Evaluation and Management of the Thyroid Nodule

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“Thyroid? Big deal--you’ve got one test (TSH), and one pill (L-T4)”

Jon Singer

Thyroid Nodule Facts in the U.S.

- Prevalence (of palpable lesions) 5% = ~10,000,000
- Incidence 0.1% = ~300,000 new palpable nodules per year
- Nodules on ultrasound 40% = ~112,000,000
- Prevalence of cancer in nodules 5% = ~560,000
- Incidence of cancer 0.004% = ~34,000 new cases per year

“Oh, I get it, the TSH goes up and down”
Thyroid Nodules

Types of Thyroid Nodules

Benign (90+ %)
- Colloid, hyperplastic
- Hashimoto's
- Cysts
- Follicular adenoma
- Hurthle cell lesion

Malignant (< 10%)
- Papillary cancer
- Follicular cancer
- Medullary cancer
- Anaplastic cancer
- Thyroid lymphoma
- Metastatic

60 Year Old Man with Thyroid Nodule

History: Healthy man noticed non-tender swelling right side of neck while shaving. Feels mild increase in pressure with swallowing for the past 6 months; no change in voice; no XRT or FH thyroid ca.  Symptomatically euthyroid.  PMH: HTN

Exam: 4 cm oblong, firm, mobile right thyroid nodule.

What is the likelihood of Ca?
Degree of Clinical Concern for Carcinoma in a Thyroid Nodule Based on History and Physical Exam

**Less Concern**
- Chronic stable exam
- Evidence of a functional disorder (eg. Hashimoto's toxic nodule)
- Multinodular gland without dominant nodule?

**More Concern**
- Age <20, >60 years
- Males
- Rapid growth, pain
- History of radiation therapy
- Family history thyroid ca
- Hard, fixed lesion
- Lymphadenopathy
- Vocal cord paralysis
- Size > 4 cm
- Tracheo-esophageal pressure (eg. stridor, dysphagia)

Cancer Risk in Solitary or Multiple Thyroid Nodules

<table>
<thead>
<tr>
<th>Study (yr, location)</th>
<th>Individuals (no.)</th>
<th>Definition of nodularity</th>
<th>FNA technique</th>
<th>Cancer rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCall et al (1986 U.S.)</td>
<td>442</td>
<td>Scan/Hx</td>
<td>Palpation</td>
<td>17</td>
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<tr>
<td>Sachmechi et al (2000 U.S.)</td>
<td>443</td>
<td>Scan</td>
<td>Palpation</td>
<td>8</td>
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<tr>
<td>Papini et al (2002 Italy)</td>
<td>494</td>
<td>US</td>
<td>US</td>
<td>9</td>
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<tr>
<td>Deandrea et al (2002 Italy)</td>
<td>420</td>
<td>US</td>
<td>US</td>
<td>6</td>
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</tbody>
</table>

60 year old man with nodule—workup?

- Blood tests?
  - TSH—2.6 miu/ml
  - TPO—not done
  - Tg—not indicated
- Imaging?
  - Nuclear scan?
  - US?

EVALUATION OF THE THYROID NODULE – THE EXPERTS OPINIONS

*ATA Membership Survey

| Technique | (%)
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>FNAB</td>
<td>96</td>
</tr>
<tr>
<td>Scan</td>
<td>56</td>
</tr>
<tr>
<td>US</td>
<td>28</td>
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<tr>
<td>TSH</td>
<td>93</td>
</tr>
<tr>
<td>Antibodies</td>
<td>31</td>
</tr>
<tr>
<td>Tg</td>
<td>14</td>
</tr>
<tr>
<td>CBC</td>
<td>12</td>
</tr>
<tr>
<td>Chem Panel</td>
<td>10</td>
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</table>

**ATA Standards of Care Committee

<table>
<thead>
<tr>
<th>Committee</th>
<th>It all depends</th>
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<tbody>
<tr>
<td>Yes</td>
<td>It all depends</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Not mentioned</td>
<td>Not mentioned</td>
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</table>

### IMAGING OF THE THYROID NODULE – THE EXPERTS OPINIONS (%)

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Scan</strong></td>
<td>56</td>
<td>23</td>
<td>66</td>
<td>prn</td>
</tr>
<tr>
<td><strong>US</strong></td>
<td>28</td>
<td>34</td>
<td>80</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Scan + US</strong></td>
<td>--</td>
<td>13</td>
<td>58</td>
<td>--</td>
</tr>
</tbody>
</table>

JCEM 81:333, 1996  
JCEM 85:2493, 2000  
Thyroid 18: 2006

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**Adenomatous goiter**
Advantages of Ultrasound in Evaluation of Nodules

- Delineates lesion with unclear findings on palpation
- Detects nonpalpable lesions (esp with XRT)
- More accurate follow-up
- More accurate FNA, esp with cystic lesions

US Characteristics of Thyroid Nodules

- Echogenicity (hypo*, hyper-, iso-)
- Calcifications (micro*, dense, eggshell-89)
- Margins (infiltrative, spiculated, irregular*, well-defined)
- Halo (absent*, irregular*, present and regular)
- Colloid (comet tails)
- Vascularity (intranodular*, peripheral, absent, spoke and wheel)
- Shape (taller than wide*)

*associated with thyroid cancer

Ajuga et al, JCU 1996;24:139

Papillary CA
Spoke & Wheel = Follicular Lesion?

