



Approach to the Patient with Thyroid nodule and Differentiated Thyroid Cancer



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Outline

- Approach to a patient with a thyroid nodule less than 1 cm
- Approach to a patient with a cytopathological diagnosis of follicular neoplasm by FNA

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GUIDELINES

2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer

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AJCC/UICC TNM Staging

TABLE 6. AJCC/UICC TNM STAGING: THE 8TH EDITION TNM^{27,595}

<i>TNM</i>		
<i>CATEGORY^a</i>	<i>Code</i>	<i>Description</i>
Primary tumor (pT)	TX	Primary tumor cannot be assessed
	T0	No evidence of primary tumor
	T1	Tumor ≤2 cm limited to thyroid
	• T1a	Tumor ≤1 cm limited to thyroid
	• T1b	Tumor >1 cm but ≤2 cm limited to thyroid
	T2	Tumor >2 cm but ≤4 cm limited to thyroid
	T3	Tumor >4 cm or minimal extrathyroidal extension
	• T3a	Tumor >4 cm limited to thyroid
	• T3b	Gross extrathyroidal extension to strap muscles
	T4	Gross extrathyroidal extension to major neck structures
	• T4a	Invading soft tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve
	• T4b	Invading prevertebral fascia or encasing carotid/mediastinal vessels

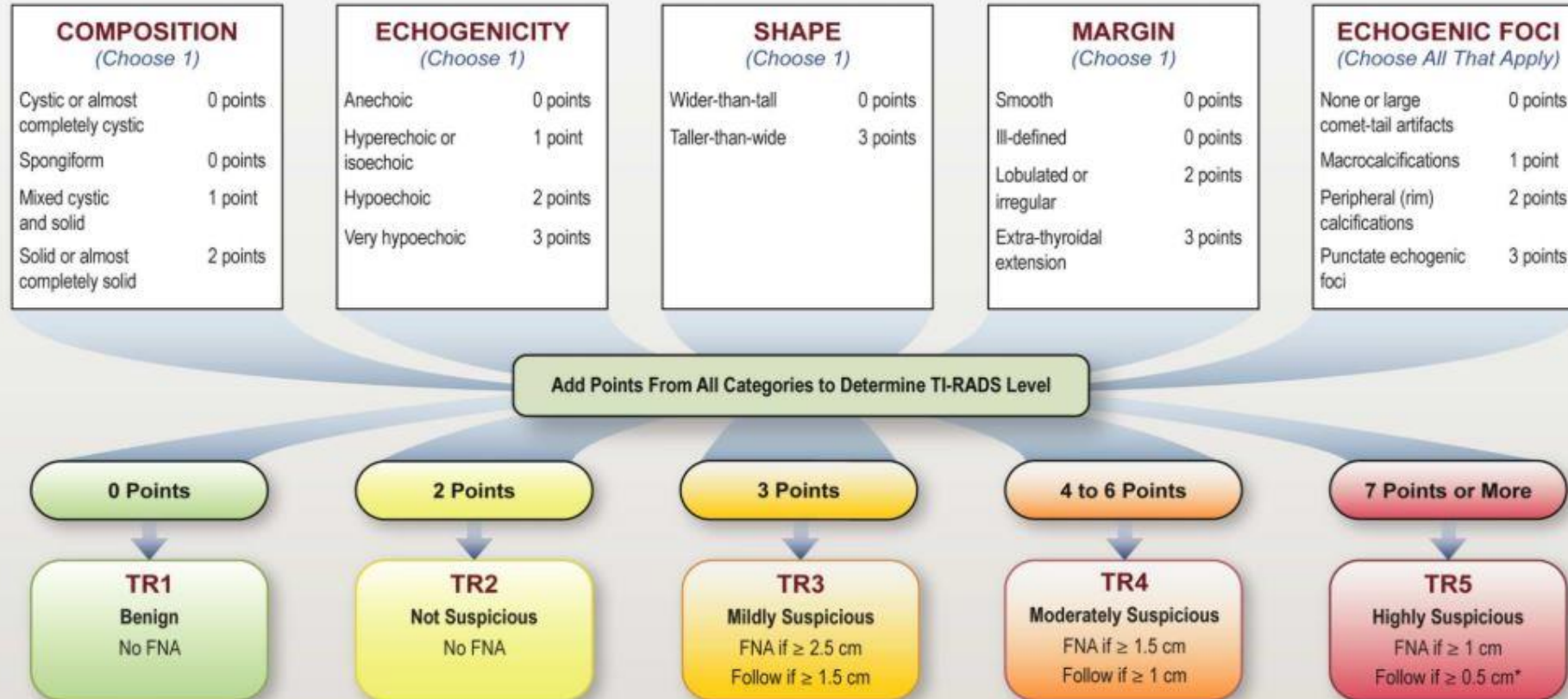
Case 1

- A 53-year-old woman was found to have a thyroid nodule measuring approximately 9 x 8 mm in diameter.
- Thyroid function tests were within normal range.
- An ultrasound (US) examination revealed heterogeneous echotexture nodule 8*7.5*6 mm within the thyroid gland, with microcalcifications, hypo-echogenicity, irregular margins, taller-than-wide shape of the nodule, consistent with Papillary Thyroid Carcinoma (PTC).
- Additionally, several reactive lymph nodes were identified bilaterally in the neck which the greatest diameter was 14 mm.

Questions

- How should a thyroid nodule be described in a radiology report?
- What is the role of US in detecting suspicious cervical LNs?
- Is Fine Needle Aspiration (FNA) indicated in this clinical scenario?

