Management of Thyroid Nodules

February 2nd, 2018
Sarah Hopkins
No disclosures
Goals:

• Review Initial Evaluation of Thyroid Nodules
• Review Indications for Biopsy
  – Approach to Multinodular Goiter
• Review Management of Biopsy Results
  – Benign, Indeterminate, and Malignant Pathology Results
  – Utility of molecular testing
• Review Long Term Follow Up of Nodules
• Briefly, Discuss Alternatives to Surgery
Indications for Thyroid Ultrasound

- Palpable anterior neck mass
- Incidental thyroid mass detected on CT, MRI, PET, or carotid duplex
- Thyroid ultrasound is not a functional exam, so it is not indicated for hyper- or hypothyroidism alone

➔ Always evaluate nodules with TSH prior to ordering imaging.
Nodule Discovered Clinically or Incidentally

#1: TSH

Low

Not low
21 y/o woman presented to new primary care provider with worsening anxiety and palpitations.

- Physical exam notable for diffuse left sided thyroid enlargement without lymphadenopathy. Nodule is mobile with swallowing.
- She denied compressive symptoms – No hoarseness, no trouble swallowing, no trouble lying flat
- No family history of thyroid disease
- No family history of radiation exposure
TSH and U/S were ordered

- TSH <0.01, FT4 1.4 (ULN 1.2), Total T3 elevated
Ultrasound

- 5cm mixed solid cystic, hypoechoic components, increased vascularity
- FNA recommended, performed, and benign
Uptake and Scan
Toxic Nodules

• Very low risk of malignancy

→ American Thyroid Associations, AACE, recommend against biopsy of hyperfunctioning nodules
Euthyroid patients

<table>
<thead>
<tr>
<th>TSH range (mIU/liter)</th>
<th>No. of patients</th>
<th>No. with malignancy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.40–1.39</td>
<td>347</td>
<td>85 (25%)</td>
<td>0.002</td>
</tr>
<tr>
<td>1.40–4.99</td>
<td>308</td>
<td>109 (35%)</td>
<td></td>
</tr>
</tbody>
</table>
Nodule Discovered with Low TSH = Pause before Biopsy and Appropriate to Refer

- TSH
  - Low
    - Uptake and Scan
      - Normal uptake
        - Evaluate nodule based on U/S
      - Hot nodule
        - No BX: Treat hyperthyroidism
      - Cold nodule
        - Consider BX based on U/S
Normal or high TSH
Indications for Biopsy:

Brief Review of guidelines:
- ATA
- AACE
- TI-RADS
Ultrasound Characteristics and Cancer Risk

<table>
<thead>
<tr>
<th>Sonographic pattern</th>
<th>US features</th>
<th>Estimated risk of malignancy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>High suspicion</td>
<td>Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small exsusive soft tissue component, evidence of ETE</td>
<td>&gt;70–90&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Intermediate suspicion</td>
<td>Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape</td>
<td>10–20</td>
</tr>
<tr>
<td>Low suspicion</td>
<td>Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETE, or taller than wide shape.</td>
<td>5–10</td>
</tr>
<tr>
<td>Very low suspicion</td>
<td>Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Benign</td>
<td>Purely cystic nodules (no solid component)</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
When to Biopsy:

AACE versus ATA Guidelines

- AACE recommends against biopsying nodules < 5mm regardless of sonographic appearance.
- AACE 5-10mm and high risks can proceed to FNA or watch. FNA recommended if evidence of extrathyroidal spread, subcapsular or paratracheal position, positive personal or family history of thyroid cancer or other clinically suspicious findings
- Otherwise cutoffs are
  - 1cm for high risk lesions
  - 2cm for intermediate risks nodules
  - Low risk > 2cm with increasing size or high risk history

Garibe et al. Endocr Practice. 2016;22(Suppl 1)
ACR TI-RADS

**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
- Hypoechoic or isoechoic: 1 point
- Hyperechoic: 2 points
- Very hyperechoic: 3 points

