Is immediate surgery always necessary for low risk differentiated thyroid cancer?

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Disclosures
No relevant conflicts of interest

Overview
When to operate, when to watch

Active Surveillance for Low Risk Papillary Thyroid Cancer

Minimalist Surgical Options for Low Risk Papillary Thyroid Cancer

Emphasis on Proper Patient Selection, Shared Decision Making, and Development of a Unified Management Philosophy

Management Philosophies in Low Risk Thyroid Cancer

Don't just do something, STAND THERE!

Typical Case

82 year old man
Avoided health care for more than 50 years
Wife insisted on a carotid US for screening
Incidental thyroid nodule detected
Thyroid US confirms a single 5 mm thyroid nodule
FNA confirms papillary thyroid cancer

What now?

Surgery Vs Observation

Typical Case

65 year old man
Diabetes, HTN, A fib
Metastatic colon cancer to lung, liver and bone
Thyroid US confirms a single 5 mm thyroid nodule
FNA confirms papillary thyroid cancer

What now?

Surgery Vs Observation
**Typical Case**

- 25 year old female
- Getting married in 3 months
- Does not want a scar on her neck before the wedding
- After wedding wants to wait another 3 months to go on her honeymoon
- After honeymoon, wants to wait another 3 months because of new job

**Thyroid US confirms a single 5 mm thyroid nodule**

**FNA confirms papillary thyroid cancer**

**What now?**

- Surgery
- Observation

**Framing the Issue**

- Active surveillance (deferred intervention)
  - Active observation approach
  - Medication delayed has no clinically significant impact
  - Therapy, when indicated, still effective
  - Not palliative care/watchful waiting (non-curative)

- Classic examples
  - Small volume prostate cancer
  - Urethral cancer
  - Some lymphomas

**Observational Management Approach to Papillary Microcarcinoma**

- 2,153 Low Risk Papillary Microcarcinoma Patients
- Active Surveillance 1,179 (55%)
- Immediate Surgery 974 (45%)
- Continued Observation 1,085 (92%)

**2015 ATA Guidelines**

A cytology diagnostic for a primary thyroid malignancy will almost always lead to thyroid surgery. However, an active surveillance management approach can be considered as an alternative to immediate surgery in:

(a) patients with very low risk tumors (e.g. papillary microcarcinomas without clinically evident metastases or local invasion, and no convincing cytologic evidence of aggressive disease),

(b) patients at high surgical risk because of co-morbid conditions,

(c) patients expected to have a relatively short life span (e.g. serious cardiopulmonary disease, other malignancies, very advanced age), or

(d) patients with concurrent medical or surgical issues that need to be addressed prior to thyroid surgery.

**Tumor Progression During Active Surveillance**

<table>
<thead>
<tr>
<th>n</th>
<th>Tumor size</th>
<th>Follow-Up</th>
<th>Increase ≤ 3 mm</th>
<th>Stable ± 3 mm</th>
<th>Decrease ≥ 3 mm</th>
<th>LN Mets</th>
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</thead>
<tbody>
<tr>
<td>USA</td>
<td>291</td>
<td>≤ 1.5 cm</td>
<td>2 yrs</td>
<td>4%</td>
<td>92%</td>
<td>4%</td>
</tr>
<tr>
<td>Korea</td>
<td>192</td>
<td>≤ 1 cm</td>
<td>2.5 yrs</td>
<td>2%</td>
<td>95%</td>
<td>3%</td>
</tr>
<tr>
<td>Korea</td>
<td>370</td>
<td>≤ 1 cm</td>
<td>2 yrs</td>
<td>4%</td>
<td>96%</td>
<td>-</td>
</tr>
<tr>
<td>Japan</td>
<td>1.23</td>
<td>≤ 1 cm</td>
<td>5 yrs</td>
<td>9%</td>
<td>95%</td>
<td>-</td>
</tr>
<tr>
<td>Japan</td>
<td>415</td>
<td>≤ 1 cm</td>
<td>10 yrs</td>
<td>8%</td>
<td>92%</td>
<td>-</td>
</tr>
<tr>
<td>Japan</td>
<td>1</td>
<td>1-2 cm</td>
<td>6.5 yrs</td>
<td>6%</td>
<td>91%</td>
<td>3%</td>
</tr>
<tr>
<td>Japan</td>
<td>61</td>
<td>≤ 1 cm</td>
<td>7 yrs</td>
<td>7%</td>
<td>93%</td>
<td>-</td>
</tr>
<tr>
<td>Japan</td>
<td>360</td>
<td>≤ 1 cm</td>
<td>7 yrs</td>
<td>8%</td>
<td>92%</td>
<td>-</td>
</tr>
<tr>
<td>Japan</td>
<td>57</td>
<td>≤ 1.5 cm</td>
<td>1 yr</td>
<td>4%</td>
<td>96%</td>
<td>-</td>
</tr>
</tbody>
</table>