60 Year Old Man with Thyroid Nodule

FNA (by palpation) done

FNA Classification and Results

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Results (%)</th>
<th>Probability of malignancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign (negative)</td>
<td>65</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Malignant (positive)</td>
<td>5</td>
<td>&gt;99</td>
</tr>
<tr>
<td>Nondiagnostic (unsatisfactory)</td>
<td>20</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Suspicious (indeterminate)</td>
<td>10</td>
<td>20</td>
</tr>
</tbody>
</table>

Probability of malignancy (%)

- <1
- >99
- <3
- 20

Gharib H and Papini E: Endocrinol Metabol Clin N Am, 2007

FNAB Imperatives

- Must have adequate material—if inadequate, repeat.
- Must have experienced cytopathologist
- Examine all of your slides with the cytopathologist!
Nondiagnostic Rates of Palpation FNA and US FNA

<table>
<thead>
<tr>
<th></th>
<th>Palpation FNA</th>
<th>USGFNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takashima, 1994</td>
<td>19% (12/62)</td>
<td>4% (10/256)</td>
</tr>
<tr>
<td>Carmeci, 1998</td>
<td>16% (60/370)</td>
<td>7% (9/127)</td>
</tr>
<tr>
<td>Danese, 1998</td>
<td>9% (433/4986)</td>
<td>4% (167/4697)</td>
</tr>
<tr>
<td>Hatada, 1998</td>
<td>30% (28/94)</td>
<td>17% (12/72)</td>
</tr>
</tbody>
</table>


60 year old man with thyroid nodule

FNA result—follicular lesion—now what’s the likelihood of Ca?
60 year old man with thyroid nodule

- So, what do you advise?—lobectomy? “total” tdx?

60 Year Old Man with Thyroid Nodule

- Because of high degree of suspicion of Ca, total thyroidectomy recommended.
- He opted for lobectomy
- Right lobectomy = minimally invasive follicular CA; foci of papillary CA
60 year old man with thyroid nodule

- Now what?
- Completion surgery—no tumor

What About The Thyroid Incidentaloma?

- PTC found in 7/119 (6%) of USG FNA for incidentally detected lesions > 1 cm (Hagag, et al. Thyroid 1998; 8:989)
- PTC in 23/450 (5%) of non-palpable nodules, most <1.5 cm. Non-diagnostic FNA in 30% of lesions <1 cm (Leenhardt, et al. J Clin Endocrinol Metab 1999; 84:24)
- 162 pts with PTC dx by USG FNA; avg nodule size 6.9 mm; half had f/u for 3-4 yrs -70 % stable or reduced in size -1.2 % developed LN mets (Ito, et al. Thyroid 2003; 13:381)
Proposed 2008 ATA Guidelines for FNA

- <1 cm: high risk Hx, or abnormal Cx nodes
- >1 cm: hypoechoic and solid, or microCa++
- 1.5-2 cm: solid and iso/hyperechoic
- >2 cm: predominantly cystic or spongiform without suspicious US findings
- Pure cystic: not indicated
- Spongiform nodule: may defer
- Multiple nodules:
  - Prioritize based on above
  - If multiple similar on US, coalescent nodules w/o suspicious US features, FNA the largest.

Here’s What’s New--Is Serum TSH a Predictor for Malignancy?

- Prospective study (1984-2002) of 1500 pts (1304 female, 196 male, mean age 47.8 yrs) with thyroid enlargement, evaluated with TSH, FNAB, histology.
- Clinical exam: diffuse goiter (12 %), single nodule (57 %), MNG (31 %).
- Open bx or surgery (for FNA malignant, suspicious, or obstructive sxs) in 553 pts (37 %).

Risk Factors for Malignancy

- Sensitivity and specificity of FNA to predict malignancy 88 % and 84 %.
- Independent risk factors were younger and older age, males, and solitary nodules by palpation.
- Risk for malignancy higher with baseline TSH (> 0.9 mU/L)

Serum TSH - a new risk factor for thyroid cancer in nodule

- Prevalence (%) of malignancy
- * p < 0.05
- ** p < 0.01
- *** P < 0.001
Finally, when are US and FNA not indicated?
OK, I get it now—can we discuss $$?