**SHAPE**
- Wider-than-tall: 0 points
- Taller-than-wide: 3 points

**MARGIN**
(Choose 1)
- Smooth: 0 points
- Irregular or lobulated: 2 points
- Extra thyroid extension: 3 points

**ECHOCENIC FOCI**
(Choose All That Apply)
- None or large comet-tail artifacts: 0 points
- Macrocipifications: 1 point
- Peripheral (rim) calcifications: 2 points
- Punctate echogenic foci: 3 points

**Add Points From All Categories to Determine TI-RADS Level**

- **0 Points**
  - TR1: Benign
  - No FNA

- **2 Points**
  - TR2: Not Suspicious
  - No FNA

- **3 Points**
  - TR3: Mildly Suspicious
  - FNA if ≥2.5 cm
  - Follow if ≥1.5 cm

- **4 to 6 Points**
  - TR4: Moderately Suspicious
  - FNA if ≥1.5 cm
  - Follow if ≥1 cm

- **7 Points or More**
  - TR5: Highly Suspicious
  - FNA if ≥1 cm
  - Follow if ≥0.5 cm

**COMPOSITION**
Spongiform: Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories.
- Mixed cystic and solid: Assign points for predominant solid component.
- Assign 2 points if composition cannot be determined because of calcification.

**ECHOGENICITY**
- Anechoic: Applies to cystic or almost completely cystic nodules.
- Hypoechoic/isoechoic/hyperechoic: Compared to adjacent parenchyma.
- Very hyperechoic: More hyperechoic than strap muscles.
- Assign 1 point if echogenicity cannot be determined.

**SHAPE**
- Taller-than-wide: 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.

**MARGIN**
- Lobulated: Protrusions into adjacent tissue.
- Irregular, jagged, speculated, or sharp angles.
- Exophytic/extension: Obvious invasion = malignancy.
- Assign 0 points if margin cannot be determined.

**ECHOCENIC FOCI**
- Large comet-tail artifacts: Valpaped, >1 mm, in cystic components.
- Macrocipifications: Cause acoustic shadowing.
- Peripheral Complete or Incomplete along margin.
- Punctate echogenic foci: May have small comet-tail artifacts.

*Refer to discussion of papillary microcarcinoma for 5-9 mm TR3 nodules.*
Approach to Multinodular Goiter
57 y/o woman with history of Type 2 diabetes, hypertension presents for evaluation of thyroid nodules.

- CT chest performed during evaluation of shortness of breath revealed partially calcified and partially imaged nodule in the left thyroid.
- No family history of thyroid cancer or radiation exposure.
- Denied compression symptoms including change in voice or dysphasia. Had trouble lying flat due to CHF.
- TSH 1.97
U/S 12/2016

- Right lower pole spongiform nodule 1.8 x 1.2 x 1.8 cm
- Right upper pole spongiform nodule 1.5 x 1.3 x 1.6 cm.
- Left lower posterior solid hypoechoic nodule with egg shell calcifications 1.8 x 1.2 x 1.2 cm
- Left lower pole solid isoechoic vaguely delineated 2.1 x 0.9 x 1.3 cm
- Isthmic solid hypoechoic nodule 1.5 x 1.0 x 1.2 cm
- All wider than tall, no ETE, no other calcifications other than noted, smooth, well defined borders (if not otherwise noted)
ATA Criteria/TIRADS

- Right sided nodules spongiform, low suspicion ATA / TIRADS 1
- Larger left sided nodule solid, hypoechoic, with rim calcifications → high suspicion ATA / TIRADS 5
- Other left nodule and isthmus nodule, intermediate suspicion ATA / TIRADS 4 based on echogenicity and vague delineation
What about multiple nodules?

- ATA recommends risk evaluation of each nodule and biopsy accordingly
- AACE and TI-RADS biopsy of no more than 2 nodules at a time
Providence Portland Approach

- Biopsy cutoff 1cm even for highly suspicious nodules
- TI-RADS will now be reported but will also include description of nodules
- Biopsy of no more than 2 nodules at a time

→ She had FNA of both left sided nodules and both benign
Interpreting the pathology report:

**Table 8. The Bethesda System for Reporting Thyroid Cytopathology: Diagnostic Categories and Risk of Malignancy**

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

\(^a\)As reported in The Bethesda System by Cibas and Ali (1076).