**Thyroid cancers are three dimensional structures**

- Usually ellipsoid (not spherical)

**Thyroid Volume:** \( \frac{\pi}{6} (\text{length} \times \text{width} \times \text{height}) \)

- 40 yr old male, PMC
- 1.03 x 0.64 x 0.93 cm
Active Surveillance of Low Risk Papillary Thyroid Cancer

Demonstrate remarkably consistent classic exponential growth curves

Tuttle et al, JAMA Otolaryngology–Head & Neck Surgery, 2017

40 yr old female
Papillary Microcarcinoma
4 yrs of active surveillance

Tuttle et al, JAMA Otolaryngology–Head & Neck Surgery, 2017

42 yr old female
Papillary Microcarcinoma
5 yrs of active surveillance

Tuttle et al, JAMA Otolaryngology–Head & Neck Surgery, 2017

Kuma Hospital [http://www.kuma-h.or.jp/index.php?id=293]
Tuttle et al, JAMA Otolaryngology–Head & Neck Surgery, 2017

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Indications for Transition from Active Surveillance to Surgical Intervention

- Increase in size of primary tumor
  - ≥ 3 mm increase in tumor diameter and/or
  - ≥ 100% increase in tumor volume
  - Identification of metastatic disease
  - Direct invasion into surrounding structures
  - Patient preference

- Surgical intervention can be considered with a confirmed 50% increase in tumor volume based on factors such as (i) proximity of the tumor to the thyroid capsule, (ii) patient preference, or (iii) primary tumor size > 1 cm.

- Conversely, even with documented increase in the size of the primary tumor by diameter or volume, surgery may be deferred in patients without other indications for intervention if they have (i) a maximum tumor diameter of < 15 mm, and/or (ii) a tumor volume doubling time > 2 years.

Tuttle/Miyauchi 2019, in Surgery of the Thyroid and Parathyroid glands, 3rd Edition, Greg Randolph, ed
Key Factors in Clinical Decision Making

Active Surveillance of Known or Suspected Thyroid Cancer

- Tumor Size (Tumor Volume)
- Doubling Time (Rate of Change)
- Location
- Patient Preference

Implementing Active Surveillance in the US

Requires concurrent evaluation of three inter-related domains

- Tumor/US Characteristics
- Medical Team Characteristics
- Patient Characteristics

Proper Patient Selection

- Inappropriate
- Appropriate

Intrathyroidal PTC
- Bethesda VI
- Bethesda V with highly suspicious US
- US highly suspicious adenopathy US without FNA
- BRAF V600E mutated Bethesda III/IV/V/VI

Cytology interpretation and US examination at MSKCC
- Primary tumor up to ≈1.5 cm

Acceptable Features
- Background thyroid abnormalities (Hashimoto’s, MNG)
- BRAF V600E mutation (genetic testing not required)
- Documented increase in size
- LN metastases
- Extrathyroidal extension
- Subcapsular location adjacent to trachea/RLN

Relationship of Nodule to Thyroid Capsule

Ideal: normal thyroid tissue surrounding the PMC

Inappropriate

Appropriate

Nodule Abuts the Thyroid Capsule But Not Invasive

Anterior Capsule

Posterior Capsule

67 yr old female, right anterior superior pole, 8x7x9mm, definite anterior extrathyroidal extension, confirmed by histology (7mm TCV PTC, minor ETE)
**Relationship of Nodule to Thyroid Capsule**

*Isthmus Nodules Rarely Appropriate*

*Usually Touch the Anterior and Posterior Thyroid Capsule*

- Nodule: 0.5 x 0.6 cm
  - Isthmus: 0.3 cm wide
- Nodule: 0.4 x 0.3 cm
  - Isthmus: 0.5 cm wide

**Course of the Recurrent Laryngeal Nerves Relative to the Intact Thyroid Gland**

- Left Lower Medial Pole Nodule (13x10x11mm)
- Posterior Right Lobe Nodule (6x8x6mm)
- Posterior Right Lobe Nodule (7x6x7mm)
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Multidisciplinary Management Team
Shared Treatment Philosophy
Quality Ultrasonography
Prospective Data Collection
Tracking System

Motivated
Compliant
Supportive Family/Clinicians
Differences in Patient Decision Making

How do patients perceive initial treatment options?

SURGERY
ACTIVE SURVEILLANCE

Sense of urgency
Perception as potentially life-threatening disease
Fear of disease progression & uncertainty with active surveillance
Surgery as a means of control and potential cure

BOTH


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Openness to reconsidering surgery over the long run

BOTH


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Deep level of trust & confidence in physician & cancer center
Use of physician & internet as 1st sources treatment-related info

Openness to reconsidering surgery over the long run

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How do patients perceive initial treatment options?