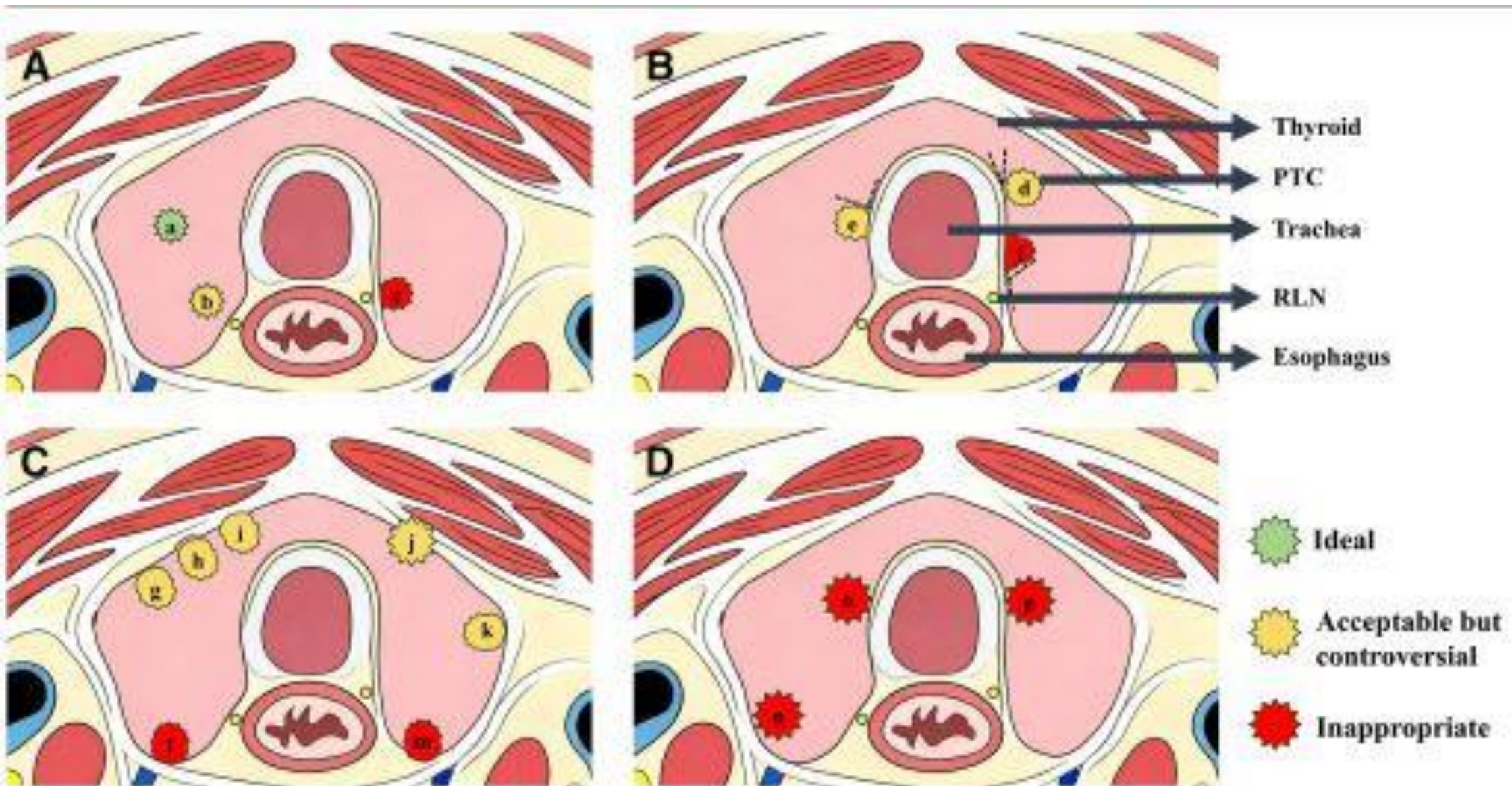
ACR TI-RADS

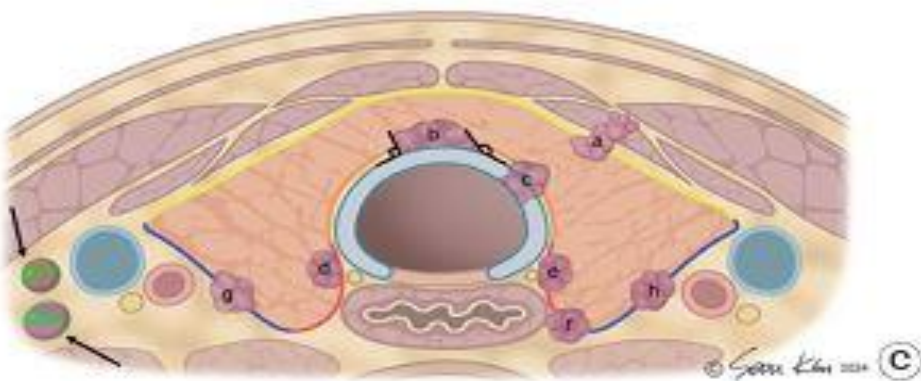
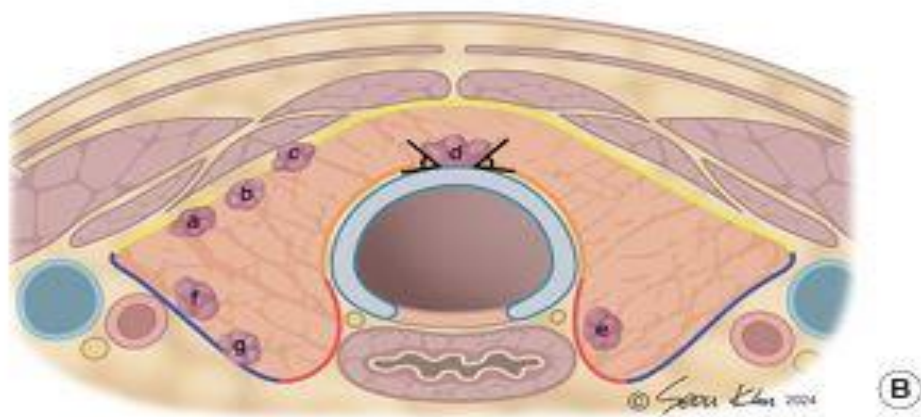
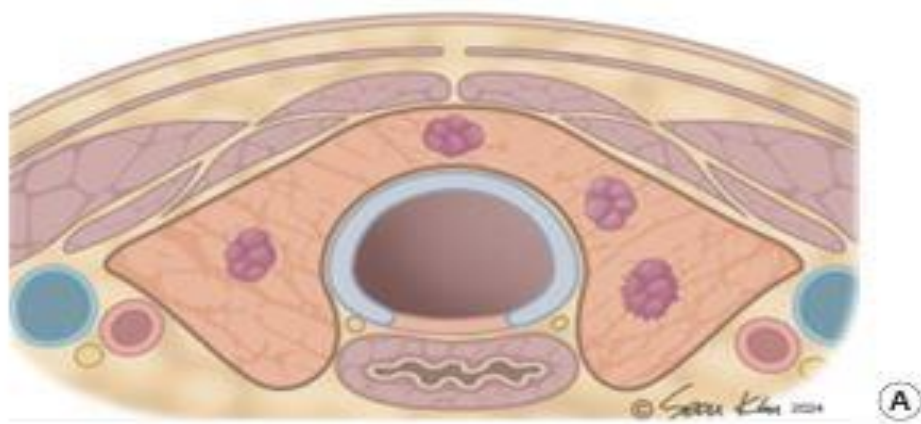


