Thyroid Nodule

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4/10/2018

Objectives

- Prevalence of thyroid nodule
- Evaluation for thyroid nodule
  - History and physical exam
  - Work up for thyroid nodule
  - US features
  - Cytology
- Thyroid nodule follow up
- Thyroid cancer incidence and mortality

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Thyroid Nodules

Kenneth D. Burman, M.D., and Leonard Wartofsky, M.D.

This *Journal* feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

A 40-year-old woman presents with a thyroid nodule, 2.0 cm by 2.0 cm on palpation. The nodule, located on the right side of the gland, was found on routine physical examination. She has no history of childhood radiation exposure or family history of thyroid abnormalities. She reports no symptoms of nervousness, weight loss, palpitation, fatigue, or neck discomfort. Ultrasonography confirms a thyroid nodule, 2.0 cm by 2.0 cm by 2.5 cm (volume, 5.23 cm^3), on the right side of the gland that does not have ultrasonographic characteristics associated with an increased risk of cancer; there is no cervical adenopathy. How should her case be managed?

Why do we care?

- Thyroid nodules are common
- Not all are benign, but thyroid cancer is uncommon
- We need cost effective way to find uncommon cancer in common nodules
- Size is not the only reason for FNA
- Ultrasound every 6 months is not required for every thyroid nodule

Journal of Community Hospital Internal Medicine Perspectives

RESEARCH ARTICLE

Initial evaluation of thyroid nodules by primary care physicians and internal medicine residents

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Table 1. Frequencies of laboratory tests ordered

Test	Frequency
TSH + other lab test	84/113
TSH alone	45
Free T4	24
Total T4	12
Total T3	3
Free T3	3
T3 resin uptake	1
Thyroglobulin	2
Thyroid peroxidase antibody	5
Thyroid panel	2
No data	27

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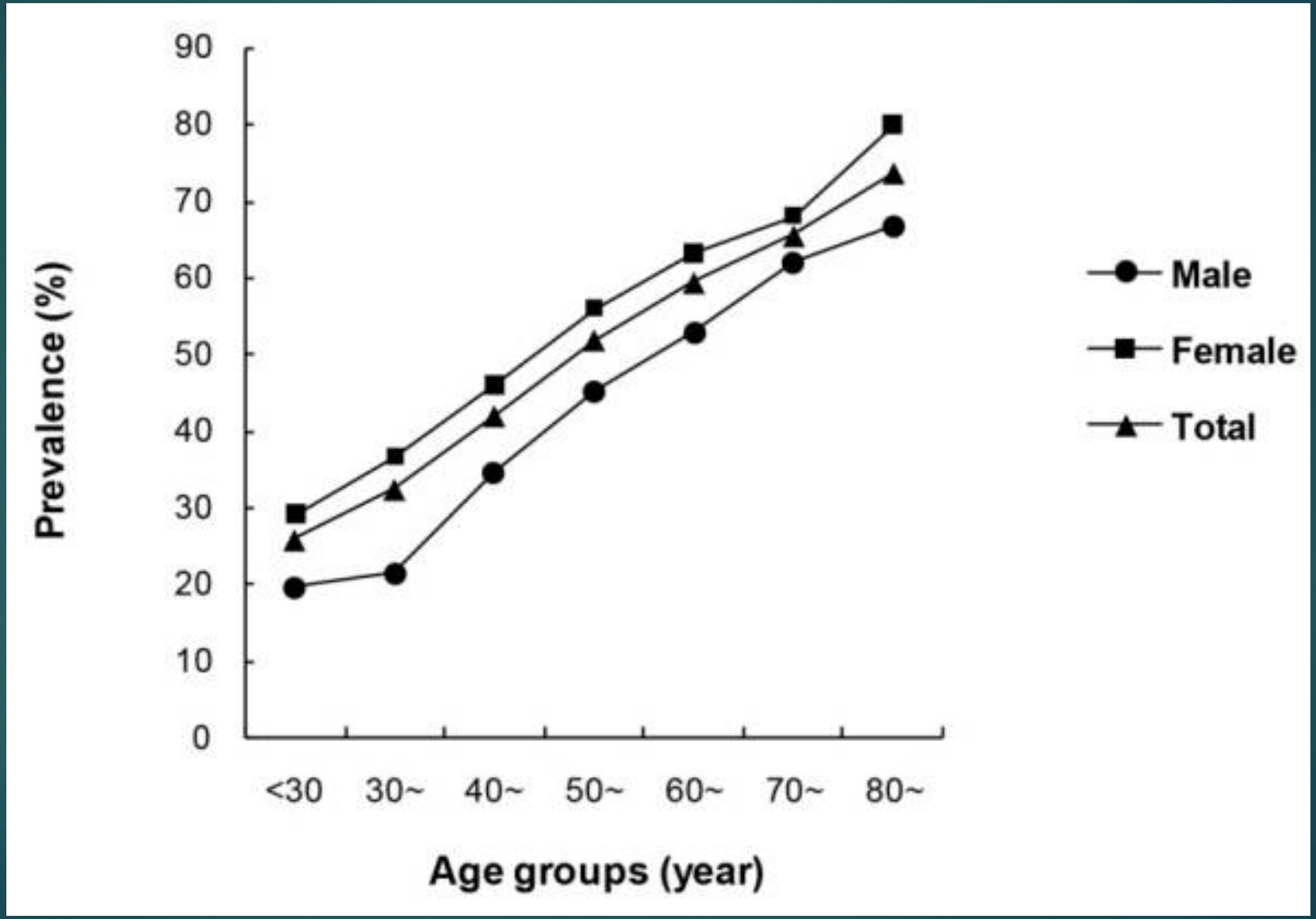
Imaging studies	Frequency
Thyroid ultrasound alone	64/113
Thyroid ultrasound + radionuclide scan	10
Thyroid ultrasound + neck CT scan	2
Thyroid uptake and scan alone	2
Cervical x-ray	1

Prevalence of Thyroid Nodule



Prevalence of Thyroid Nodule

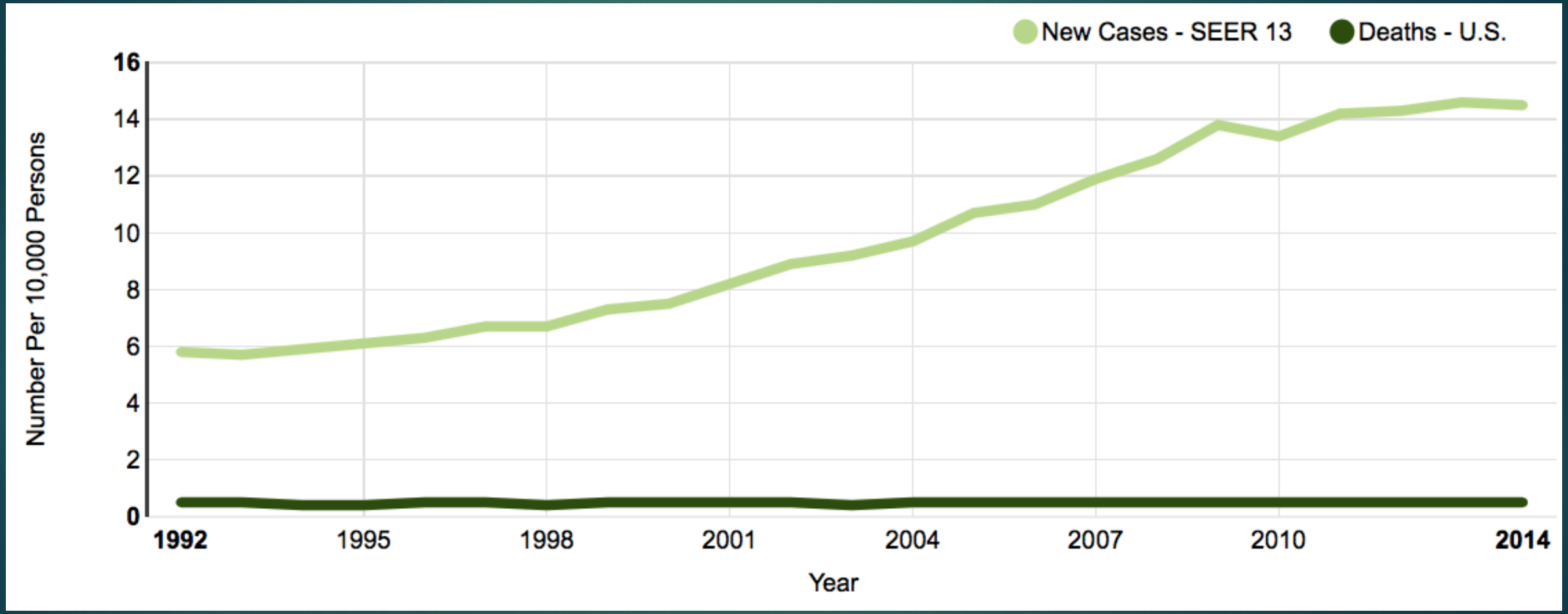
- Thyroid nodules are very common
- More common in women, F:M is 4:1
- The prevalence of palpable thyroid nodules in the US has been estimated to be
  - Adult population: 4%
  - Young children: <1%
  - Age 11-18: 1.5%
  - >60 year old: 5%
- Thyroid nodules detected on US is up to 50% of healthy individuals, especially middle aged or older women