\(^b\)Based 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.
Annual 2016 TBS Diagnostic % Rates

- pos VI, 5.6
- susp V, 1.3
- atyp (FN/SFN) IV, 2.9
- incon (AUS/FLUS) III, 7.8
- neg II, 78.7
- non-dx I, 3.6
- TBS
Interpreting the pathology report:

Nodule Follow Up - Providence Portland Approach:

- Nodules not undergoing FNA
  - Annual follow up for 5 years
    - No growth - stop at 5 years
    - > 50% growth in volume or development of suspicious features → FNA
- Nodules with benign FNA
  - Repeat U/S 1, 3 and 5 years if no significant change
  - If new symptoms, significant change or > 50% growth → FNA
  - 2 benign FNA, no further follow up required
Interpreting the pathology report:

Non-diagnostic

• Repeat FNA
• Consider surgery if high suspicion U/S pattern, > 20% growth in two dimensions, > 50% increase in volume, or other risk factors for malignancy

Interpreting the pathology report:

55 y/o woman with history of multiple sclerosis presenting for evaluation of thyroid nodule.

- Nodule palpated on exam by PCP
- No additional risk factors for thyroid malignancy (family history, radiation exposure, hoarseness, dysphasia)
- TSH 1.8
Ultrasound:
1.1 x 1.0 x 1.0 cm solid hypoechoic nodule with peripheral vascularity but otherwise without concerning features. → TIRADS 4

FNA → FLUS

... now what?
Interpreting the pathology report:

<table>
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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.
Tools to further classify risks for AUS/FLUS

- Repeat FNA
- Second pathology opinion
- U/S characteristics
- Close follow up with repeat U/S
- Molecular testing

Indeterminate pathology – Role of molecular testing

• “It is important to note that long-term outcome data on companion use of molecular marker status to guide therapeutic decision-making is currently lacking, and therefore we do not know if implementation of molecular marker use in routine clinical practice would result in a significant overall benefit in health outcomes in patients with thyroid nodules”

Molecular Testing Basics

• Rule in Test: 7 panel Gene Mutation (BRAF, RAS, RET/PTC, PAX8/PPARc)
• Rule Out Test: Afrima GEC (167 genes)

Rule in Test: 7 Panel Gene Mutations

• Specificity 86-100%
• PPV 84-100%
• Sensitivity 44-100%
• This test was often used to inform surgical planning → with positive test leading to total thyroidectomy versus possible lobectomy

Rule Out Test: 167 GEC

• Sensitivity 92%
• NPV 93%
• Specificity 48-53% → Not good for ruling in malignancy
• Limitations:
  – Negative result has led to conservative follow up without surgery in many cases and therefore long term data limited.
  – Long term follow up is limited to 8.5 months.

Our patient...

- Elected for close U/S follow up
- U/S at 6 months with 40% interval volume increase
- U/S at 12 months with 70% interval volume increase but no other changes in the appearance of the nodule. Still very reluctant to proceed to surgery and overall size of nodule < 1.5 cm.
Afirma: GEC

RESULT DETAILS

NODULE A

- Size: 1.1 cm  Location: Upper Left
- Cytopathology Diagnosis: Indeterminate - Follicular Neoplasm (FN - Bethesda Category IV)
- Diagnostic Comments: These features are best categorized as suspicious for follicular neoplasm.

Microscopic Description:
The cytologic and cell block preparations are mildly to moderately cellular, with numerous microfollicles, trabecular arrangements and some macrofollicles; follicular cells are enlarged and crowded and there is relatively little colloid present.

Afirma GEC Result: Suspicious
Afirma MTC Result: Negative
Afirma MTC Comments: A gene expression signature for medullary thyroid carcinoma (MTC) was not identified. A negative Afirma MTC result does not significantly change the risk of malignancy (ROM) of the Afirma GEC Suspicious result.

