A Human Intelligence “HI” Approach to Incidental Thyroid Nodules: JACR White Paper Algorithm is About More Than Nodule Size and Patient Age
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- No conflicts to disclose
Background - Thyroid Nodules:

- **Incidental thyroid nodule (ITN)** – nodule detected on study not done to assess thyroid

- **ITN pose challenges for radiologists**

- **Thyroid nodules (TN) - extremely common**
  - At least one nodule in half of people over 50 years old
  - Nodules found in up to 25% CT scans and 67% thyroid ultrasounds

- **Thyroid cancer - largely indolent** –
  - 20-year survival rate of 97%
  - > 85% of all thyroid cancers are papillary thyroid cancer (PTC)
  - Early detection of PTC has not been shown to impact survival

- **0.5% death rate has not increased despite ~3 fold increase in thyroid cancer**

1. Nguyen et al. 2013. ANJR
3. Ito et al World Journal Surgery 2018
4. USPSTF Recommendation Statement JAMA 2017
ACR white paper algorithm for managing ITN aims to provide practical approach to ITN and reduce unnecessary thyroid nodule workup

Project:
- Initial aim: Determine if algorithm is effective in triaging nodules to thyroid ultrasound when focus limited to nodule size and patient age
- Secondary aim: Determine impact of following all algorithm steps compared with focus on nodule size and patient age
Methods: Retrospective Review:

- 245 consecutive patients who underwent biopsy of ITN detected on prior CT or MR (2012-2016)
- **Assess thyroid cancer rate by:**
  - **1st phase** categories
    - total cohort
    - nodule size
    - patient age
  - **2nd phase:** sub-categories
    - Clinical findings/risk factors for thyroid cancer
    - Comorbidities/NTM which may limit life expectancy- primarily collected NTM
    - Low-risk ITN have neither of above
FIRST PHASE Analysis Based on White Paper Algorithm

Final Steps: Patient Age and Nodule Size –

- Suspicious CT or MRI findings
  - Limited life expectancy and comorbidities
  - Evaluate with thyroid ultrasound
  - No further evaluation
- No suspicious CT or MRI findings
  - General population
  - Age <35 years
    - <1 cm: No further evaluation
    - >1 cm: Evaluate with thyroid ultrasound
  - Age ≥35 years
    - <1.5 cm: No further evaluation
    - ≥1.5 cm: Evaluate with thyroid ultrasound

Hoang, J. et al. 2015. JACR
SECOND PHASE Analysis Based on White Paper Algorithm

Early steps: Ensure Proper Patient Selection

Patients with clinical findings or risk factors for thyroid cancer—
not eligible

Patients with extrathyroidal extension or cervical LN—
not eligible

Patients with severe comorbidities/NTM with limited life expectancy will not benefit from further evaluation—
not eligible

Incidental Thyroid Nodule Detected on CT or MRI

Suspicious CT or MRI findings

Limited life expectancy and comorbidities

No suspicious CT or MRI findings

General population

Follow age and nodule size algorithm

Hoang, J. et al. 2015. JACR
Human Intelligence “HI” Approach to ITN
Before Recommending Thyroid Ultrasound Consider the Following:

<table>
<thead>
<tr>
<th>PATIENT CENTERED</th>
<th>RADIOLOGIST CENTERED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs or symptoms concerning for thyroid cancer</td>
<td>Clinical risk factors for thyroid cancer</td>
</tr>
<tr>
<td>Palpable or enlarging lump</td>
<td>Family history of thyroid cancer</td>
</tr>
<tr>
<td>Enlarged cervical LN</td>
<td>Radiation exposure to neck</td>
</tr>
<tr>
<td>Persistent hoarseness or voice change</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Inherited conditions, eg MEN</td>
</tr>
<tr>
<td>Dysphagia</td>
<td></td>
</tr>
<tr>
<td>Pain neck/jaw/ear</td>
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</tbody>
</table>
Results: Cohort Patient Profile

- 238 after 7 patients excluded*

**Phase 1:**
- Age: 97% patients 35 and older
- Size: 30% patients under size threshold

**Phase 2:**
- 70% of patients low-risk ITN
- 30% not eligible for algorithm

* suspicious findings- cervical lymph nodes- on CT/MR
Results: Total Number of Thyroid Cancers by Categories and Subcategories of Algorithm

### Categorization by SIZE

- **1st phase: size only**
  - Low Risk ITN: 5
  - Clinical/Risk Factors: 2
  - Comorbidities: 1

- **1st phase: age only**
  - Low Risk ITN: 3
  - Clinical/Risk Factors: 2
  - Comorbidities: 1

### Categorization by AGE

- **Over 35yo**
  - Below size threshold: 1
  - Above size threshold: 9

- **Over 35yo**
  - Below size threshold: 6
  - Above size threshold: 1
Results: White Paper size threshold is effective when follow all steps of algorithm

- NO thyroid cancers detected in low-risk ITN below size threshold (24% of cohort)
- All sizes of low-risk ITN - 70% of cohort but only 10% of thyroid cancers
- Only 2 (0.6%) of 165 patients with low-risk ITN had PTC

Compare biopsy yield of thyroid cancers vs breast cancer
Thyroid cancer: 0.6 per 100 biopsies
Breast cancer: 20 – 35 per 100 biopsies
Conclusions:

• **Decision to proceed to thyroid US for ITN is an important check point**

• 220 patients (92%) of patients benign* after diagnostic work-up

• 19 (8%) had thyroid cancer

• 2 (~1%) of low-risk ITN had PTC when apply full algorithm

• None were under size threshold

*Includes benign and lost to follow up
Diagnostic cascade and steps to avoid it:

• **Diagnostic cascade may lead to low-yield overdiagnosis**

• **DO NOT recommend thyroid ultrasound in patients with:**
  - Low-risk ITN under the size threshold
  - Metastatic cancers
  - Too sick to undergo biopsy or thyroidectomy
  - Severe comorbidities which limit life expectancy
  - Possibly in patients with low-risk ITN over size threshold

**Diagnostic Cascade**

1. ITN Detection
2. Thyroid US
3. Biopsy
   - If inconclusive: repeat biopsy and molecular imaging
4. Thyroidectomy

**Alternate Cascade**

1. ITN Detection
2. Avoid Thyroid US
3. Avoid Biopsy
4. Avoid repeat biopsy
5. Avoid Thyroidectomy
6. Spared anxiety and financial sequelae
Take Home: Algorithm is Effective When Apply **ALL** Steps, Not Just Nodule Size and Patient Age

<table>
<thead>
<tr>
<th>What to do when you have NO clinical information regarding patient with ITN</th>
</tr>
</thead>
</table>
| • Include in report impression-  
  • **clinical findings** and/or **risk factors** for thyroid cancer and **comorbidities/NTM** which limit life expectancy should **factor into decision** to ultrasound or not  
  • For example: An incidental thyroid nodule has been detected for which thyroid ultrasound may be considered however these are frequently benign or indolent cancers and diagnostic tests are not always decisive. In the absence of clinical findings or risk factors for thyroid cancer the risk of cancer is small. Further evaluation is not recommended in patients with comorbidities which limit life expectancy or are not surgical candidates as they will not benefit from the results. |
References


• Hoang, J et al. Managing Incidental Thyroid Nodules Detected on Imaging: White Paper of the ACR Incidental Thyroid Findings Committee. JACR. 2015; 12(2):143-150


• UPSTF. Screening for Thyroid Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2017; 217(18):1882-1887