Prevalence of Thyroid Nodule

- The vast majority (95%) of thyroid nodules are benign
- Thyroid cancer is a relatively rare condition
- Annual incidence 8.7 per 100,000 population
- In 2017:
  - 56,870 cases of newly diagnosed thyroid cancer
  - 3.4% of all new cancer cases

  - 2,010 cancer deaths from thyroid cancer
  - 0.3% of all cancer deaths

Prevalence of Thyroid Cancer



Benign Thyroid Nodules

Benign conditions can produce nodularity in the thyroid tissue

- Focal thyroiditis
- Dominant nodule in a multinodular goiter (cyst, colloid-filled, hyperplastic)
- Benign adenomas (Follicular and Hurthle cell)
- Thyroid, parathyroid or thyroglossal cyst
- Agenesis of a thyroid lobe
- Postsurgical remnant hyperplasia
- Postradioiodine remnant hyperplasia

Differentiation of Benign and Malignant Lesions

Risk factors useful in distinguishing benign from malignant thyroid lesions

- History
- Physical characteristics
- Serum factors
- Scanning techniques
  - Radioactive iodine or TcO_4 scan
  - US
  - CT head and neck or MRI
- Cytology

Differentiation of Benign and Malignant Lesions

	More likely benign	More likely malignant
History:	Family history of benign goiter Residence in endemic goiter area	Family history of medullary thyroid cancer , MEN2 Previous therapeutic irradiation of head or neck Recent growth in the nodule Hoarseness, dysphagia, or obstruction History of thyroid cancer
Physical characteristics	Older woman Soft nodule	Child, young adult, male Solitary, firm nodule clearly different from the rest of the gland (dominant nodule) Vocal cord paralysis, firm lymph nodes, distant metastases
Serum factors:	High titers of serum antibodies	Elevated calcitonin
Radioactive iodine or TcO_4 scan	Hot nodule	Cold nodule
US:	Pure cyst	Solid or complex
CT head and neck or MRI:	No lymph nodes	Lymph nodes
Cytology:	Benign appearance on cytology examination	Malignant or suggestive of malignancy

Case 1

- 27 year old healthy woman during GYN evaluation was found to have a left side thyroid nodule approximately measuring 3 cm.
- She does not have history of thyroid cancer
- Denied radiation exposure
- No clinical sx/sx of hyperthyroidism
- No compressive symptoms
- No family history of thyroid cancer

- Next step?

Evaluation of Thyroid Nodules

TSH is the first step in evaluating a thyroid nodule

- TSH normal in most of the case
- TSH is below normal → radionuclide thyroid scan ***should be considered***
- A high normal or elevated TSH has been associated with a modestly higher risk of thyroid cancer

- TSH: 1.8
- Thyroid Ultrasound?

Thyroid imaging

Thyroid ultrasound:

- Confirm if cervical mass is within the thyroid
- Measure nodules size
- Distinguish solid from cystic
- Certain US characteristics can suggest malignancy
  - Irregular borders
  - Extrathyroidal invasion
  - Capsule invasion
  - Taller more than wide
  - Microcalcifications
- Can favor benign nodule (comet tail, colloid within the nodule)

Thyroid imaging

- **Radionuclide scan:**
  - **Hot nodule**, takes up more radioactive iodine than surrounding tissue, almost never malignant
  - 5-10% of **cold nodules** may be malignant
- **PET scan:** 1/3 of hypermetabolic nodules are malignant