SURGERY
ACTIVE SURVEILLANCE

Sense of urgency
Perception as potentially life-threatening disease
Fear of disease progression & uncertainty with active surveillance
Surgery as a means of control and potential cure

View as a common, indolent, low-risk disease
Concerns about adjusting to life without a thyroid/reliance on hormone replacement

BOTH


Weighing the Risks and Benefits of Treatment

Medical Decision Making

Maximalists
Minimalists
Weighing the Risks and Benefits of Treatment

Medical Decision Making

Maximalists
“be ahead of the curve”
“why wait”
“more is better”

Minimalists
“less is more”
“unintended consequences outweigh potential benefits”

Cancer
Blood pressure
Cholesterol
Glucose
BMI

Development of the Medical Maximizer-Minimizer Scale.

Availability Bias

Medical Decision Making

Availability Bias is the tendency to let an example that comes easily to mind affect decision-making or reasoning. This can occur when a story you can readily recall plays too big a role in how you reach your conclusion.

My sister had thyroid surgery and gained 100 lbs.
Dr Google says that thyroid hormone pills are ineffective.
My thyroid support group says the sooner thyroidectomy is done the better the outcome will be.
I had a patient with small thyroid cancer that had a brain metastasis (or lung metastasis/bone metastasis).
Last month, one of my patients had bilateral vocal cord paralysis as a result of thyroidectomy for a 5 mm PTC.

Availability Bias Medical Decision Making

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Medical Team Characteristics
Motivated
Compliant
Supportive Family/Clinicians
Differences in Patient Decision Making

Patient Characteristics

Observational Management Strategy

• Serial US evaluations of the thyroid and neck
  • Q 6 months for 2 years
  • Then less frequently
• TSH suppression is not recommended
  • Goal TSH 0.5-3 mIU/L
• Thyroid function tests
  • Yearly

• Indications for surgical intervention
  • Increase in size of primary tumor* 
    • ≥ 3mm increase in tumor diameter and/or 
    • ≥ 100% increase in tumor volume
  • Identification of metastatic disease
  • Direct invasion into surrounding structures
  • Patient preference

Typical Case

36 year old female
Incidental finding of asymptomatic thyroid nodule
Normal thyroid function
Wants to avoid thyroid hormone replacement
Thyroid US confirms a single 2.0 cm thyroid nodule
Contralateral lobe is normal, no abnormal lymph nodes
FNA confirms papillary thyroid cancer

What now?
Total Thyroidectomy
Vs
Thyroid Lobectomy

Selecting Patients for Lobectomy

Intra-operative Findings
Post-operative Path Report

Tumor/US Characteristics

Medical Team Characteristics

Patient Characteristics

Selecting Patients for Lobectomy

- **Intra-operative Findings**
  - Tumor/US Characteristics
  - Medical Team Characteristics
  - Patient Characteristics

- **Post-operative Path Report**
  - Immediate Completion 6-20%
  - Delayed Completion 5-10%

- **Effective Salvage Therapy**

- **Inappropriate**

- **Appropriate**

**Tumor/Imaging characteristics**

- **TSH goal**
  - 0.5-2.5 mIU/mL
  - With or without levothyroxine

- **Clinic visits**
  - Post-op (to review path, check TSH, Tg)
  - Then 6-12 month follow-up
  - Yearly for 2-3 years with exam
  - TSH, Free T4, Tg, TgAb with each clinic visit

- **Imaging**
  - Neck US 6-12 months, 3 yrs, and 5 yrs
  - Then very rarely

- **Late completion thyroidectomy**
  - Physical exam findings
  - Neck US findings
  - Need for RAI
  - Sustained, serial rise in Tg over time

Post-operative Decision Making

- **Ideal**
  - Features

- **Appropriate**

- **Inappropriate**

Risk Stratification in Thyroid Cancer

A dynamic, iterative, active process

<table>
<thead>
<tr>
<th>Features</th>
<th>Candidates for Minimalistic Management</th>
</tr>
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<tbody>
<tr>
<td>Ideal</td>
<td>Peri-Diagnostic Risk Assessment</td>
</tr>
<tr>
<td>Appropriate</td>
<td>ATA Risk Recurrent/Persistent Disease</td>
</tr>
<tr>
<td>Inappropriate</td>
<td>AJCC 8th Edition</td>
</tr>
</tbody>
</table>

Suspicous Nodule Diagnosis Thyroid Surgery Adjuvant Therapy Follow up

- Excellent Biochemical Structural
  - Excellent
  - Incomplete

Response to Therapy Management recommendations

- ATA Risk Recurrent/Persistent Disease
  - Low, Intermediate, or High

Tuttle, Alzahrani, Mini-review, JCEM expected in early 2019