BACKGROUND INFORMATION FOR InterPRETING AFIRMA RESULTS

<table>
<thead>
<tr>
<th>CYTOPATHOLOGY DIAGNOSIS</th>
<th>Non-Diagnostic</th>
<th>Benign</th>
<th>Indeterminate</th>
<th>Suspicious for Malignancy</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afirma Gene Expression Classifier Results</td>
<td>Asymptomatically GEC Benign (ROM &lt;5%)</td>
<td>GEC Suspicious (ROM ~40%)</td>
<td>MTC BRAF</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What about other indeterminate scores:

- Follicular neoplasm/suspicious for follicular neoplasm:
  - Diagnostic surgical excision is favored
  - Studies looking at utility of molecular testing are ongoing but again no perfect test to rule in or out. Recent studies suggest GEC with NPV of 75-94%

- Suspicious for malignancy:
  - Surgery recommended
  - Can consider BRAF or 7 gene mutation panel if this will change surgical management
Is Surgery Necessary with PTC?

- MicroPTC (< 1 cm) present in up to 5-10% of people on autopsy studies (which would indicate 16 million people should be diagnosed in US)
  - Prevalence in US 0.5 million → < 3% of these cases are diagnosed
  - Most subclinical PTC do not progress or do so very slowly
- 2015 ATA Guidelines
  - Advise against biopsy of nodules < 1 cm
  - Acknowledge that active surveillance may be an appropriate alternative to surgery in patients with low risk microPTC

Oda et al. 2016. Thyroid 26;150-155.
FIG. 1. Flow of the management and oncological outcomes of 2153 patients with low-risk papillary microcarcinoma (PMC). Of the observation group, 94 patients underwent surgery for various reasons. Rec: recurrence; DOO, died of other causes unrelated to thyroid cancer.
Table 1. Clinical Characteristics of Low-Risk PMC Patients Who Chose Active Surveillance and Those Who Chose Immediate Surgery

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Active surveillance</th>
<th>Immediate surgery</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>142/1037</td>
<td>117/857</td>
<td>n.s.</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 (15–88)</td>
<td>55 (15–84)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Tumor size (mm)</td>
<td>7 (2–10)</td>
<td>8 (3–10)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Study period (months)</td>
<td>47 (12–116)</td>
<td>47 (12–116)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Multiplicity</td>
<td>71/1179 (6.0%)</td>
<td>132/974 (13.6%)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>51/1179 (4.3%)</td>
<td>30/974 (3.1%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>TgAb (+) or TPOAb (+)</td>
<td>363/1179 (30.8%)</td>
<td>260/974 (26.7%)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Familial history: yes</td>
<td>36/1179 (3.1%)</td>
<td>34/974 (3.5%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Benign thyroid nodule (&gt;20 mm): yes</td>
<td>200/1179 (17.0%)</td>
<td>174/974 (17.9%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

aMedian value (range).
PMC, papillary microcarcinoma; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies; n.s., not significant.
### Table 2. Unfavorable Events Following Active Surveillance and Immediate Surgery

<table>
<thead>
<tr>
<th>Unfavorable events</th>
<th>Active surveillance, 1179 pts</th>
<th>Immediate surgery, 974 pts</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Later surgery (pts)</td>
<td>94</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Temporary VCP (%)</td>
<td>7 (0.6%)</td>
<td>40 (4.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Permanent VCP (%)</td>
<td>0 (0%)</td>
<td>2 (0.2%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Temporary Hypo-PT (%)</td>
<td>33 (2.8%)</td>
<td>163 (16.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Permanent Hypo-PT (%)</td>
<td>1 (0.08%)</td>
<td>16 (1.6%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>On L-thyroxine (%)</td>
<td>244 (20.7%)</td>
<td>644 (66.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Postsurgical hematoma (%)</td>
<td>0 (0%)</td>
<td>5 (0.5%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Postsurgical abscess (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Surgical scar (%)</td>
<td>94 (8.0%)</td>
<td>974 (100%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Recurrence in neck (pts)</td>
<td>1</td>
<td>5</td>
<td>n.s.</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3 (0.3%)</td>
<td>5 (0.5%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

VCP and Hypo-PT in the active surveillance group occurred in patients who converted to surgery later for various reasons, except for one patient who developed idiopathic Hypo-PT and another who developed transient idiopathic VCP contralateral to the microcarcinoma. All deaths in the present series were due to causes unrelated to thyroid cancer.