- 1 cr
- 1 cr
- 1.5 cm
- 2 c
- No FNA

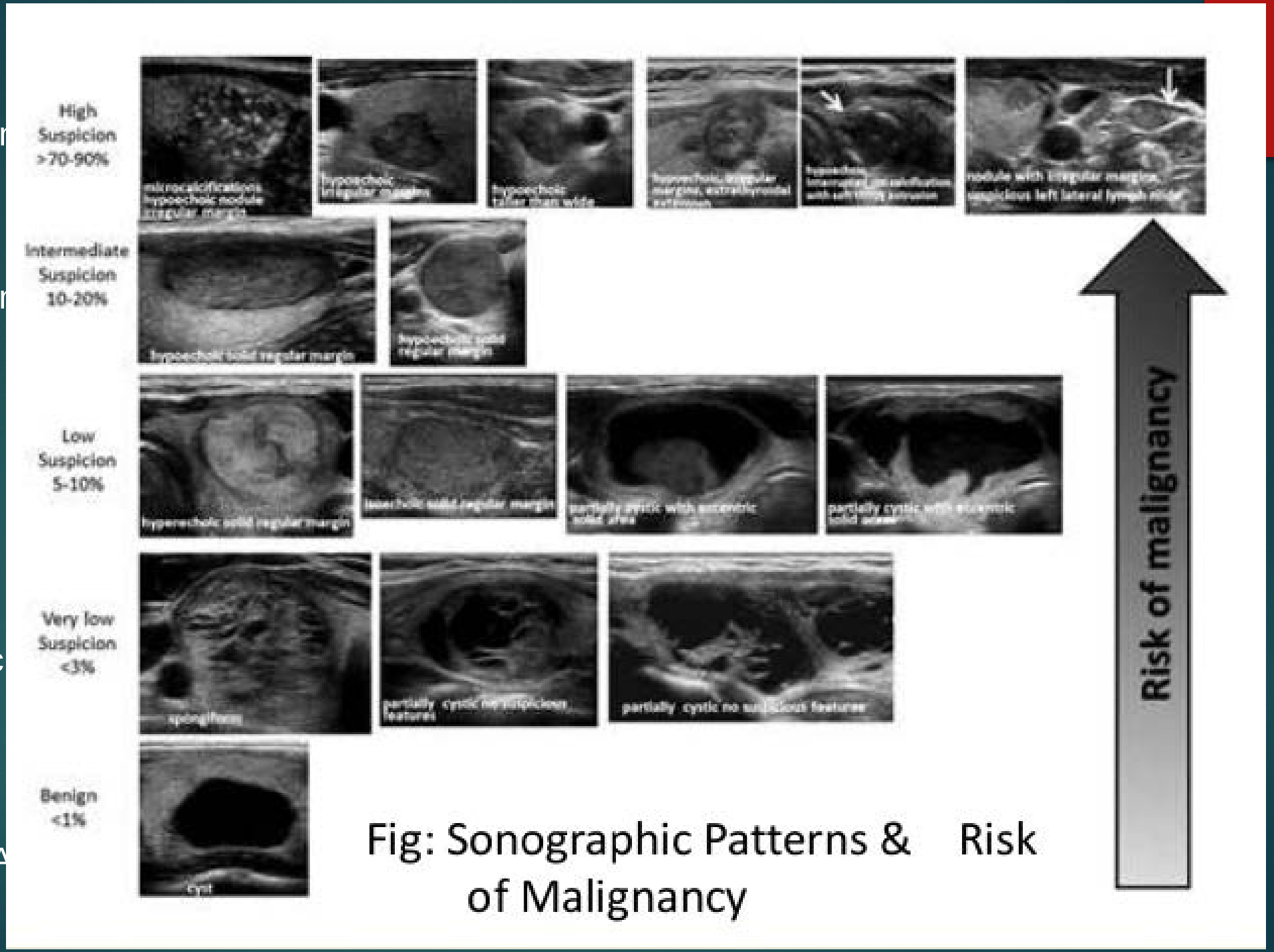
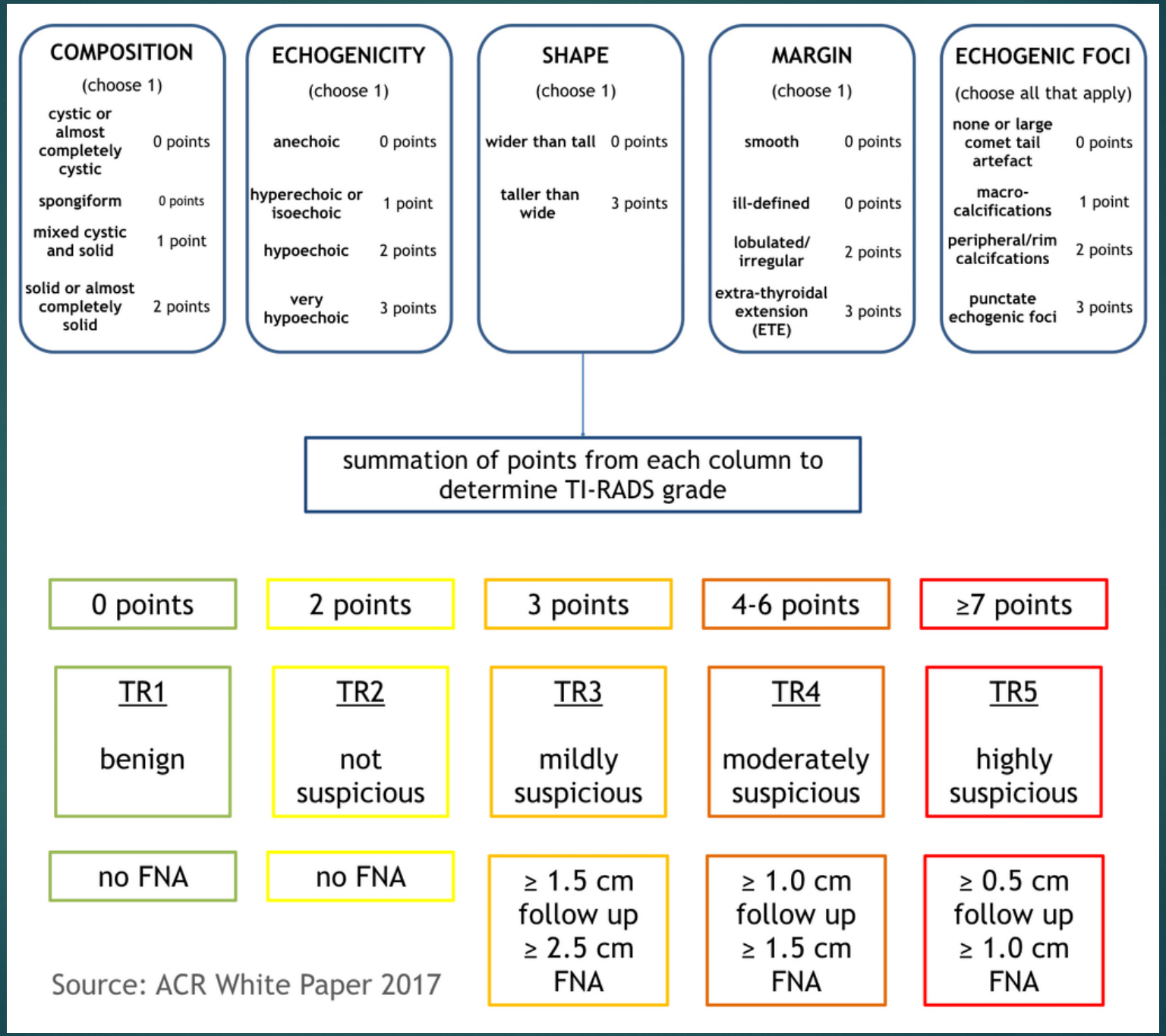
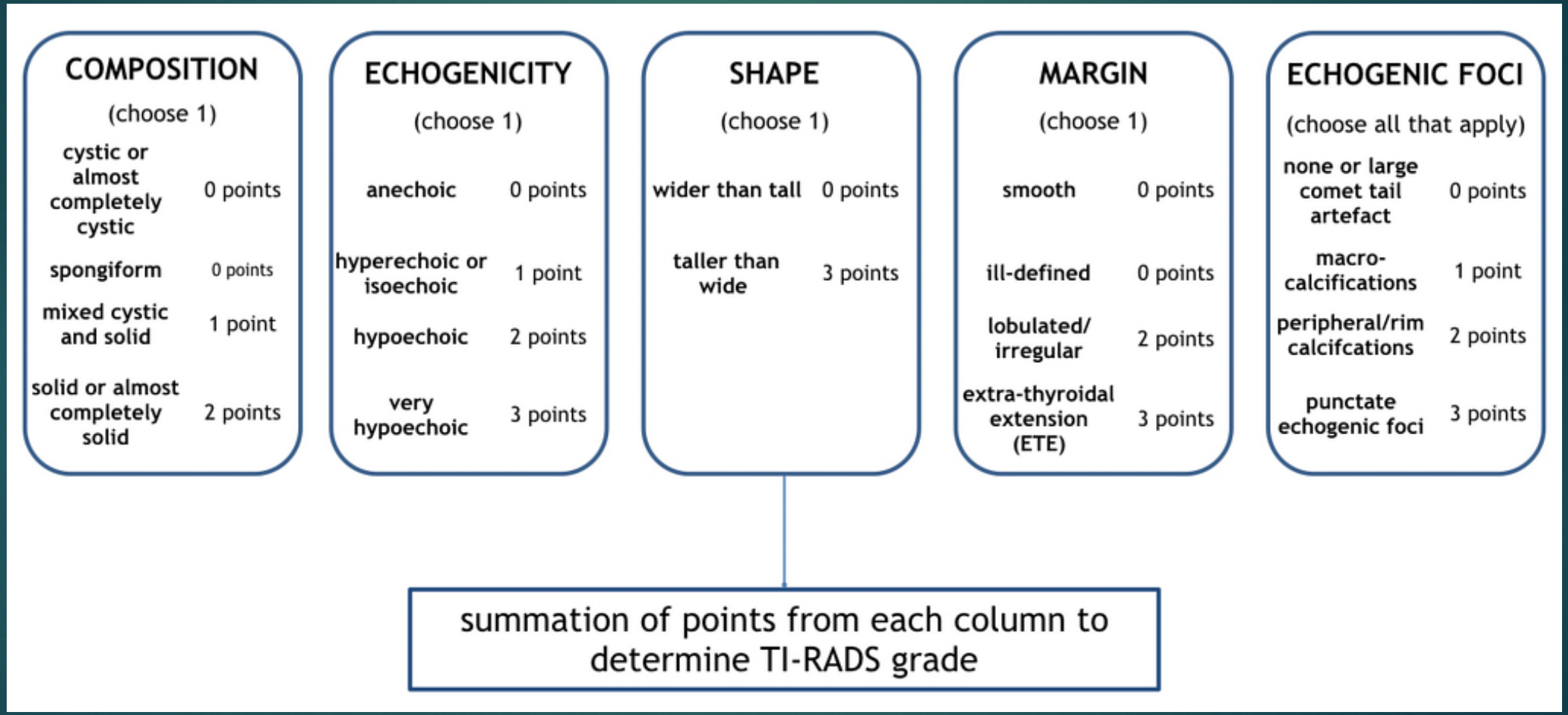


Fig: Sonographic Patterns & Risk of Malignancy


COMPOSITION
(choose 1)
cystic or almost completely cystic 0 points
spongiform 0 points
mixed cystic and solid 1 point
solid or almost completely solid 2 points
ECHOGENICITY
(choose 1)
anechoic 0 points
hyperechoic or isoechoic 1 point
hypoechoic 2 points
very hypoechoic 3 points
SHAPE
(choose 1)
wider than tall 0 points
taller than wide 3 points
MARGIN
(choose 1)
smooth 0 points
ill-defined 0 points
lobulated/ irregular 2 points
extra-thyroidal extension (ETE) 3 points
ECHOGENIC FOCI
(choose all that apply)
none or large comet tail artefact 0 points
macro-calcifications 1 point
peripheral/rim calcifcations 2 points
punctate echogenic foci 3 points
summation of points from each column to determine TI-RADS grade
0 points
2 points
3 points
4-6 points
≥7 points
TR1 benign
TR2 not suspicious
TR3 mildly suspicious
TR4 moderately suspicious
TR5 highly suspicious
no FNA
no FNA
≥ 1.5 cm follow up ≥ 2.5 cm FNA
≥ 1.0 cm follow up ≥ 1.5 cm FNA
≥ 0.5 cm follow up ≥ 1.0 cm FNA
Source: ACR White Paper 2017


