New Perspectives in Thyroid Cancer

Jennifer Sipos, MD
Assistant Professor of Medicine
Division of Endocrinology
The Ohio State University

Outline

- Thyroid Nodules
- Thyroid Cancer Epidemiology
- Initial management
- Long-term follow up
- Disease-free status

Incidence of thyroid nodules

Likelihood of malignancy 14%

Palpation vs. Ultrasound

How good are we at finding nodules?
Ultrasound vs. Palpation

# Nodules found

- 36
- 35
- 34
- 33
- 32

Nodule size by US

- <1cm
- 1-2cm
- >2cm

Nodules FOUND by palpation
Nodules MISSED by palpation

Yassa 2007 Cancer Cytopathology 111:508-16

Yassa 2007 Cancer Cytopathology 111:508-16
TSH predicts malignancy risk and cancer stage

<table>
<thead>
<tr>
<th>TNM stage</th>
<th>No. of patients</th>
<th>Mean TSH</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I and II</td>
<td>204</td>
<td>2.1±0.24</td>
<td>0.002</td>
</tr>
<tr>
<td>III and IV</td>
<td>35</td>
<td>4.9±1.59</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05  ** p<0.01  *** p<0.001


Percentages of thyroid carcinoma by histologic subtype

- Papillary: 80%
- Follicular: 11%
- Hurthle cell: 3%
- Medullary: 4%
- Anaplastic: 2%

Hundahl 1998 Cancer 83: 2368-48

FNA Cytology Diagnostic Categories

<table>
<thead>
<tr>
<th>National Cancer Institute Classification</th>
<th>Alternate classification</th>
<th>% Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td></td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Follicular Lesion of Undetermined Significance</td>
<td>Atypia</td>
<td>5-10%</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>Follicular Neoplasm</td>
<td>20-30%</td>
</tr>
<tr>
<td></td>
<td>Hurthle Neoplasm</td>
<td></td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td></td>
<td>50-75%</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
<td>98-100%</td>
</tr>
<tr>
<td>Non-diagnostic</td>
<td>Unsatisfactory</td>
<td></td>
</tr>
</tbody>
</table>

Baloch ZW., 2008 Diag Cytopath 36:425-437

Epidemiology of Thyroid Cancer

- 48,020 new cases in 2011
- 1,740 deaths
- Females 5 year survival rates increasing significantly, from 93% in 1974 to 97.4% in 2001
- Survival rates in men have decreased significantly, by 2.4%
- Rates of distant metastases in men were over 2-fold higher than women (9% vs 4%)

The prevalence of microcarcinoma in 24 autopsy series with 7,156 cases

Incidence rates of PTC by tumor size

Adapted from: Pazaitou-Panayiotou, et al. 2007 Thyroid 17 (11): 1085-92

Adapted from: Pazaitou-Panayiotou, et al. 2007 Thyroid 17 (11): 1085-92

Adapted from: Sipos, Mazzaferri. 2010 Clinical Oncology 22: 395-404
Mortality and Recurrence Rates for Thyroid Cancer

Relative survival of papillary thyroid carcinoma by AMES risk levels

10 Year recurrence rates by tumor size

Ten year mortality by tumor size

Hundahl et al 1998 Cancer 83: 2638

Bilimoria 2007 Annals Surg 246: 375-84

Bilimoria 2007 Annals Surg 207: 375-84
Initial Treatment and Long-Term Management

Recurrence Rates as a Function of Treatment

Levels of TSH Suppression

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>TSH (mU/L)</th>
<th>Duration of Therapy</th>
<th>Strength of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent Disease</td>
<td>&lt;0.1</td>
<td>Indefinitely in absence of contraindications</td>
<td>B</td>
</tr>
<tr>
<td>NED; High risk tumor</td>
<td>0.1-0.5</td>
<td>10 years then low risk range</td>
<td>C</td>
</tr>
<tr>
<td>NED; Low risk tumor</td>
<td>0.3-2.0</td>
<td>Indefinite in absence of recurrence</td>
<td>B</td>
</tr>
</tbody>
</table>

Recurrence Rates as a Function of Treatment:

- No T4 or RAI
- T4 alone
- T4 + RAI

Role of Thyroglobulin in Diagnostic F/U

- Important modality to monitor patients for residual or recurrent disease
- In absence of antibody interference, Tg has high sensitivity and specificity to detect thyroid cancer
- Highest sensitivity is following thyroid hormone withdrawal or stimulation using rhTSH

Derived from: Cooper et al. 2009 Thyroid 19(12) 1-48.
Criteria for absence of persistent tumor

After total or near-total thyroidectomy and remnant ablation (RAI), disease-free status comprises ALL of the following:

1. No clinical evidence of tumor.
2. No imaging evidence of tumor.
3. Undetectable serum Tg levels during TSH suppression and stimulation in the absence of interfering antibodies.

