Papillary Thyroid Microcarcinoma

Haruko Akatsu, M.D.
Medical Director, Thyroid Cancer Program
Clinical Associate Professor
Division of Endocrinology, Gerontology and Metabolism
Stanford University

Papillary Thyroid Cancer Management

- Initial treatment
  - Thyroidectomy
  - I-131 ablation
- Surveillance
  - TSH suppression
  - Following Tg
  - Imaging studies
- Subsequent treatment
  - Surgery
  - I-131 ablation
  - XRT
  - Chemo protocol

American Thyroid Association Consensus Report

Initial treatment
- Thyroidectomy
- I-131 ablation

6-12 months follow up
- Neck ultrasound, Tg on TSH suppression
- rhTSH stimulated Tg, neck ultrasound

* Negative

- TgAb negative patients,
  - Tg <1ng/ml with TSH suppression
  - Tg <2ng/ml with TSH stimulation

- Chest CT without contrast
- Surgery
- LT4 withdrawal I-131 Rx

Papillary Thyroid Cancer Management

**WHO Definition:**
- ~2003: Papillary CA ≤1cm
- 2004+: Incidentally found papillary CA ≤1cm

For this talk “microcarcinoma” = “≤1cm papillary CA”

ATA 2009 Guideline RECOMMENDATION 26:
“Lobectomy alone may be sufficient for small <1cm, low-risk, unifocal, intrathyroidal papillary CA with no previous radiation exposure or clinically involved cervical LN”

No consensus or clear guidelines for papillary microcarcinoma management

---

Papillary Microcarcinoma

1. **Epidemiology**
   *Why we cannot ignore microcarcinoma*

2. **Diagnosis of papillary microcarcinoma**
   *Three possibilities*

3. **Management of papillary microcarcinoma**
   *Risk stratification*

4. **Goal of management**
   *Avoid over and under treatment*

---

Papillary Microcarcinoma

1. **Epidemiology**
   *Why we cannot ignore microcarcinoma*

2. **Diagnosis of papillary microcarcinoma**
   *Three possibilities*

3. **Management of papillary microcarcinoma**
   *Risk stratification*

4. **Goal of management**
   *Avoid over and under treatment*

---

Increase in Thyroid Cancer Incidence

The Surveillance, Epidemiology, and End Results Program (SEER)
Increase in Thyroid Cancer Incidence


Increase in Thyroid Cancer Incidence
~International Data~


Increasing Incidence of Papillary CA


Increasing Incidence of Papillary Microcarcinoma

49% of the rising incidence consisted of papillary carcinoma ≤1cm

1. Epidemiology
   *Why we cannot ignore microcarcinoma*

2. Diagnosis of papillary microcarcinoma
   *Three possibilities*

3. Management of papillary microcarcinoma
   *Risk stratification*

4. Goal of management
   *Avoid over and under treatment*

---

**Diagnosis of \( \leq 1\) cm Papillary CA**

- Metastatic disease found first
- Thyroidectomy performed for other reasons
- \( \leq 1\) cm nodule FNA positive or suspicious

**Diagnosis of Papillary Microcarcinoma**
Papillary Microcarcinoma

1. Epidemiology
   Why we cannot ignore microcarcinoma
2. Diagnosis of papillary microcarcinoma
   Three possibilities
3. Management of papillary microcarcinoma
   Risk stratification
4. Goal of management
   Avoid over and under treatment

Diagnosis of ≤1cm Papillary CA

- Metastatic disease found first
- Thyroidectomy performed for other reasons
- ≤1cm nodule FNA positive or suspicious

Diagnosis of Papillary Microcarcinoma

Management of ≤1cm Papillary CA

Metastatic disease found first
Thyroidectomy performed for other reasons
≤1cm nodule FNA positive or suspicious

Same as >1cm papillary management

Management of ≤1cm Papillary CA

Metastatic disease found first
Thyroidectomy performed for other reasons
≤1cm nodule FNA positive or suspicious

Same as >1cm papillary management

Controversial
Persistently Low Mortality

Thyroid Cancer Incidence and Mortality


Management of ≤1cm Papillary CA

Metastatic disease found first

Thyroidectomy performed for other reasons

≤1cm nodule FNA positive or suspicious

Diagnosis of Papillary Microcarcinoma

Risk Stratification

Same as >1cm Papillary

Risk Stratification

High risk

Low risk

Controversial
Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

✓ Age
✓ Lymph node metastases
✓ Multifocality
✓ Capsular invasion
✓ Vascular invasion
✓ BRAF mutation

High risk

Low risk

Risk Stratification

✓ Age
✓ Lymph node metastases
✓ Multifocality
✓ Capsular invasion
✓ Vascular invasion
✓ BRAF mutation

High risk

Low risk

Increased recurrence with young age <45 years


Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

✓ Age
✓ Lymph node metastases
✓ Multifocality
✓ Capsular invasion
✓ Vascular invasion
✓ BRAF mutation

High risk

Low risk

Risk Stratification

✓ Age
✓ Lymph node metastases
✓ Multifocality
✓ Capsular invasion
✓ Vascular invasion
✓ BRAF mutation