COMPOSITION
(choose 1)
cystic or almost completely cystic
0 points
spongiform
0 points
mixed cystic and solid
1 point
solid or almost completely solid
2 points
ECHOGENICITY
(choose 1)
anechoic
0 points
hyperechoic or isoechoic
1 point
hypoechoic
2 points
very hypoechoic
3 points
SHAPE
(choose 1)
wider than tall
0 points
taller than wide
3 points
MARGIN
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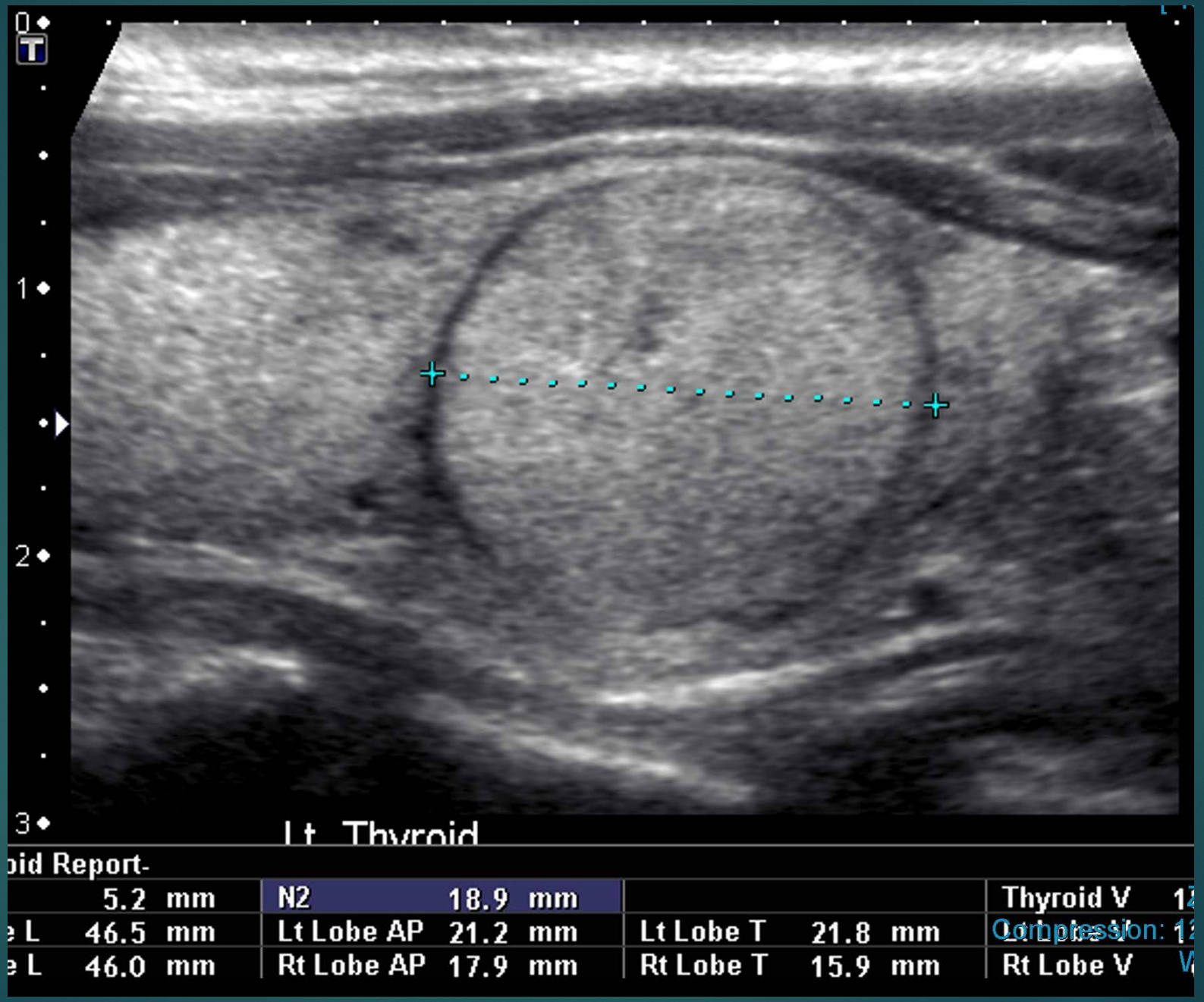
summation of points from each column to determine TI-RADS grade


Lt Thyroid
oid Report-
5.2 mm
N2 18.9 mm
Thyroid V
e L 46.5 mm
Lt Lobe AP 21.2 mm
Lt Lobe T 21.8 mm
e L 46.0 mm
Rt Lobe AP 17.9 mm
Rt Lobe T 15.9 mm
Rt Lobe V

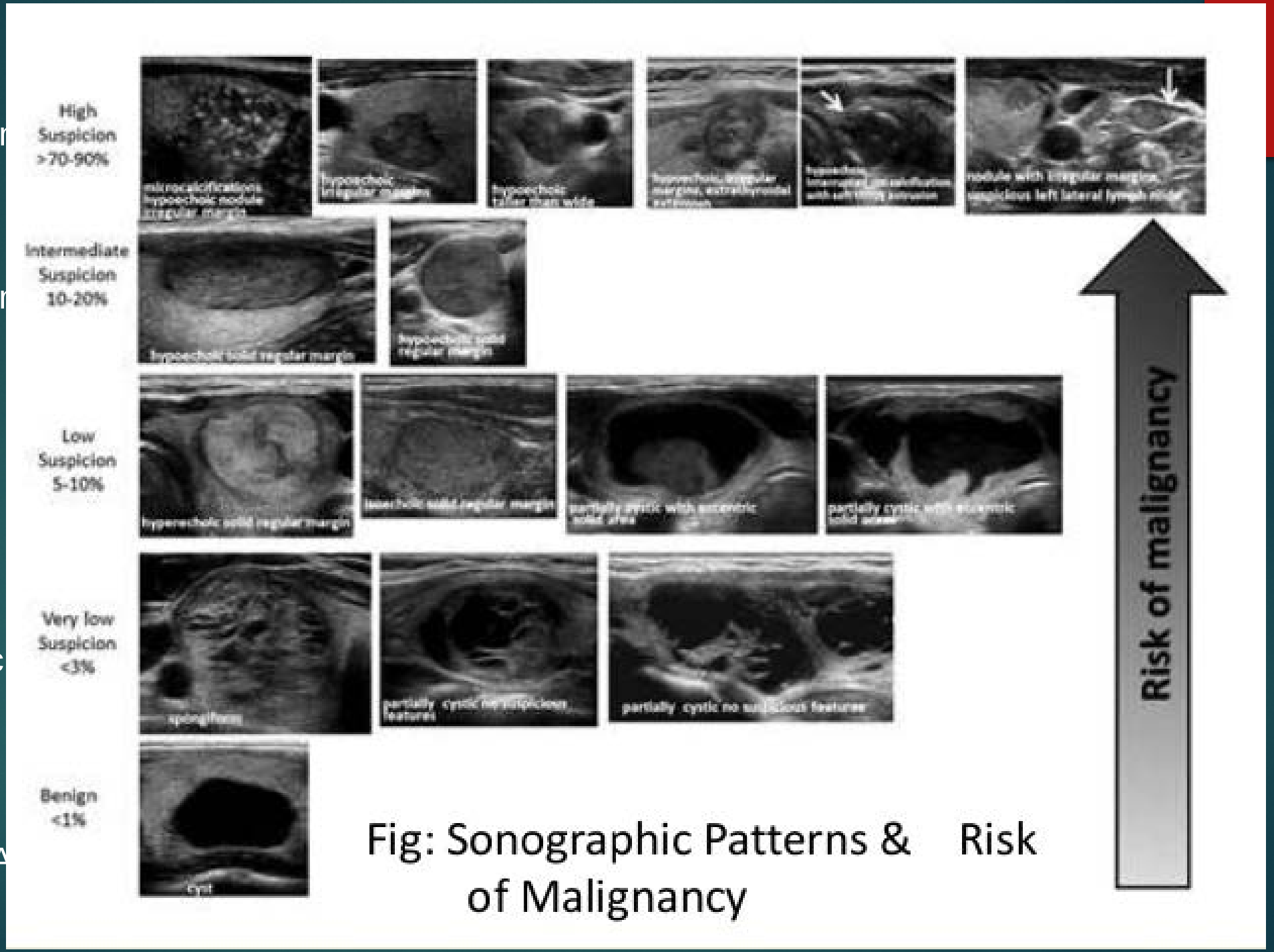
- US: 1.7 cm solid nodule, isoechoic, regular borders, no microcalcification, Grade I vascularity.

1. Patient is asking about risk of having cancer

2. Does she need a biopsy every 6 months

3. She wants to get US in 2 months to evaluate for growth

- 1 cr
- 1 cr
- 1.5 cm
- 2 c
- No FNA



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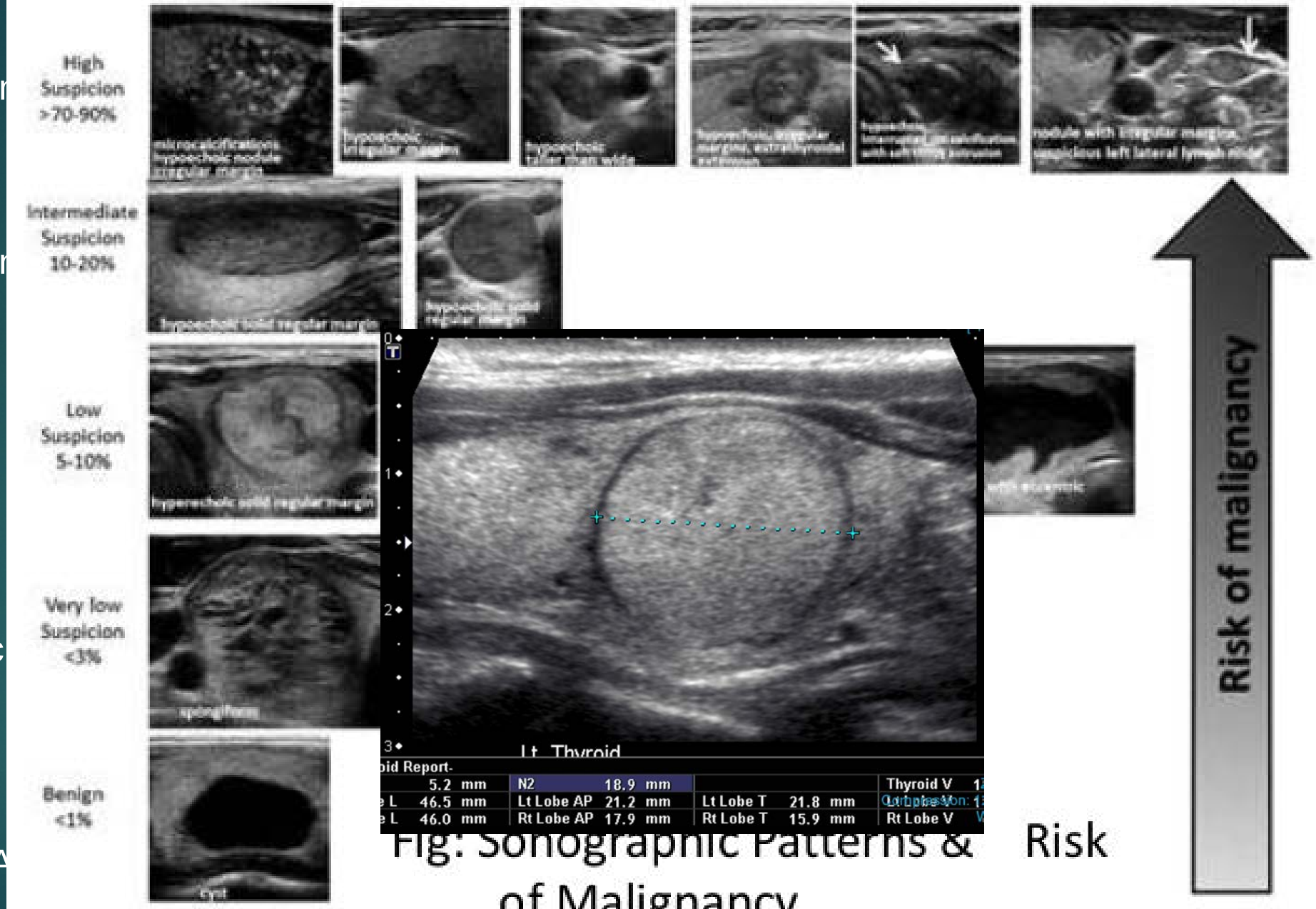