COMPOSITION	ECHOGENICITY	SHAPE	MARGIN	ECHOGENIC FOCI
<i>Spongiform</i>: Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories. <i>Mixed cystic and solid</i>: Assign points for predominant solid component. Assign 2 points if composition cannot be determined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

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

Ultrasound Anatomy – Based Decision Making in Low Risk PTMC





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**Review
Article**

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Ultrasound Imaging Criteria and Protocols for Active Surveillance of Low-Risk Thyroid Cancer: A Review of International Consensus Guidelines

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Question

- Is Fine Needle Aspiration (FNA) indicated in this clinical scenario?

Thyroid nodule diagnostic FNA recommendation

- I. Thyroid nodule diagnostic FNA is recommended for:
 - Nodules $\geq 1\text{cm}$ in greatest dimension with high suspicion sonographic pattern.
(Strong recommendation, Moderate-quality evidence)
 - Nodules $\geq 1\text{cm}$ in greatest dimension with intermediate suspicion sonographic pattern.
(Strong recommendation, Low-quality evidence)
 - Nodules $\geq 1.5\text{cm}$ in greatest dimension with low suspicion sonographic pattern.
(Weak recommendation, Low-quality evidence)
- II. Thyroid nodule diagnostic FNA may be considered for:
 - Nodules $\geq 2\text{cm}$ in greatest dimension with very low suspicion sonographic pattern (e.g., spongiform). Observation without FNA is also a reasonable option.
(Weak recommendation, Moderate-quality evidence)
- III. Thyroid nodule diagnostic FNA is not required for:
 - Nodules that do not meet the above criteria.
(Strong recommendation, Moderate-quality evidence)
 - Nodules that are purely cystic.
(Strong recommendation, Moderate-quality evidence)

FNA:

- A Fine-Needle Aspiration (FNA) biopsy of the thyroid nodule was performed.
- The cytopathology results showed, pale-staining nuclei with finely dispersed chromatin, nuclear grooves, nuclear pseudoinclusions and a colloid background all highly suggestive of PTC.

Question

- What are the standardized criteria for reporting the cytopathology of a thyroid nodule following fine-needle aspiration (FNA)?

Optional approaches? Which one works the best?

1-Active surveillance

2- Surgery, total thyroidectomy Vs lobectomy

3- Percutaneous ablation/Radiofrequency, microwave, laser, ethanol ablation

Active surveillance

- 1- Who is candidate for active surveillance?
- 2- Role of neck ultrasound in monitoring disease progression
- 3- Should serum Tg and TgAb levels be measured during active surveillance?
- 4- Role of LT4 suppression therapy
- 5- when do you recommend surgery during an active surveillance?

Question

- Who is candidate for active surveillance?

Determining which patients are candidates for active surveillance

- Shared decision-making among the patient, endocrinologist, surgeon, and other clinicians.
- Some patients may not want active surveillance, whereas for others the benefit of avoiding surgical complications.
- Consideration should be given to the tumor and patient characteristics (non-compliance) and the medical team's ability to provide long-term observation.

Con't

- If thyroid cancer is diagnosed in a tumor $\leq 1\text{cm}$ by FNA, active surveillance is an acceptable management option in selected patients.
- In adults with small, low-risk DTC, active surveillance and immediate resection are associated with similar, low risk of all-cause or cancer-specific mortality, distant metastasis, and recurrence after thyroidectomy.

- Ito Y.etal. Thyroid 2003;13(4):381–387;
- Tuttle RM,etal. JAMA Otolaryngol Head Neck Surg 2017;143(10):1015–1020;

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Active Surveillance Versus Thyroid Surgery for Differentiated Thyroid Cancer: A Systematic Review

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Ralph P. Tufano,^{5,6} Julie Ann Sosa,⁷ and Matthew D. Ringel⁸

Seven studies (five cohort studies N = 5432 and two cross-sectional studies N= 53) of active surveillance vs. immediate surgery, and seven uncontrolled treatment series of active surveillance (N = 1219) were included.

	<i>Outcome</i>	<i>No. of studies study design</i>	<i>Risk of bias</i>	<i>Inconsistency</i>	<i>Indirectness</i>	<i>Imprecision</i>	<i>Quality of evidence</i>	<i>Main findings</i>
Key Question 1: Active surveillance vs. immediate surgery, low-risk differentiated thyroid cancer <2 cm	All-cause mortality	3 cohort studies (N=2982) 7 uncontrolled treatment series or active surveillance (N=1219)	High	Consistent	Direct	Precise	Low	Cohort studies: 0.3% vs. 0.5% (1 study); no cases (2 studies) Treatment series: No cases (7 studies)
	Thyroid cancer mortality	4 cohort studies (N=4377) 7 uncontrolled treatment series of active surveillance (N=1219)	High	Consistent	Direct	Precise	Low	Cohort studies: 0% vs. 0.2% (1 study); no cases (3 studies) Treatment series: No cases (6 studies)
	Recurrence after surgery	3 cohort studies (N=2574) 4 uncontrolled treatment series of active surveillance (N=80)	High	Consistent	Direct	Precise	Low	Cohort studies: 0% vs. 3.0%, 1.1% vs. 0.5%, and 0% vs. 2.4% (3 studies) Treatment series: No cases (3 studies)
	Lymph node metastasis	3 cohort studies (N=2574) 5 uncontrolled treatment series of active surveillance (N=1004)	High	Consistent	Direct	Precise	Low	Cohort studies: 0.1% vs. 0.3%, 0.8% (T1a) and 3.3% (T1b) vs. 1.5% (T1b), and 0% vs. 5.6% (3 studies) Treatment series: Range 0% to 2.9% (5 studies)
	Distant metastasis	4 cohort studies (N=4388) 4 uncontrolled treatment series of active surveillance (N=946)	High	Consistent	Direct	Precise	Low	Cohort studies: 0% vs. 0.3% (1 study); no cases (3 studies) Treatment series: No cases (4 studies)
	Tumor growth ≥3 mm in persons undergoing active surveillance	4 cohort studies (N=2026) 6 uncontrolled treatment series of active surveillance (N=996)	High	Inconsistent	Direct	Precise	Low	Cohort studies: Range 1.4% to 7.5% (4 studies) Treatment series: Range 2.1% to 20% (6 studies)
	Subsequent surgery in persons undergoing active surveillance	4 cohort studies (N=2160) 7 uncontrolled treatment series of active surveillance (N=1240)	High	Inconsistent	Direct	Precise	Low	Cohort studies: Range 2.6% to 32% (4 studies) Uncontrolled treatment series: 3.5% to 23% (7 studies)
	Temporary vocal cord paralysis, temporary hypoparathyroidism, thyroid replacement	1 cohort study (n=1179)	High	Unable to determine	Direct	Precise	Low	Temporary vocal cord paralysis: 0.6% vs. 4.1% (1 cohort study) Temporary hypoparathyroidism: 2.8% vs. 16.7% (1 cohort study) Thyroid replacement: 20.7% vs. 66.1% (1 cohort study)

