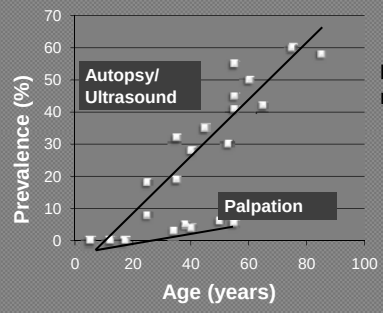
New Perspectives in Thyroid Cancer

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

Incidence of thyroid nodules



Likelihood of malignancy 14%[1]

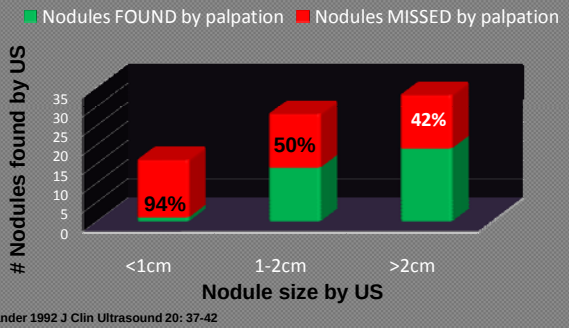
Mazzaferri 1993 NEJM 328 (8): 553-9

[1] Yassa 2007 Cancer Cytopathology 111:508-16

Outline

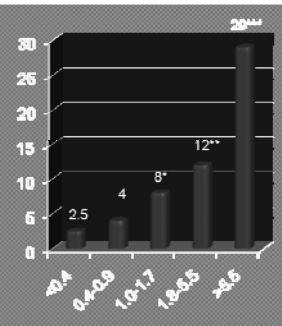
- Thyroid Nodules
- Thyroid Cancer Epidemiology
- Initial management
- Long-term follow up
- Disease-free status

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



Brander 1992 J Clin Ultrasound 20: 37-42

TSH predicts malignancy risk and cancer stage



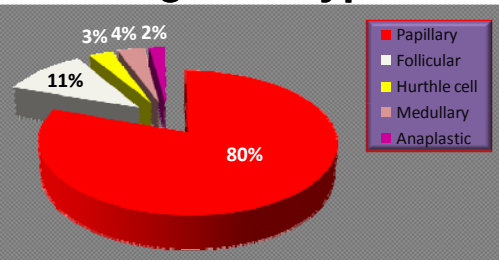
TNM stage	No. of patients	Mean TSH	*p* value
I and II	204	2.1±0.24	0.002
III and IV	35	4.9±1.59	

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

Boelaert 2006 JCEM 91:4295-4301

Haymart, et al. JCEM, March 2008, 93(3):809–814

Percentages of thyroid carcinoma by histologic subtype



Hundahl 1998 Cancer 83: 2368-48

FNA Cytology Diagnostic Categories

National Cancer Institute Classification	Alternate classification	% Malignant
Benign		<1%
Follicular Lesion of Undetermined Significance	Atypia	5-10%
Neoplasm	Follicular Neoplasm Hurthle Neoplasm	20-30%
Suspicious for malignancy		50-75%
Malignant		98-100%
Non-diagnostic	Unsatisfactory	

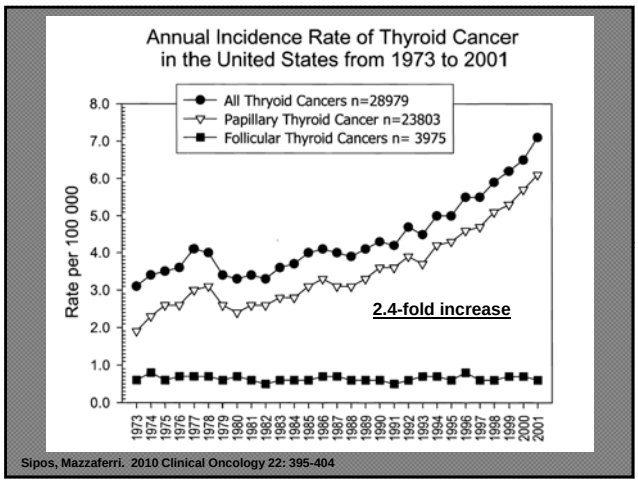
Baloch ZW., 2008 Diag Cytopath 36:425-437