Fig: Sonographic Patterns & Risk of Malignancy

Table 2 The 2017 Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management.

Diagnostic category	Risk of malignancy if NIFTP = CA (%)	Usual management[a]
Nondiagnostic or Unsatisfactory	5-10	Repeat FNA with ultrasound guidance
Benign	0-3	Clinical and sonographic follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~10-30	Repeat FNA, molecular testing, or lobectomy
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	25-40	Molecular testing, lobectomy
Suspicious for Malignancy	50-75	Near-total thyroidectomy or lobectomy[b,c]
Malignant	97-99	Near-total thyroidectomy or lobectomy[c]

Abbreviations: NIFTP, non-invasive follicular thyroid neoplasm with papillary-like nuclear features; CA, carcinoma; FNA, fine-needle aspiration.

[a]Actual management may depend on other factors (eg, clinical, sonographic) besides the FNA interpretation.

[b]Some studies have recommended molecular analysis to assess the type of surgical procedure (lobectomy versus total thyroidectomy).

[c]In the case of "Suspicious for metastatic tumor" or a "Malignant" interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated.

Adapted from Ali and Cibas[7] with permission of Springer.

Follow up after the First Benign FNA

- Nodules with **high suspicion US pattern**
  →repeat **US and US-guided FNA within 12 months**

- Nodules with **low to intermediate suspicion US pattern**
  → repeat US at **12–24 months:** FNA could be repeated if sonographic evidence of **growth or development of new suspicious sonographic** features

- 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

Follow up after the Second Benign FNA

- 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

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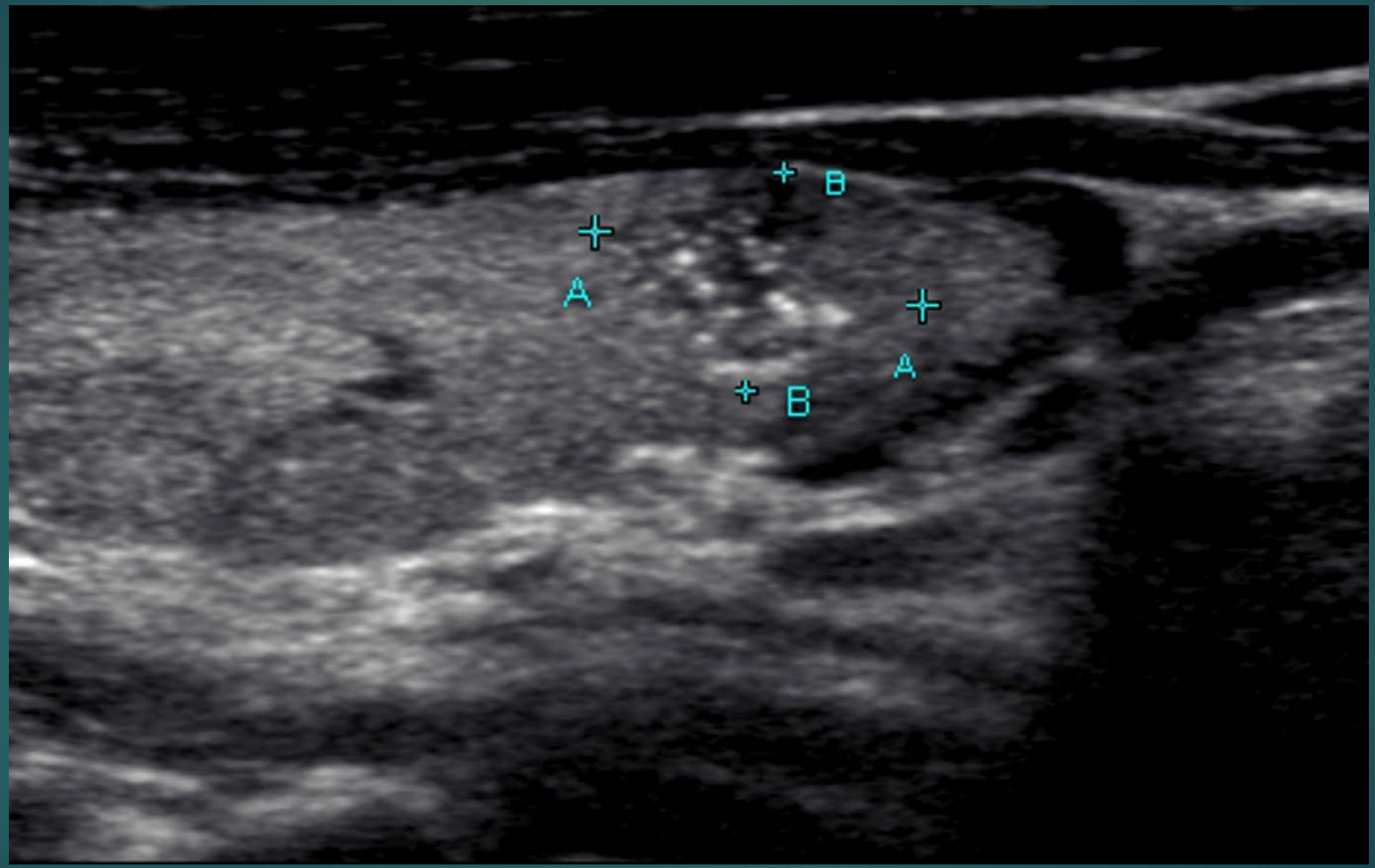
Case 2

- 67 year old man was found to have a thyroid nodule with microcalcification during carotid US. He was told he needs a biopsy and surgery.
- Clinically, no sx/sx of hyperthyroid
- No history of thyroid cancer in the patient or first degree relatives.
- He denied compressive symptoms
- Annual labs showed normal TSH 4 months ago.

Next step?


