margins or clear invasion of surroundings structures such as cartilage, trachea... It is frequently seen in anaplastic carcinoma of the thyroid, lymphoma and sarcoma.

10.- Tumor vascularity ( Fig. 8 on page 11 )

- Peripheral vascularization
- Hipervascularity
- Avascular

The vascular pattern more frequently present in malignant nodules is hypervascularity, in other words, more flow in the central part of the nodule than at the periphery. Perinodular blood flow (at least in 25% of the nodule circumference) is more likely present in benign lesions. Absence of internal flow in a nodule is very unlikely to represent malignancy.
All in all, the sonographic characteristics of a thyroid nodule which are associated with a higher likelihood of malignancy are: a solid hypoechoic nodule, the presence of microcalcifications, flow predominantly in the central portion of the nodule with color Doppler US, taller than wider, absence halo and irregular-infiltrative margins. On the contrary, a nodule is more likely to be benign if it is cystic, spongiform, iso- or hyperechoic and has halo.

**Ultrasound features that suggest histological type**

The findings that suggest papillary carcinoma are a predominantly solid, hypoechoic, hypervascular nodule with microcalcifications and irregular-infiltrating margins. The ultrasound features of medullary carcinoma are a predominantly solid, iso/ hyperechogenic nodule with an irregular thickened capsule.

**Images for this section:**
**Fig. 1:** INTERNAL CONTENT of a nodule can be solid (1), mixed solid-cystic (predominantly solid (2) or predominantly cystic (c)). Image 4 demonstrates two examples of spongiform nodules.

**Fig. 2:** ECHOGENICITY: (1) Hyperechogenic nodule compared with the surrounding thyroid parenchyma. (2) Isoechogenic nodule regarding to thyroid parenchyma. Also note the fine hypoechoic rim delimitating the nodule. (3) Hypoechoic nodule compared with the surrounding thyroid parenchyma and similar to strap muscle.
Fig. 3: ECHOESTructure. (1) homogeneous (2) heterogeneous.
Fig. 4: SHAPE. Schematic drawings show round and ovoid shape on the right lobe and taller-than-wide shape on the left thyroid lobe, which has high specificity for malignancy.
Fig. 5: MARGINS. (1) Blur margins; color doppler improves its demarcation. (2) well-defined border with a thin hypoechoic halo (3).
Fig. 6: CALCIFICATIONS:(1) microcalcifications depicted as tiny bright dots without posterior shadow. (2) coarse calcification casting a shadow. (3) rim calcification whose posterior shadow hides nodule depiction in depth.
Fig. 7: EXTRACAPSULAR INVASION in anaplastic thyroid carcinoma. 80 year-old woman who suffered from airway obstruction due to a fast growing cervical mass. Ultrasound image(1) shows a huge mass replacing the left thyroid lobe, which surrounds and displaces the trachea(T). The CT image(2) depicts the mass (star) that infiltrate the surrounding tissues (strap muscles, inferior pharyngeal constrictor muscle and right thyroid lobe-arrowhead-). The double arrow signals the jugular vein and common carotid artery on the right, while on the left the jugular vein is collapsed.
Fig. 8: VASCULARIZATION: Peripheral vascularization(1) vessels define the nodule ringlike margins. Central vascularization(2) almost the entire nodule shows intense hypervascularization (A indicates carotid artery). Flow absence in a cyst (3).
Findings and procedure details

Guidelines

- American Thyroid Association (ATA)
- American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association (AACE/AME/ETA)
- Korean Society of Radiology (KSTR)

American Thyroid Association (ATA)

The ATA guidelines, revised in 2009, recommend FNA of thyroid nodules according to two items: risk factors and ultrasound features.

The risk factors included in the ATA guidelines are:

- family history of thyroid cancer
- radiation exposure during childhood or adolescence
- multiple endocrine neoplasia syndrome
- familial medullary thyroid cancer-associated RET protooncogene mutation
- calcitonin > 100pg/mL
- FDG avidity on PET scanning

All nodules that exceed 5 mm in diameter (with or without suspicious ultrasound features) in patients with high-risk history should undergo FNA, under the ATA.

The suspicious ultrasound features defined by ATA guidelines are:

- hypoechoic nodule
- increased intranodular vascularity
- irregular infiltrative margins,
- microcalcifications
- absent halo
- taller than the width shape

ATA recommends FNA of thyroid nodules when exceeding 1 cm in diameter and show microcalcifications; in solid nodules, above 1 cm in diameter if hypoechoic and above 1-1.5 cm when isoechoic or hyperechoic; in mixed cystic-solid nodules, if they have suspicious ultrasonographic features then the cut-off diameter is 1 to 1.5 cm and if not,
the chosen diameter is larger than 2 cm, spongiform nodules are included in this latter category. FNA is not advised for cystic nodules.

Also, FNA of abnormal cervical lymph nodes is mandatory even in the absence of suspicious thyroid nodule.