High risk

Low risk
Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation

Nodal Status


Nodal Status

Increased recurrence with positive nodes


Near total/total thyroidectomy

No initial distant metastases

~50% nodal removal

~17% RAI

Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation
**Management of ≤1cm Papillary CA**

Diagnosis of Papillary Microcarcinoma

**Risk Stratification**

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation

**Increased recurrence with multifocality**


**Near total/total thyroidectomy**

No initial distant metastases

Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation

High risk

Risk Stratification

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation

High risk

Capsular and Vascular Invasion

<table>
<thead>
<tr>
<th>Cancer-related death, Tg &gt;2, +/-macroscopic disease</th>
<th>N</th>
<th>Yes</th>
<th>No</th>
<th>OR (95% CI)</th>
<th>*p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsular Invasion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>71</td>
<td>69</td>
<td>2</td>
<td>12.7</td>
<td>(2.4-66.2)</td>
</tr>
<tr>
<td>Yes</td>
<td>26</td>
<td>19</td>
<td>7</td>
<td>*p 0.001</td>
<td></td>
</tr>
<tr>
<td>Vascular Invasion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>82</td>
<td>78</td>
<td>4</td>
<td>9.8</td>
<td>(2.2-42.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>10</td>
<td>5</td>
<td>*p 0.004</td>
<td></td>
</tr>
</tbody>
</table>

### BRAF Mutation

<table>
<thead>
<tr>
<th>Papillary &lt;2cm</th>
<th>N</th>
<th>BRAF positive</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>277</td>
<td>46%</td>
<td>0.005</td>
</tr>
<tr>
<td>≥45</td>
<td>299</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>LN metastasis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>34</td>
<td>59%</td>
<td>0.03</td>
</tr>
<tr>
<td>No</td>
<td>544</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>Multifocality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>196</td>
<td>41%</td>
<td>0.6</td>
</tr>
<tr>
<td>No</td>
<td>382</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>Extrathyroidal extension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>98</td>
<td>65%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No</td>
<td>480</td>
<td>34%</td>
<td></td>
</tr>
</tbody>
</table>


### BRAF Mutation

<table>
<thead>
<tr>
<th>Papillary ≤1cm</th>
<th>LN positive</th>
<th>LN negative</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.1±20.8</td>
<td>10.5±16.5</td>
<td>0.39</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>0.7±0.58</td>
<td>0.5±0.33</td>
<td>0.1076</td>
</tr>
<tr>
<td>Extrathyroidal extension</td>
<td>66%</td>
<td>13%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multicentric</td>
<td>21%</td>
<td>10%</td>
<td>0.0739</td>
</tr>
<tr>
<td>BRAF</td>
<td>77%</td>
<td>32%</td>
<td>0.0016</td>
</tr>
</tbody>
</table>

Akatsu-Kuffner, Nikiforov et al. Univ of Pittsburgh

### BRAF Mutation

<table>
<thead>
<tr>
<th>Papillary carcinoma of all sizes N=105</th>
<th>BRAF</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>53%</td>
<td>61%</td>
</tr>
<tr>
<td>≥45</td>
<td>47%</td>
<td>39%</td>
</tr>
<tr>
<td>LN metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>64%</td>
<td>56%</td>
</tr>
<tr>
<td>Yes</td>
<td>36%</td>
<td>44%</td>
</tr>
<tr>
<td>Extrathyroidal invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>45%</td>
<td>52%</td>
</tr>
<tr>
<td>Yes</td>
<td>55%</td>
<td>48%</td>
</tr>
<tr>
<td>Multifocal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40%</td>
<td>42%</td>
</tr>
<tr>
<td>Yes</td>
<td>60%</td>
<td>58%</td>
</tr>
</tbody>
</table>


### Management of ≤1cm Papillary CA

- **Diagnosis of Papillary Microcarcinoma**
  - **Risk Stratification**
    - Age
    - Lymph node metastases
    - Multifocality
    - Capsular invasion
    - Vascular invasion
    - BRAF mutation

High risk
Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

- Age
- Lymph node metastases
- Multifocality
- Capsular invasion
- Vascular invasion
- BRAF mutation

High risk

Low risk

Clinical judgment & patient’s preference

Management of ≤1cm Papillary CA

Diagnosis of Papillary Microcarcinoma

Risk Stratification

- High risk
- Low risk

Same as >1cm Papillary

Conservative

Clinical judgment & patient’s preference
1. Epidemiology
   Why we cannot ignore microcarcinoma
2. Diagnosis of papillary microcarcinoma
   Three possibilities
3. Management of papillary microcarcinoma
   Risk stratification
4. Goal of management
   Avoid over and under treatment

Papillary Thyroid Microcarcinoma
Management Goal

Avoid both over and under treatment!
Papillary Microcarcinoma

1. Epidemiology
   *Why we cannot ignore microcarcinoma*

2. Diagnosis of papillary microcarcinoma
   *Three possibilities*

3. Management of papillary microcarcinoma
   *Risk stratification*

4. Goal of management
   *Avoid over and under treatment*

Papillary Thyroid Microcarcinoma

1. Epidemiology
   *Why we cannot ignore microcarcinoma*

2. Diagnosis of papillary microcarcinoma

3. Management of papillary microcarcinoma
   *[Thank you for your attention!]*

4. Goal of management
   *Avoid over and under treatment*