B
A
A
B

1 cm

1 cm

1.5 cm

2 cm

No FNA

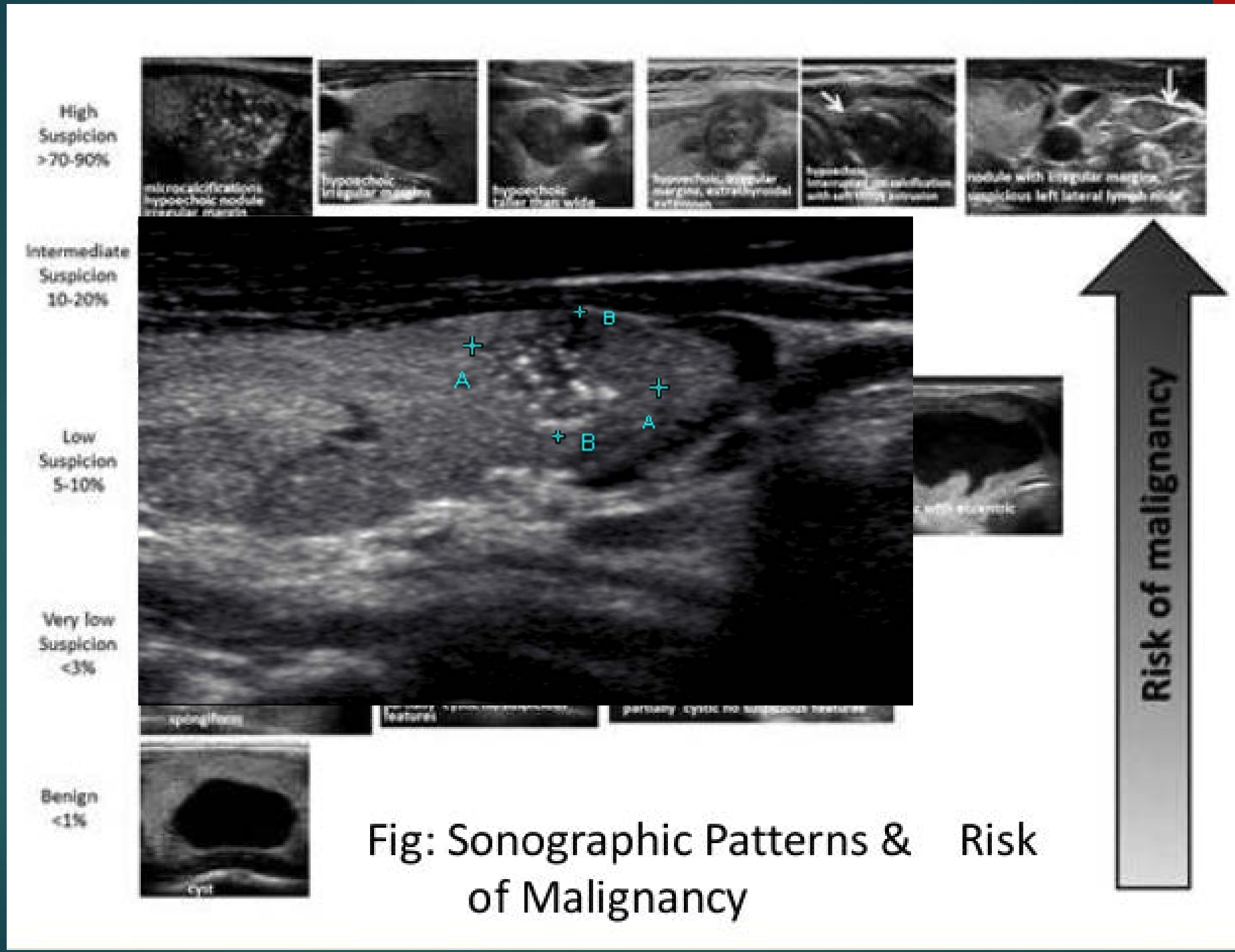
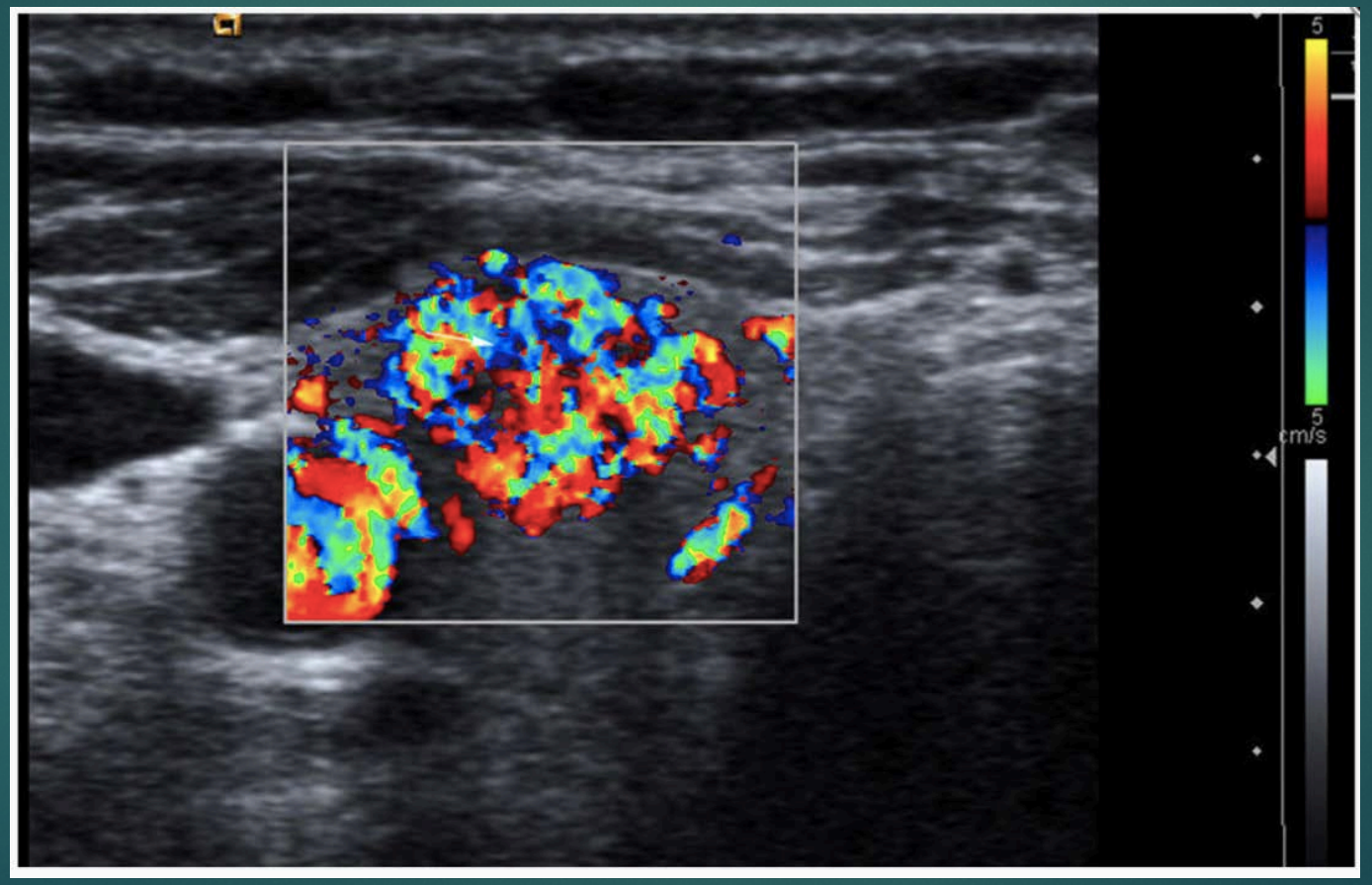


Fig: Sonographic Patterns & Risk of Malignancy

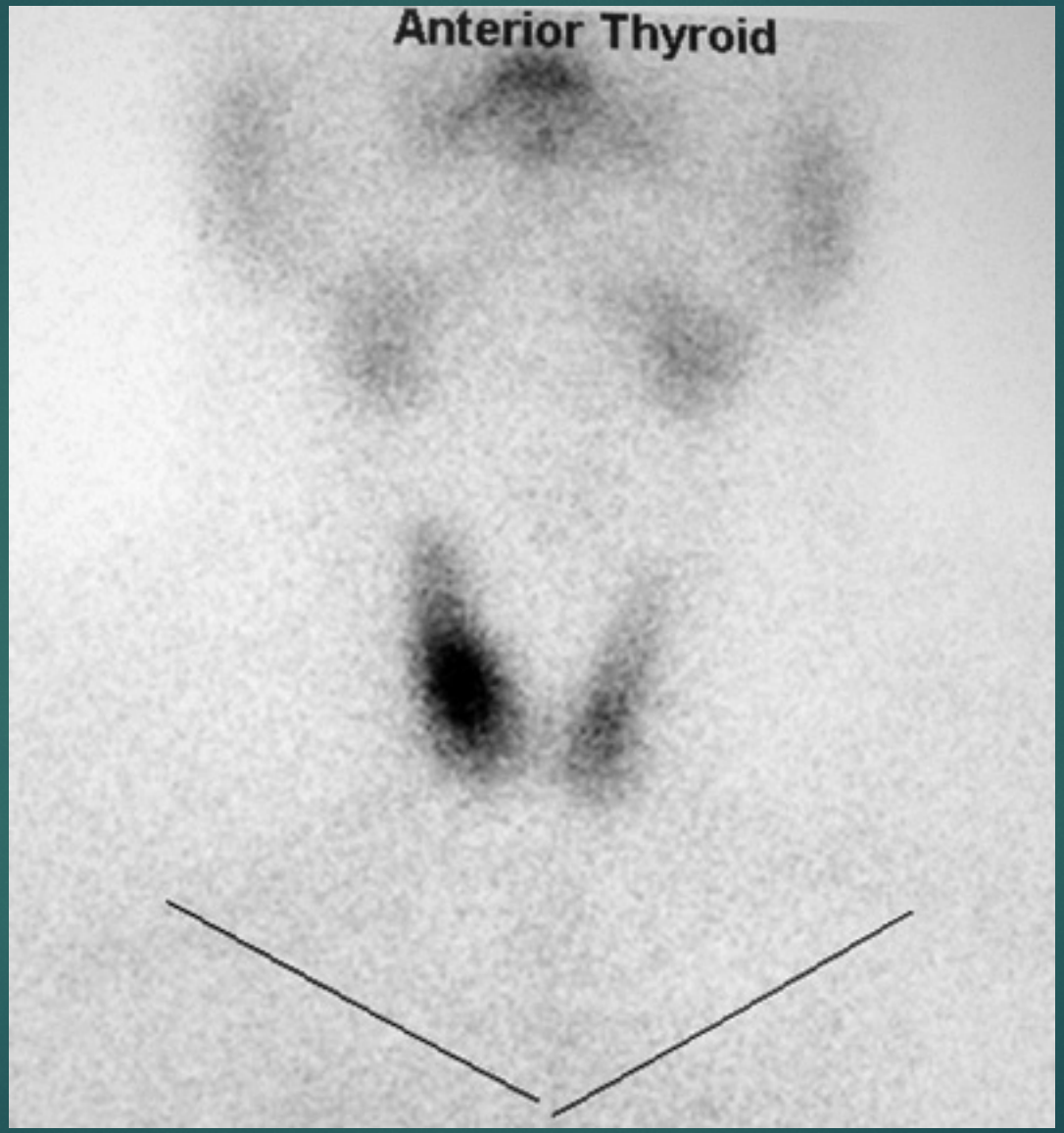
Case 3

- 57 year old man was admitted for new onset Afib. Labs showed TSH 0.01, with Free T4 3.5.
- CT scan showed Rt side thyroid nodule.
- Clinically, the patient has nonspecific symptoms for the last year and he was treated for anxiety and insomnia.