For active surveillance versus surgery, the quality of evidence was assessed as low for all outcomes, being based on observational studies with high risk of bias.

Conclusions: In patients with small low-risk (primarily papillary) DTC, active surveillance and immediate surgery may be associated with similar mortality, risk of recurrence, and other outcomes

RECOMMENDATION 11A

- Active surveillance may be offered as an appropriate management option for some patients with cT1aN0M0 (Tumor size ≤ 1 cm) PTCs.
- Shared clinical decision-making between the patient and clinical team regarding risks and benefits of this approach is essential.
(Conditional recommendation, Low certainty evidence)

Question

- What is the role of neck ultrasound in monitoring disease progression?

Role of the neck ultrasound

- It is important that members of the medical team offering active surveillance have experience and confidence in their use of neck ultrasound.
 - Neck ultrasound, assessing the thyroid gland and all cervical lymph node compartments, is key to monitoring for cancer progression.
 - Neck ultrasound should be performed every 6 months for 1–2 years and then annually.
 - The length of necessary follow-up remains unknown.
 - None of the prior studies on active surveillance used neck CT for routine follow-up.
-
- Tuttle RM et al. JAMA Otolaryngol Head Neck Surg. 2017 Oct 1;143(10):1015-1020.
 - Yasuhiro Ito et al. Thyroid. 2014 Jan;24(1):27-34.
 - ITO Y et al. World J Surg. 2010 Jan;34(1):28-35.

RECOMMENDATION 12

- For patients undergoing active surveillance, neck ultrasound should be used to monitor disease progression.
- (Good Practice Statement)

Question

- Should serum Tg and TgAb levels be measured during active surveillance?

RECOMMENDATION 13

- For patients undergoing active surveillance, routine measurement of serum Tg and/or TgAb levels is not recommended.
- (Good Practice Statement)

Question

- Does Lt4 suppression therapy play any role during active surveillance?

Question

- when do you recommend surgery during an active surveillance?

RECOMMENDATION 14

- In patients undergoing active surveillance, surgical resection is indicated if :
 - There is evidence of new biopsy-proven lymph node metastases
 - Growth of the primary tumor by ≥ 3 mm
 - Distant metastases
 - Evidence of extrathyroidal extension
 - Posterior growth
 - When there is patient anxiety
 - Inability to follow-up, and/ or expressed preference for surgery
- (Good Practice Statement)

Surgery

- 1-What is the optimal operative approach for DTC? lobectomy versus total thyroidectomy.
- 2-After lobectomy, tumor multifocality was seen in pathology report, what the next approach is.
- 3-When should completion thyroidectomy be performed?

Question

- What is the optimal operative approach for mPTC?

lobectomy Vs total thyroidectomy.

RECOMMENDATION 15

- When resection is performed for patients with thyroid cancer ≤ 2 cm without gross extra-thyroidal extension(cT1) and without metastases (cN0M0), the initial surgical procedure should be a thyroid lobectomy unless there are bilateral cancers or other indications to remove the contralateral lobe.
- (Strong recommendation, Moderate certainty evidence)

Question

- 2-After lobectomy, tumor multifocality was seen in pathology report, what the next approach is?
- 3-When should completion thyroidectomy be performed?

RECOMMENDATION 16

- Completion thyroidectomy for cancer following initial lobectomy may be considered
 - To address persistent primary malignancy
 - Facilitate RAI administration, and/ or enhance follow-up based upon higher estimated risk of recurrence identified postoperatively, accounting for recurrent laryngeal nerve function.
-
- (Conditional recommendation, Low-moderate certainty evidence)

Percutaneous ablation

- Who is the best candidate for percutaneous ablation?
- What is the comparative efficacy and safety profile of radiofrequency ablation versus lobectomy in patients diagnosed with micro-PTC?
- What do we have for long term follow up in the literature?

Question

- Who is the best candidate for percutaneous ablation?

Percutaneous ablation

- Patients who are uncomfortable with active surveillance or with surgery may prefer a percutaneous ultrasound-guided ablative treatment for their cancer.
- Compared with lobectomy, ablation has a lower likelihood of resultant hypothyroidism, but it affords less certainty of complete tumor eradication, and it does not permit histopathologic evaluation.

- Santos GPL,etal. Arch Endocrinol Metab 2024;68.

RECOMMENDATION 11 B

- Ultrasound-guided percutaneous ablation may be considered as an alternative to active surveillance or resection for cT1aN0M0 PTC (Tumor $\leq$ 1 Cm limited to thyroid) in selected patients.
- Shared clinical decision-making between the patient and clinical team regarding risks and benefits of this approach is essential.
- (Conditional recommendation, Low certainty evidence)

Question

- What is the comparative efficacy and safety profile of radiofrequency ablation versus lobectomy in patients diagnosed with micro-PTC?