![Diagram of thyroid nodule classification]

**Fig. 9**: Adapted schematic view from the ATA guidelines.

**References**: Arganda del Rey/ES

**American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association (AACE/AME/ETA)**

The **risk factors** considered by AACE/AME/ETA guidelines are:

- history of irradiation in childhood or adolescence
• family history of medullary carcinoma, multiple endocrine neoplasia type 2, or papillary thyroid carcinoma
• young (<14 years) or old patients (>70 years)
• men
• rapid firm growth of a nodule
• certain symptoms (hoarseness, vocal cord paralysis, dyspnea or difficulty swallowing).

The ultrasound findings associated with malignancy described on the AACE/AME/ETA guidelines are:

• marked hypoechoogenicity
• irregular or microlobulated margins
• a taller than wide shape
• microcalcifications
• intranodular hypervascularity

On the basis of this, AACE/AME/ETA guidelines (2010) suggest FNA biopsy of any solid and hypoechoic nodule larger than 1 cm in diameter, of nodules of any size if the patient has risk factors and of nodules smaller than 1 cm in diameter provided ultrasound findings associated with malignancy are present. FNA is proposed for the solid component of all complex solid-cystic nodules. Besides, biopsy is not required in hot nodules on scintigraphy. On the other hand, AACE/AME/ETA guidelines recommend FNA of abnormal cervical lymph nodes.
**Fig. 10:** Adapted schematic view from the AACE/AME/ETA guidelines.

**References:** - Arganda del Rey/ES
Korean Society of Radiology (KSTR)

KSTR guidelines in 2011 arrange nodules in three categories:

- probably benign
- suspicious for malignancy
- indeterminate.

-Nodules considered **probably benign** are:
  - spongiform nodules
  - completely cystic
  - predominantly cystic

-Nodules are defined as **suspicious for malignancy** when present at least one of these ultrasound features:

Fig. 11: Adapted schematic view from the AACE/AME/ETA guidelines.

References: - Arganda del Rey/ES
- Nodules that don’t meet criteria for probably benign or suspicious for malignancy categories are regarded as **indeterminate**. These characteristics include:

  - isoechogenicity, hypoechogenicity and hyperechogenicity
  - an ovoid-to-round or irregular shape
  - a smooth or ill defined margin
  - rim calcification

KSTR guidelines advise FNA of all nodules exhibiting any feature suspicious for malignancy and larger than 5 mm in size if feasible. Due to its difficulty, they recommend evaluation of risk factors of the patient and the experience of the clinician in nodules smaller than 5 mm to decide to perform the biopsy. If the solid component of a mix solid-cystic nodule exhibit suspicious ultrasound feature/s, biopsy is indicated. Moreover, repeated biopsy of any suspicious nodule with benign initial cytologic findings should be performed.

For nodules considered probably benign, the KSTR guidelines recommend: no follow-up ultrasound if smaller than 1 cm in diameter, follow-up ultrasound at 2 years and at 3 to 5 years when larger than 1 cm and FNA if larger than 2 cm.

In nodules considered indeterminate, follow-up ultrasonography is recommended for those smaller than 1 cm and biopsy for nodules larger. Also, they recommend biopsy in indeterminate nodule showing growth.

Moreover, if suspicious lymph nodes are present, should undergo biopsy.
**Fig. 12**: The table summarizes KJR Guidelines (2011) (*) follow-up US in two years and thereafter at 3-5 years. 

**NOTES**: (1) If nodule grows, perform FNA. (2) If suspicious lymph nodes present, should undergo biopsy.

**References**: - Arganda del Rey/ES

<table>
<thead>
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<th>SUSPICIOUS MALIGNANCY</th>
<th>INDETERMINATE</th>
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<td>Taller than wide shape</td>
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<td>Irregular margins</td>
<td>Hyper /iso/ hypechochogenicity</td>
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<td>Micro/macrocalcifications</td>
<td>shape</td>
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<td>Extracapsular invasion</td>
<td>Smooth or ill-defined margin</td>
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<td>Rim calcification</td>
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- FNA

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<td>FNA</td>
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<tr>
<td>FNA</td>
<td>&gt; 2 cm</td>
<td>Repeat FNA if benign cytology despite ultrasound suspicious signs</td>
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Fig. 13: Flowchart for strategy for follow-up US and US-guided fine needle aspiration (USFNA) according to KSTR

In short, the three guidelines agree to perform FNA when the nodule is 1 cm or above and has suspicious US criteria. However, they differ regarding subcentimetric nodules: AACE and KSTR recommend FNA in nodules with features suggestive of malignancy, while according to ATA only if there were clinical risk factors. Patients with iso- or hyperechoic #1-1.5 cm nodules will undergo FNA according to ATA and KSTR, while AACE doesn’t mention anything about. As for complex cystic nodules, ATA advises FNA in nodules 1.5-2 cm or more in the largest diameter, AACE, in all complex cystic nodules and KSTR only if the solid mural component has suspicious features.