Next step?

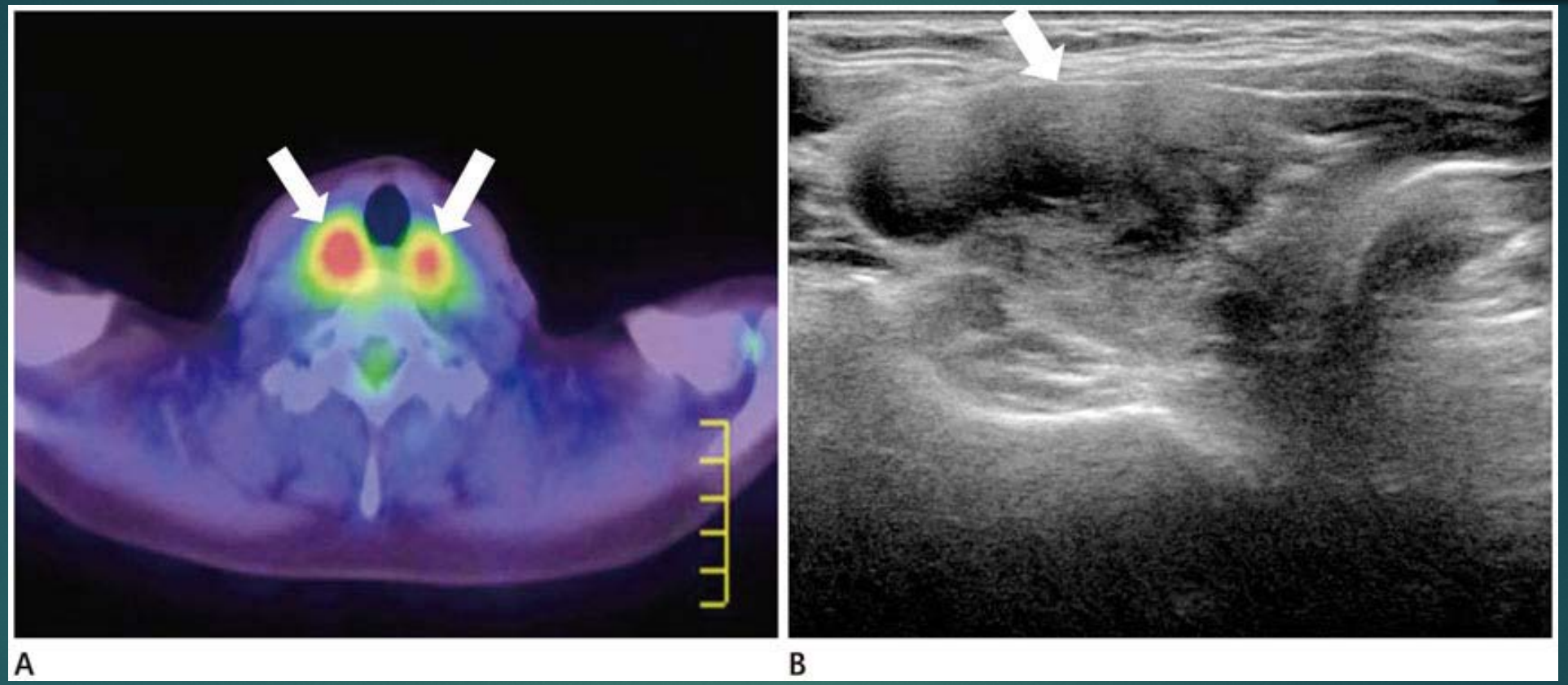

5
5
cm/s

- Next step?


Anterior Thyroid

Case 4

- 54-year-old woman underwent PET-CT for screening, and an incidental diffuse FDG uptake was observed in both lobes of the thyroid gland (SUV max = 4.2)
- TFT mild hypothyroidism
- On ultrasonography, heterogeneous parenchymal echogenicity with ill-defined heterogeneous hypoechoic nodules was observed in both lobes of the thyroid gland


A
B

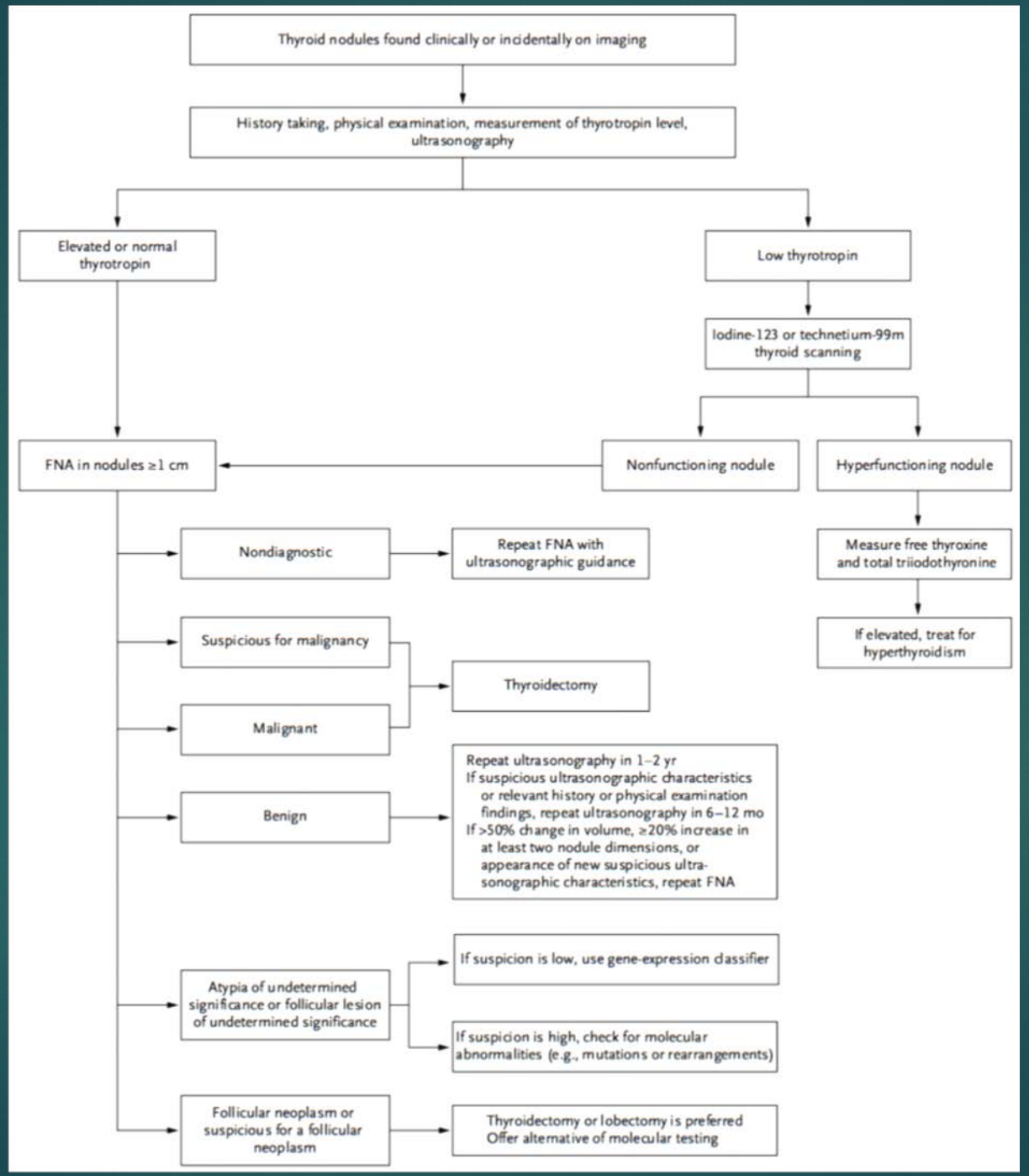
- Next step?