Assessment of Radiofrequency Ablation for Papillary Microcarcinoma of the Thyroid

A Systematic Review and Meta-analysis

JAMA Otolaryngol Head Neck Surg

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2022;148;(4):317-325. doi:10.1001/jamaoto.2021.4381

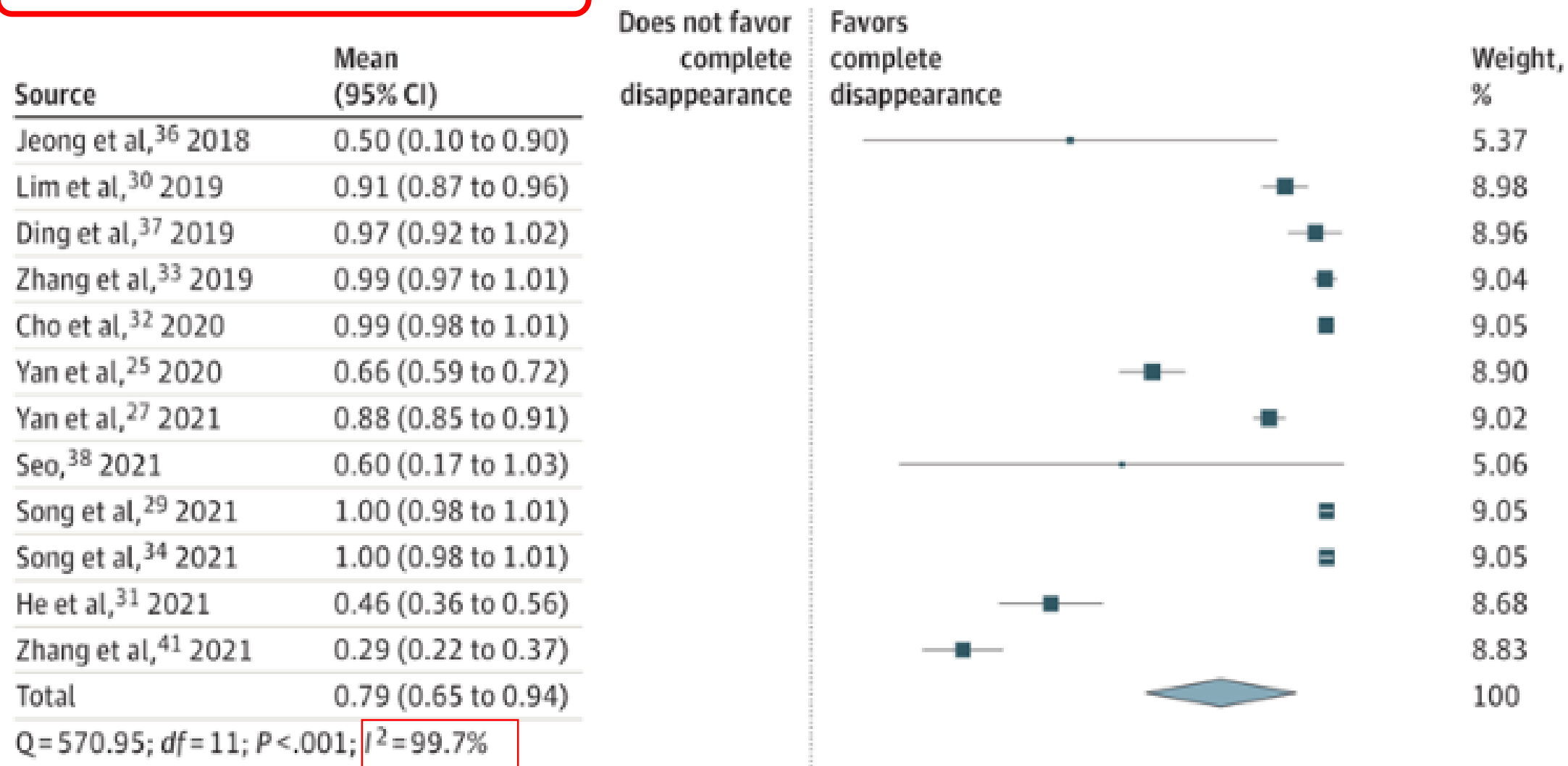
Sam P. J. van Dijk, BSc¹; Hannelore I. Coerts, BSc¹; Sabrina T. G. Gunput, PhD²; [et al](#)