Contemporary Surgical Management of Differentiated Thyroid Cancer

Matthew Old, MD, F.A.C.S.
Assistant Professor
Department of Otolaryngology-Head & Neck Surgery
The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute

Outline

Preoperative Assessment
Risk Stratification
Goals
Surgical management
Neck Dissection
Complications and Minimizing Risks
Cases
Preoperative Assessment

- Risk stratification
- Preoperative counseling/informed consent based on risk stratification
- Known or suspected cancer: Ultrasound contralateral lobe, central and lateral necks
- FNA suspicious nodes
- Routine use of MRI, CT, PET not needed

Cooper, et al 2009 Thyroid 19: 1167-1214.

Risk Stratification

Goal: place patient in a low or high risk category based on preoperative assessment

Example: Follicular or Hurthle cell neoplasm ~20% risk

High Risk Features

- >4 cm
- Atypical features or suspicious on FNA
- Family history
- Radiation exposure

Cooper, et al 2009 Thyroid 19: 1167-1214.
Surgical Goals

Goals Thyroid Cancer Surgery

Curative vs Palliative
Remove primary tumor
Remove disease extending outside primary
Remove all nodes involved
Staging
Facilitate postoperative RAI
Permit adequate surveillance (WBS + Tg)
Minimize disease recurrence and mets

Cooper, et al 2009 Thyroid 19: 1167-1214.

Extent of Surgery (lobectomy versus total)

Extent of Surgery

Thyroid lobectomy – initial approach
- Low risk undiagnosed tumors
- DTC <1 cm without contralateral nodules or nodes on US and no high risk factors or features
- 1-2 cm DTC: 24% chance recurrence, 49% increased mortality with lobectomy alone
- Individuals >45 - total thyroidectomy for tumors <1cm

Cooper, et al 2009 Thyroid 19: 1167-1214.
Extent of Surgery

Total thyroidectomy
- High risk stratification with unknown or equivocal FNA
- Improved survival with increased extent of surgery
- All patients with >1cm thyroid cancer with no contraindication to surgery

Cooper, et al 2009 Thyroid 19: 1167-1214.

Neck dissection

Neck Dissection (central +/- lateral)

Adopted from Gray’s Anatomy, Wikipedia Commons.
Post-ND Anatomy

Neck dissection

- General teaching: PTC lymph node metastases in low-risk patients not clinically significant

- 2 SEER studies recently demonstrated:
  1) lymph node metastases, age >45 years, distant mets, larger tumors predicted poor outcome
  2) lymph node mets independent for decreased survival only in follicular cancer and PTC in pts over age 45.

- Regional recurrence higher with nodal mets and ECS

Podnos et al 2005 Am Surg 71: 731-734
Cooper, et al 2009 Thyroid 19: 1167-1214.
Zaghloul et al 2008 133: 1070-1077

Neck dissection

- Risks and benefits should be weighed with surgical expertise

- Level I and VII (below manubrium) may be involved

- En-bloc, functional neck dissections favored over isolated lymphadenectomy (“cherry-picking”) with some data to suggest improved mortality and reduced recurrence

- Most common site of recurrence is in cervical lymph nodes, which comprise the majority of all recurrences

Cooper, et al 2009 Thyroid 19: 1167-1214.

Neck dissection

- Central neck dissection (VI) and lateral neck for clinically involved nodes during total thyroidectomy: Rating B

- Consider prophylatic central neck dissection with clinically uninvolved central nodes: Rating C

- Total thyroidectomy without prophylatic central neck dissection for T1 or T2, node-negative PTCs, and most follicular cancers: Rating C

Cooper, et al 2009 Thyroid 19: 1167-1214.
Minimizing Risks + Maximizing Outcome

- Preoperative counseling and assessment critical
- Hypoparathyroidism – bilateral central neck dissections
- Debate: preoperative and post-operative vocal fold assessment
- Discussion of recurrent laryngeal nerve injury and sacrifice – higher incidence with thyroid cancers
- Chyle leaks, hematomas
- Accessory (CNXI) paresis

Post-nerve Dissection Anatomy

Parapreservation

Level IV; Thoracic duct
Case 1 – Low risk

35 year old female
2 cm left nodule
No family history or risks
FNA – indeterminant
No vocal fold dysfunction
+/- Dysphagia
US – no lateral or central adenopathy

Case 2

60 year old male with hoarseness
Right neck and thyroid mass (5 cm)
Right vocal fold paralysis
No family history or risk factors
CT scan performed

Case 1

Left thyroid lobectomy – frozen: follicular neoplasm
Nerve stuck to backside of gland but dissected free
Patient did well without sequelae
Path: 2 cm angioinvasive unencapsulated follicular thyroid carcinoma
Patient underwent completion thyroidectomy and is without evidence of disease

Case 2

FNA – papillary thyroid carcinoma
Case 2
Bilateral central and lateral disease; confirmed by US

Case 2
Required vocal fold medialization
recovered near-normal voice
Post-operative RAI
No evidence of disease to date
Baseline functional status – voice, swallowing and function

Case 2
Total thyroidectomy, bilateral central and lateral neck dissections, sacrifice of right RLN and right IJ
Path: 5 cm PTC, capsular/perineural/lymphovascular r/ deep neck muscular invasion; 15/79 nodes positive with ECS