VCP, vocal cord paralysis; Hypo-PT, hypoparathyroidism.
<table>
<thead>
<tr>
<th>Candidates for observation</th>
<th>Tumor/neck US characteristics</th>
<th>Patient characteristics</th>
<th>Medical team characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal</td>
<td>• Solitary thyroid nodule</td>
<td>• Older patients (&gt;60 years)</td>
<td>• Experienced multidisciplinary management team</td>
</tr>
<tr>
<td></td>
<td>• Well-defined margins</td>
<td>• Willing to accept an active surveillance approach</td>
<td>• High-quality neck ultrasonography</td>
</tr>
<tr>
<td></td>
<td>• Surrounded by ≥2 mm normal thyroid parenchyma</td>
<td>• Understands that a surgical intervention may be necessary in the future</td>
<td>• Prospective data collection</td>
</tr>
<tr>
<td></td>
<td>• No evidence of extrathyroidal extension</td>
<td>• Expected to be compliant with follow-up plans</td>
<td>• Tracking/reminder program to ensure proper follow-up</td>
</tr>
<tr>
<td></td>
<td>• Previous US documenting stability</td>
<td>• Supportive significant others (including other members of their healthcare team)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• cN0</td>
<td>• Life-threatening comorbidities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• cM0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appropriate</td>
<td>• Multifocal papillary microcarcinomas</td>
<td>• Middle-aged patients (18–59 years)</td>
<td>• Experienced endocrinologist or thyroid surgeon</td>
</tr>
<tr>
<td></td>
<td>• Subcapsular locations not adjacent to RLN without evidence of extrathyroidal extension</td>
<td>• Strong family history of papillary thyroid cancer</td>
<td>• Neck ultrasonography routinely available</td>
</tr>
<tr>
<td></td>
<td>• Ill-defined margins</td>
<td>• Child bearing potential</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Background ultrasonographic findings that will make follow-up difficult (thyroiditis, nonspecific lymphadenopathy, multiple other benign-appearing thyroid nodules)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• FDG-avid papillary microcarcinomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate</td>
<td>• Evidence of aggressive cytology on FNA (rare)</td>
<td>• Young patients (&lt;18 years)</td>
<td>• Reliable neck ultrasonography not available</td>
</tr>
<tr>
<td></td>
<td>• Subcapsular locations adjacent to RLN</td>
<td>• Unlikely to be compliant with follow-up plans</td>
<td>• Little experience with thyroid cancer management</td>
</tr>
<tr>
<td></td>
<td>• Evidence of extrathyroidal extension</td>
<td>• Not willing to accept an observation approach</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Clinical evidence of invasion of RLN or trachea (rare)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• N1 disease at initial evaluation or identified during follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• M1 disease (rare)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Documented increase in size of ≥3 mm in a confirmed papillary thyroid cancer tumor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

US, ultrasound; RLN, recurrent laryngeal nerve; FDG, fluorodeoxyglucose; FNA, fine-needle aspiration.
Summary

• Start with TSH
  – If low, refer to endocrinology
  – Normal or high → U/S
• Ask about radiation exposure, compressive symptoms, and family history.
• Multinodular goiter → biopsy 2 most suspicious nodules
• No FNA → Monitor annual U/S x 5 years
• Benign pathology → Repeat U/S in 1, 3, and 5 years
  – Refer if >20% growth or new suspicious characteristics
• Suspicious for malignancy or + for cancer → refer to ENT
• Indeterminate pathology → Refer to endocrinology or ENT for further management and benefits and limitations of molecular testing
• Active surveillance may be more common in years to come
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