Main Outcomes and Measures

The primary outcome: the complete disappearance rate of mPTC

Secondary outcomes: tumor progression and complications

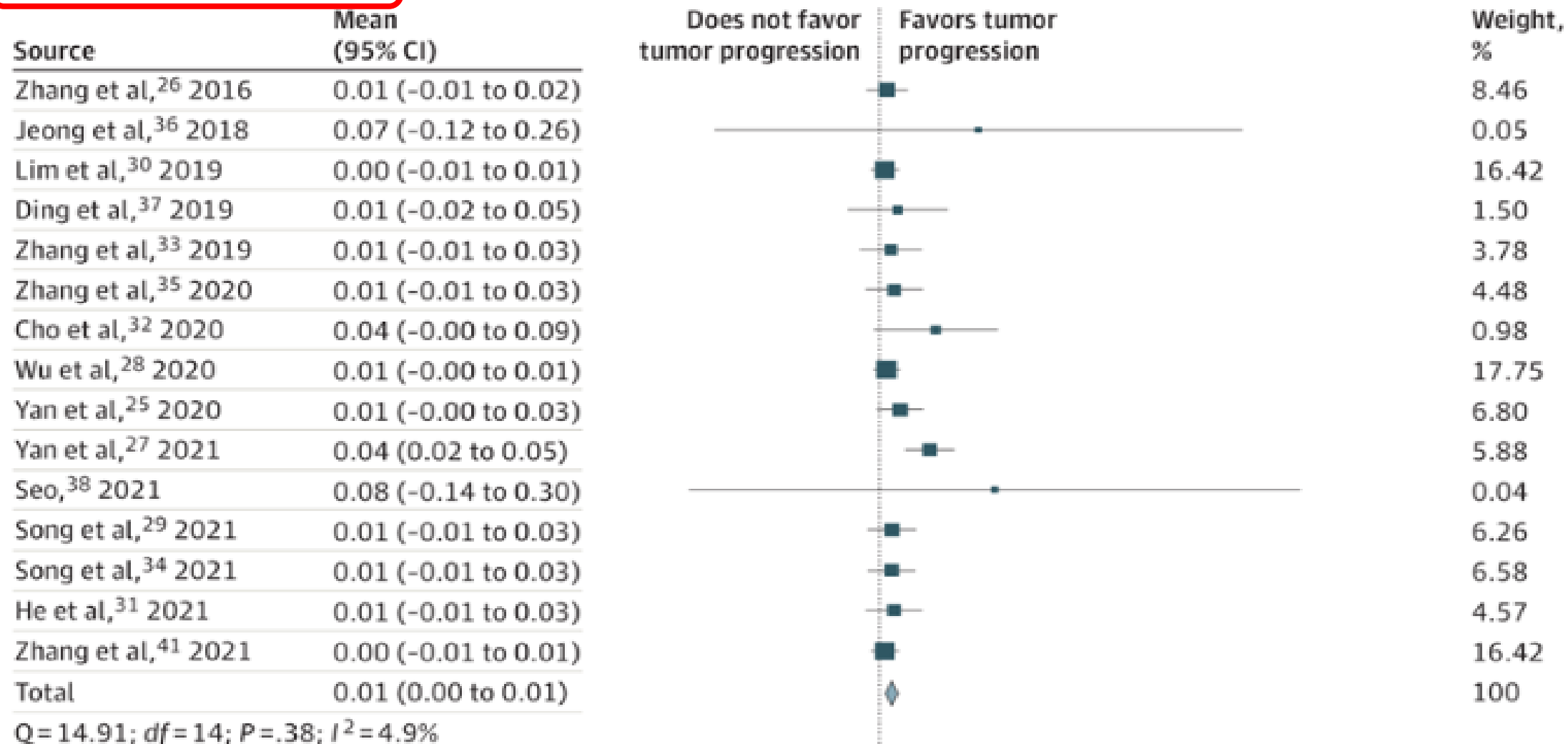
A Complete disappearance at last follow-up



The pooled complete disappearance rate at the end of follow-up was

79% (95% CI, 65%-94%)

B Overall tumor progression



The overall tumor progression rate was 1%

Conclusions and Relevance

- The findings of this systematic review and meta-analysis suggest that RFA is a safe and efficient method to treat selected low-risk mPTCs.
- Radiofrequency ablation could be envisioned as step-up treatment after local tumor growth under active surveillance for an mPTC or initial treatment in patients with mPTCs with anxiety about active surveillance.

Case 2

- A 36-year-old woman presented with a thyroid nodule located in the left lobe of her thyroid gland.
- The nodule was identified and measured by US to be 2.8 x 1.8 cm in diameter.
- On ultrasound, the nodule exhibits hypoechoic features, suggesting it may be more solid than cystic.
- The patient is clinically euthyroid.
- Thyroid function tests were within normal range.
- There is no reported family history of thyroid cancer.

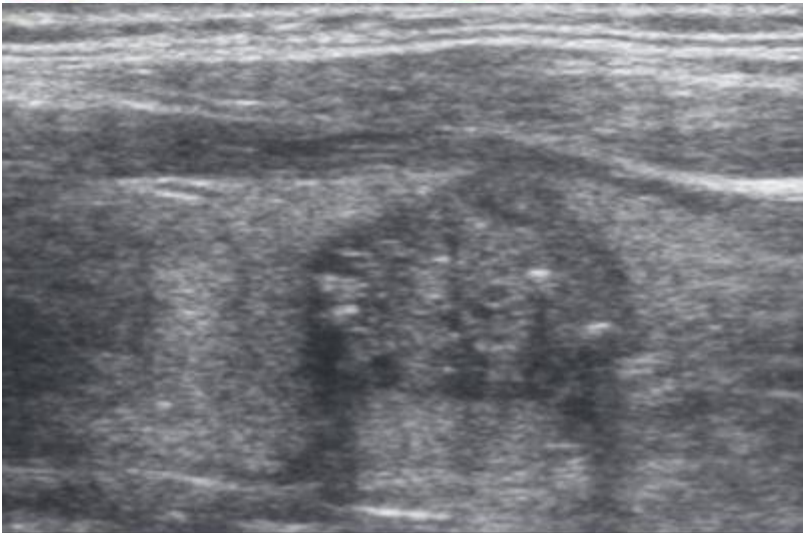
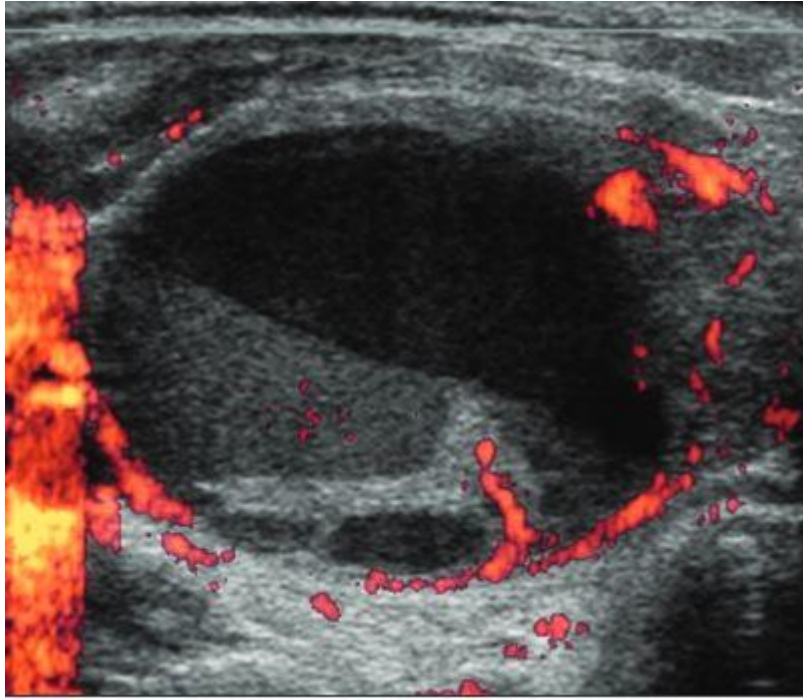
Question

- To what extent can thyroid ultrasonographic features assist in differentiating between benign follicular adenomas and malignant follicular carcinomas?”