<table>
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<tr>
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<th>KSTR</th>
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<td>FNA</td>
<td>FNA indeterminate</td>
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<td>FNA microcalcifications or solid &amp; hyperechoic</td>
<td>Suspicious US: FNA</td>
<td>Suspicious US: FNA Indeterminate: Follow-up: probably benign</td>
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**Disadvantages**

<table>
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<td>FNA &gt; 5 mm only if high risk history</td>
<td>Suspicious US: FNA</td>
<td>Suspicious US: FNA Indeterminate: Follow-up</td>
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In conclusion, the three guidelines agree to perform FNA when the nodule is 1 cm or above and has suspicious US criteria. However, they differ regarding subcentimetric nodules: AACE and KSTR recommend FNA in nodules with features suggestive of malignancy, while according to ATA only if there were clinical risk factors. Patients with iso- or hyperechoic #1-1.5 cm nodules will undergo FNA according to ATA and KSTR, while AACE doesn’t mention anything about. As for complex cystic nodules, ATA advises FNA in nodules 1.5-2 cm or more in the largest diameter, AACE, in all complex cystic nodules and KSTR only if the solid mural component has suspicious features.
Due to limited prospective studies regarding cost or outcome, many of the recommendations are based on expert opinion.

The KSTR guidelines do not take into account clinical risk factors in the decision process for biopsy nor vascularity as a risk factor.

The ATA and AACE guidelines do not consider the variations in complex cysts (ranging from predominantly cystic lesion to a predominantly solid lesion with cystic components) while KSTR does.

Following the guidelines, most thyroid nodules will undergo FNA, however, they possibly have an favorable outcome.

**Examples**

*Fig. 15 on page 27, Fig. 16 on page 28, Fig. 17 on page 29, Fig. 18 on page 30, Fig. 19 on page 31*

Images for this section:
**Fig. 9:** Adapted schematic view from the ATA guidelines.

**Fig. 10:** Adapted schematic view from the AACE/AME/ETA guidelines.
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**Fig. 12:** The table summarizes KJR Guidelines (2011) (*)follow-up US in two years and thereafter at 3-5 years NOTES: (1) If nodule grows, perform FNA. (2) If suspicious lymph nodes present, should undergo biopsy.
Fig. 13: Flowchart for strategy for follow-up US and US-guided fine needle aspiration (USFNA) according to KSTR
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**Fig. 14**
Fig. 15: FOLLICULAR THYROID CARCINOMA. Ultrasound images (1,2) show a large, iso to slightly hyperechoic nodule on the left lobe with microcalcifications and thick irregular margin. Axial CT image (3) shows two pathologic lymph nodes at level VI.
**Fig. 16:** MEDULLARY THYROID CARCINOMA. 21 year-old woman who had a cervical mass since 2 years before. Ultrasound images show on the right lobe a hypoechoic nodule with microcalcifications (image 1) and the FNA procedure of a metastatic lymph node (image 2). In post-contrast Axial T1WI (image 3), not only the conglomerate adenopathy (asterisk) enhances but also the small thyroid nodule. Coronal STIR image (image 4) shows the conglomerate adenopathy (stars) at III-IV levels. T indicates the trachea.
**Fig. 17:** PAPILLARY THYROID CARCINOMA. 32 year-old woman with palpable mass. The first ultrasound image (1) shows enlarged mix (solid-cystic) lymph nodes with calcifications, and a hyperechoic nodule on left thyroid lobe (arrow). T indicates the trachea. The CT axial image (2) shows the nodule calcification (which explains its hyperechogenicity) and the conglomerate adenopathy with calcifications. FNA procedures are shown in images 3 and 4.
**Fig. 18:** ANAPLASTIC THYROID CARCINOMA. 80 year-old woman who suffered from airway obstruction due to a fast growing cervical mass. Ultrasound image (1) shows a huge mass replacing the left thyroid lobe, which surrounds and displaces the trachea (T). The CT image (2) depicts the mass (star) that infiltrate the surrounding tissues (strap muscles, inferior pharyngeal constrictor muscle and right thyroid lobe - arrowhead -). The double arrow signals the jugular vein and common carotid artery on the right, while on the left the jugular vein is collapsed (arrow). Image 3 shows the needle on the left of the picture.
Fig. 19: BENIGN NODULE WITH MICROCALCIFICATIONS. Ultrasound images show a hypoechoic nodule with microcalcifications on the left lobe (image 1) and the FNA procedure (image 2). The pathology report concluded without evidence of malignancy and was classified benign according to Bethesda system.
Conclusion

The ultrasound features of a thyroid nodule which are associated with a higher likelihood of malignancy are: a solid hypoechoic nodule, the presence of microcalcifications, flow predominantly in the central portion of the nodule with color Doppler US, taller than wider, absence halo and irregular-infiltrative margins. When present, all guides agree to perform FNA, provided the nodule diameter is > 1 cm. If not, they disagree. More prospective studies could be done to solve this problem.

Personal information

References