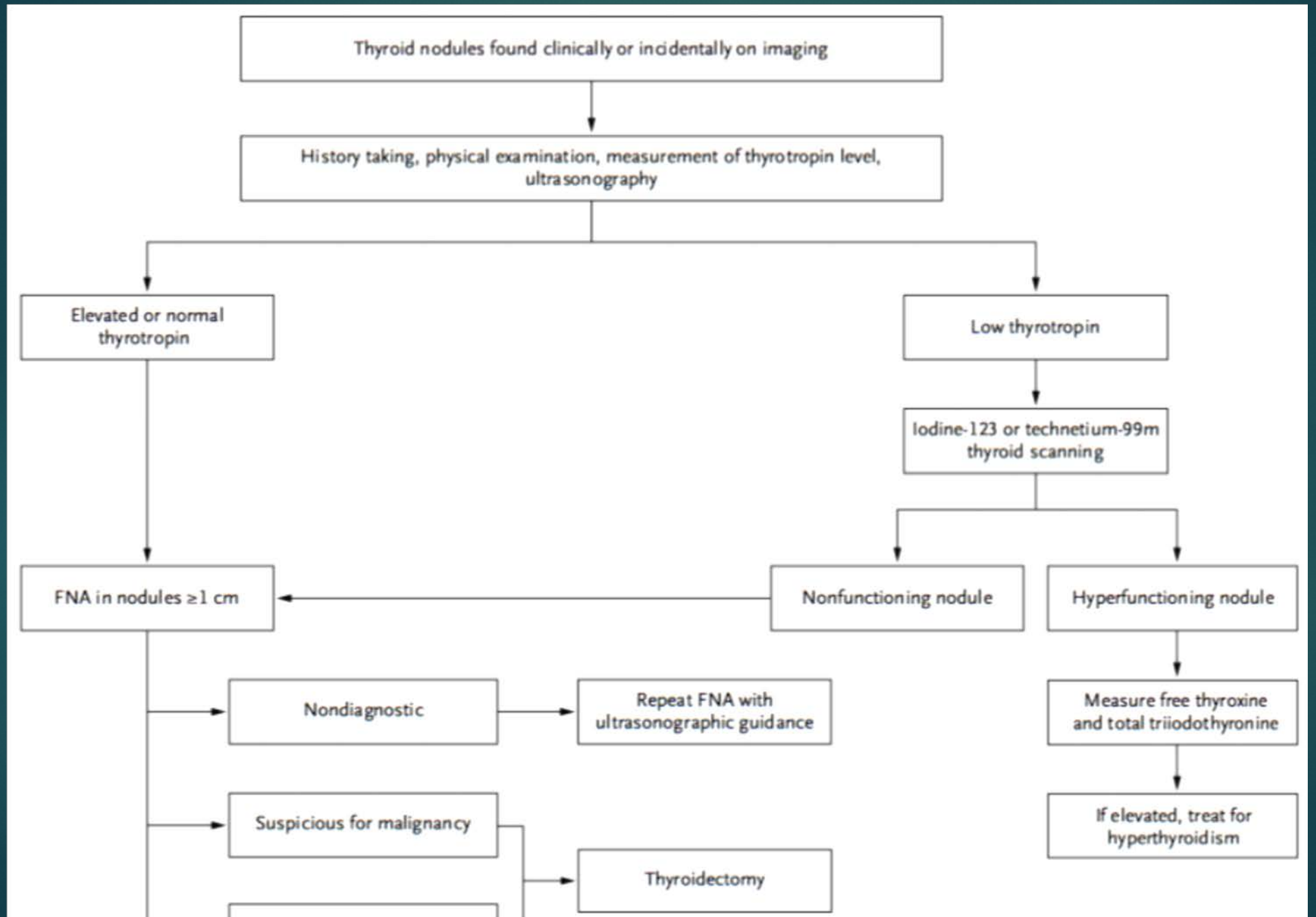
- FNA confirmed Hashimoto's thyroiditis: diffuse thyroid uptake is often associated with chronic lymphocytic

How should thyroid nodules in pregnant women be managed?

- In euthyroid and hypothyroid pregnant women:
  - FNA of clinically relevant thyroid nodules should be performed

- For women with suppressed serum TSH levels ***that persist beyond 16 weeks gestation***:
  - FNA may be deferred until after pregnancy and cessation of lactation
  - We still do labs (TSI, TRAb)


Thyroid nodules found clinically or incidentally on imaging
History taking, physical examination, measurement of thyrotropin level, ultrasonography
Elevated or normal thyrotropin
Low thyrotropin
Iodine-123 or technetium-99m thyroid scanning
FNA in nodules ≥1 cm
Nonfunctioning nodule
Hyperfunctioning nodule
Nondiagnostic
Repeat FNA with ultrasonographic guidance
Measure free thyroxine and total triiodothyronine
If elevated, treat for hyperthyroidism
Suspicious for malignancy
Malignant
Thyroidectomy
Benign
Repeat ultrasonography in 1–2 yr
If suspicious ultrasonographic characteristics or relevant history or physical examination findings, repeat ultrasonography in 6–12 mo
If >50% change in volume, ≥20% increase in at least two nodule dimensions, or appearance of new suspicious ultrasonographic characteristics, repeat FNA
Atypia of undetermined significance or follicular lesion of undetermined significance
If suspicion is low, use gene-expression classifier
If suspicion is high, check for molecular abnormalities (e.g., mutations or rearrangements)
Follicular neoplasm or suspicious for a follicular neoplasm
Thyroidectomy or lobectomy is preferred
Offer alternative of molecular testing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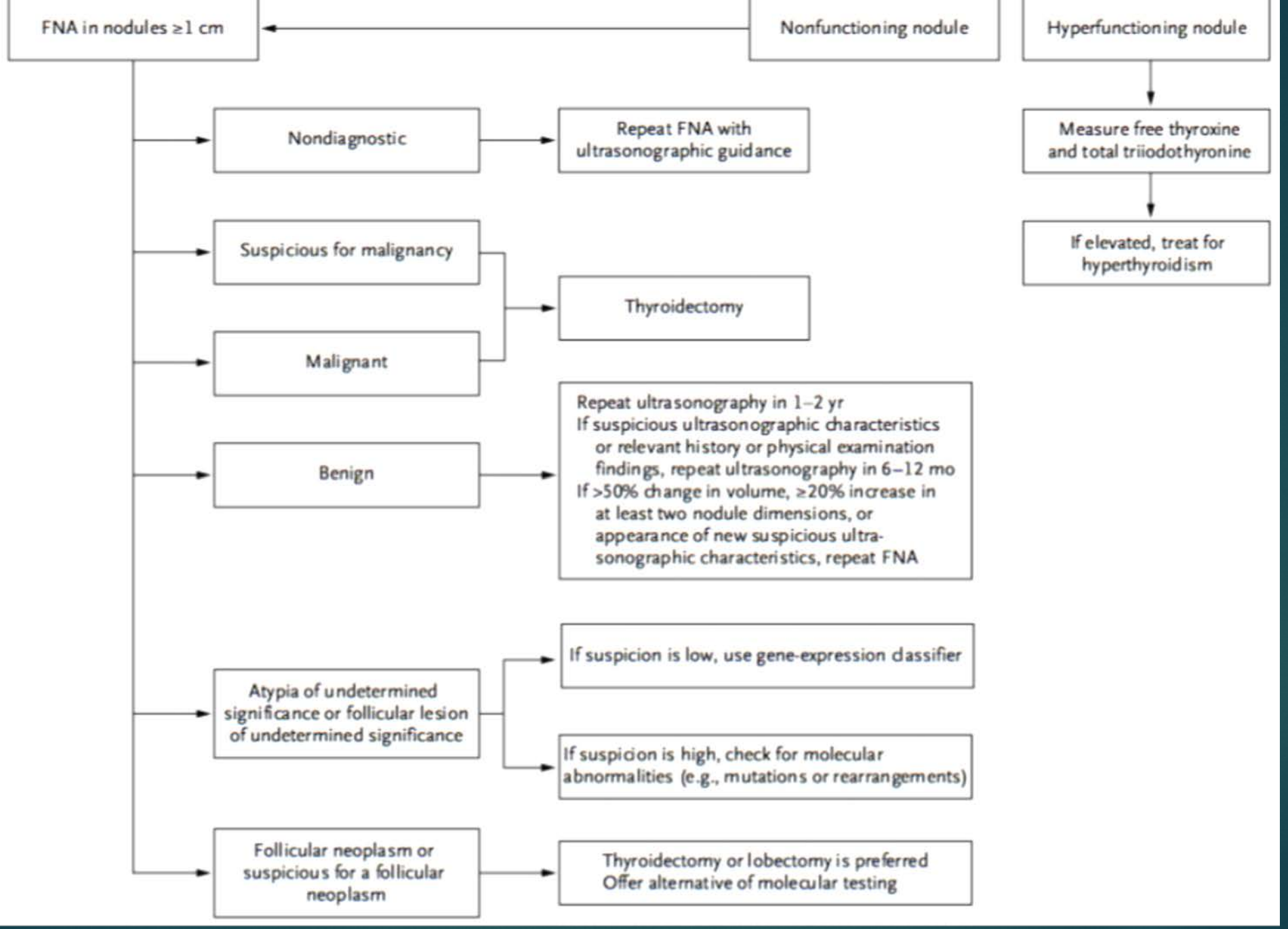
Thyroidectomy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Q&A

Thank you

Evaluation of Thyroid Nodules

- TSH, Neck ultrasound (thyroid and LN)
- Nonsuppressed TSH, single or multiple nodules
  - Biopsy larger or suspicious nodules
- Suppressed TSH, single or multiple nodules
  - I-123 thyroid scan