Follicular adenoma V Carcinoma US-features

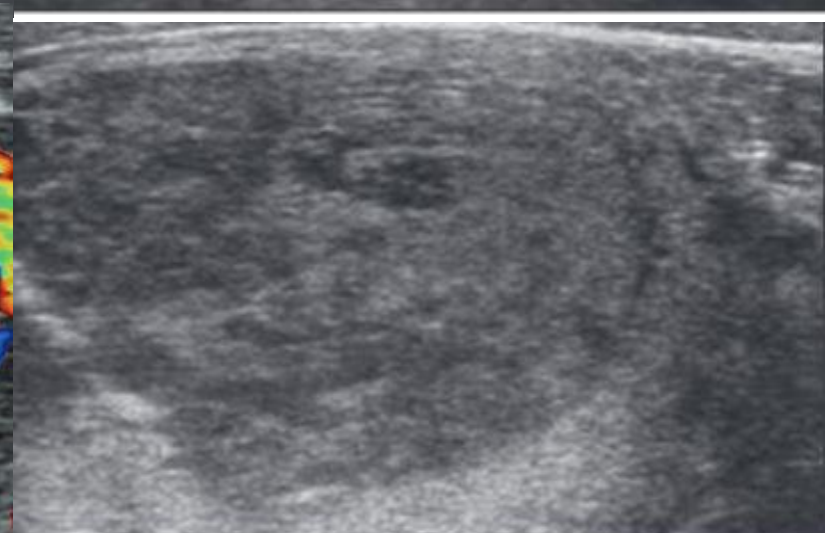
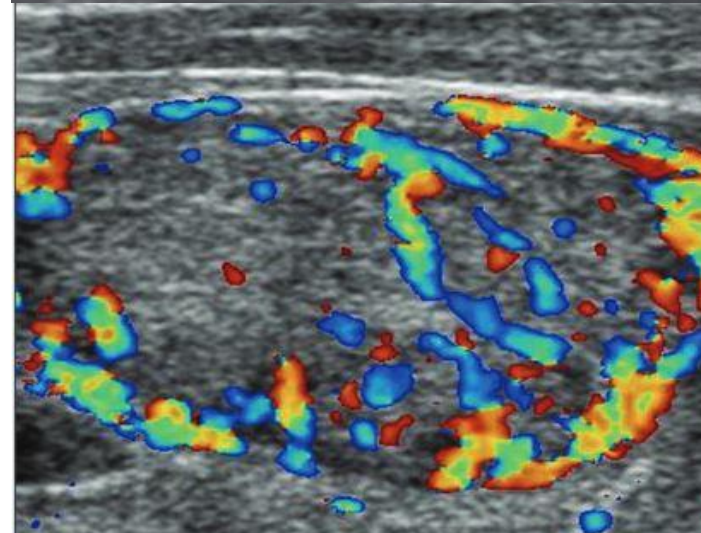
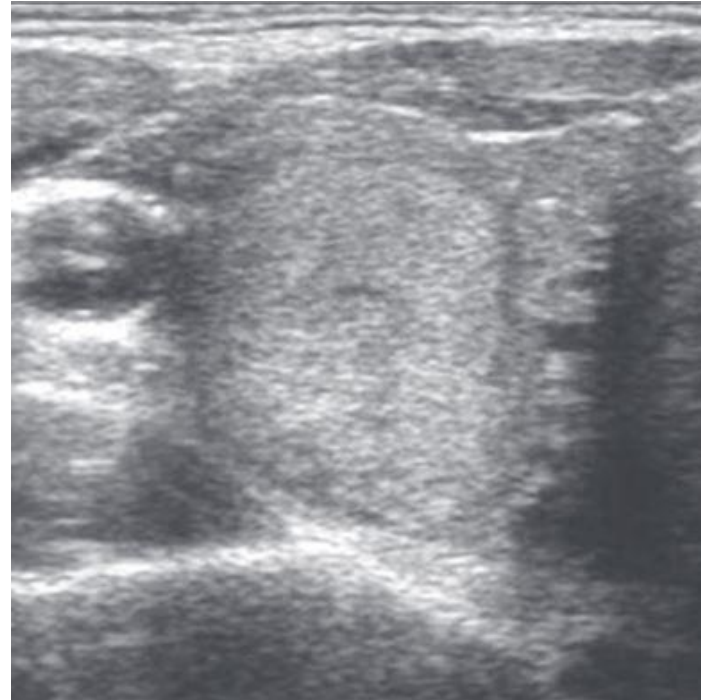
- Larger lesion size,
- Lack of a sonographic halo
- Hypoechoic appearance
- Absence of cystic change favored a follicular carcinoma diagnosis.
- Increased patient **age and male sex** are associated with malignancy.
- Within the follicular carcinoma subgroup, **Hürthle-cell variant of follicular carcinoma** is more often seen in older patients with nodules having a **heterogeneous** appearance and lacking internal calcifications

Follicular Adenoma



Vs

Carcinoma



Cytopathology report

- The aspirate showed numerous small, crowded follicular cells arranged in microfollicles, macrofollicles and occasionally as single cells or in small clusters consists with a follicular neoplasm.
- What is the diagnosis?
- Goal is to identify all potential cases of
 - Follicular carcinoma, follicular variant of papillary carcinoma and NIFTP
 - OR
 - Follicular neoplasm / suspicious for follicular neoplasm (Bethesda IV)
 - OR
 - Encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) with mild or focal nuclear atypia

The Bethesda System for Reporting Thyroid Cytopathology: Diagnostic Categories and Risk of Malignancy

<i>Diagnostic category</i>	<i>Estimated/predicted risk of malignancy by the Bethesda system, %^a</i>	<i>Actual risk of malignancy in nodules surgically excised, % median (range)^b</i>
Nondiagnostic or unsatisfactory	1–4	20 (9–32)
Benign	0–3	2.5 (1–10)
Atypia of undetermined significance or follicular lesion of undetermined significance	5–15	14 (6–48)
Follicular neoplasm or suspicious for a follicular neoplasm	15–30	25 (14–34)
Suspicious for malignancy	60–75	70 (53–97)
Malignant	97–99	99 (94–100)

^aAs reported in The Bethesda System by Cibas and Ali (1076).

^bBased on the meta-analysis of eight studies reported by Bongiovanni *et al.* (103). The risk was calculated based on the portion of nodules in each diagnostic category that underwent surgical excision and likely is not representative of the entire population, particularly of nondiagnostic and benign diagnostic categories.

Cont

- What is your next step?
- Surgery (Lobectomy Vs total Thyroidectomy)
- Role of Frozen Section
- Follow-up after lobectomy

Essential features of follicular neoplasm

- Final diagnosis is based on histological examination of the surgically resected specimen because capsular or vascular invasion are essential criteria
 - Most common histopathological diagnosis is follicular adenoma, followed by follicular nodular disease, NIFTP, follicular variant of papillary carcinoma and follicular carcinoma Impossible to distinguish follicular adenoma from follicular carcinoma by FNA cytology
-
- Diagn Cytopathol 2018:148

Question

- What is your next step?
Surgery (Lobectomy Vs total Thyroidectomy)
 - Diagnostic thyroid lobectomy
- Molecular testing may guide treatment



Frozen section

- Role of Frozen Section
- Its utility for diagnosing follicular carcinoma

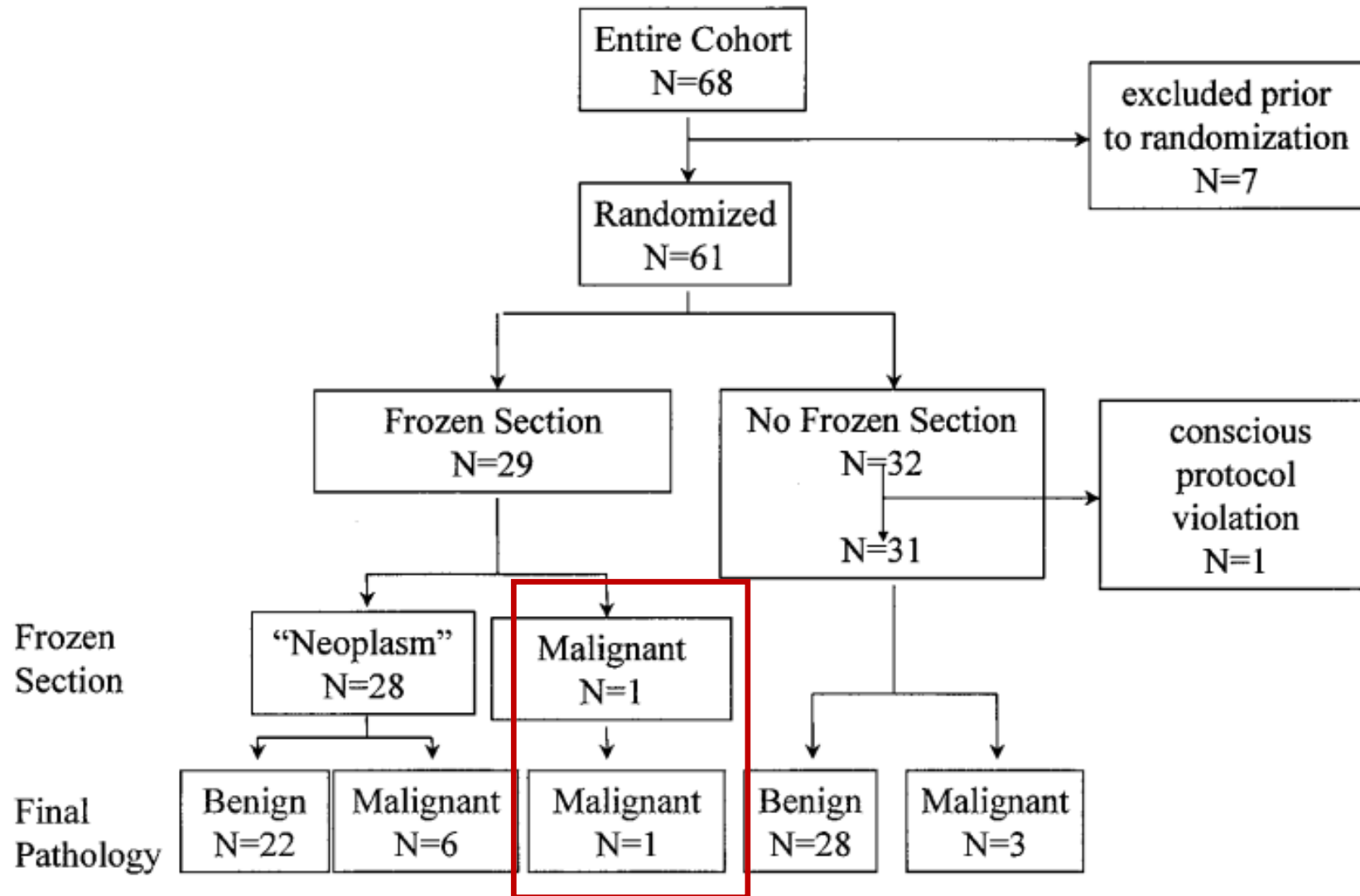
Randomized Prospective Evaluation of Frozen-Section Analysis for Follicular Neoplasms of the Thyroid

Robert Udelsman, MD, MBA,* William H. Westra, MD,† Patricia I. Donovan, RN,* Taylor A. Sohn, MD,* and John L. Cameron, MD*

*From the Departments of *Surgery and †Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland*

- Objective :To evaluate the clinical utility of frozen section in patients with follicular neoplasms of the thyroid in a randomized prospective trial
- The series comprised 68 consecutive patients with a solitary thyroid nodule in whom FNA showed a follicular neoplasm.

Randomization scheme



Cont' (case)

- The patient underwent left lobectomy and the pathology was Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)
- What is the best next option?

RECOMMENDATION 1

- NIFTP and other tumors of uncertain malignant potential (Follicular Tumor of Uncertain Malignant Potential and Hyalinizing Trabecular Tumor-FUMP) are diagnosed pathologically and have a very low malignant potential (lower than the lowest-risk DTC).
- Further treatment with completion thyroidectomy/lymphadenectomy and/or RAI is not advised routinely.
- The optimal approach to postoperative monitoring of these tumors is uncertain. (Good Practice Statement)