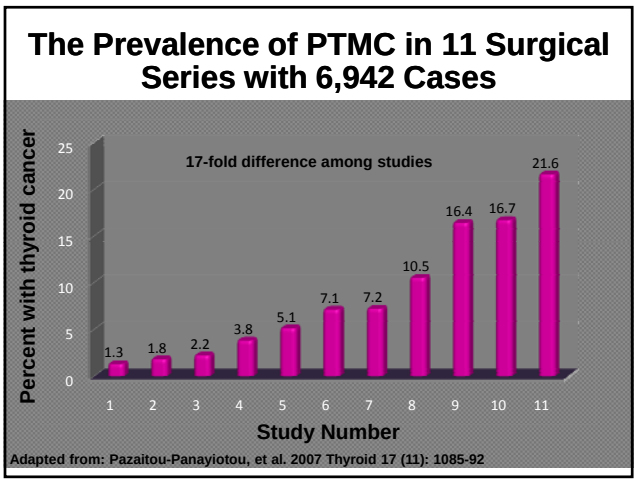
Epidemiology of Thyroid Cancer

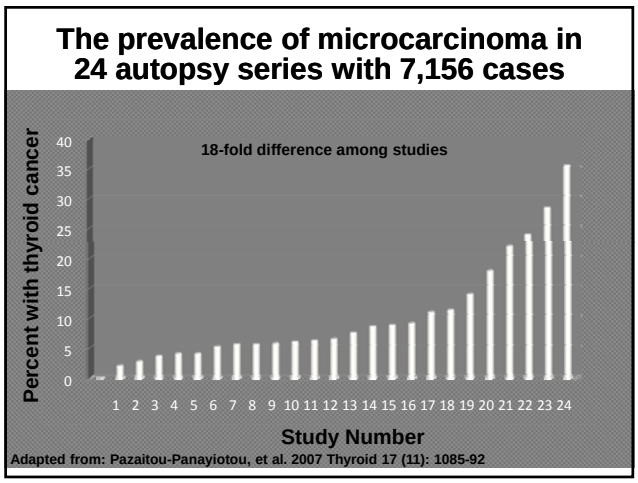
- 48,020 new cases in 2011
- 1,740 deaths

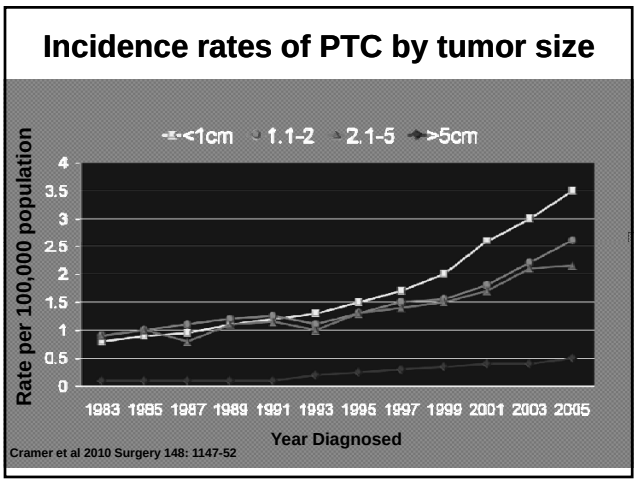
- Females 5 year survival rates increasing significantly, from 93% in 1974 to 97.4% in 2001
- Survival rates in men have decreased significantly, by 2.4%
- Rates of distant metastases in men were over 2-fold higher than women (9% vs 4%)

Cancer Facts and Figures 2011
National Cancer Institute, http://www.cancer.gov/cancertopics/types/thyroid
SEER Cancer Statistics Review, 1975-2001. http://seer.cancer.gov/csr/1975_2008/.


Annual Incidence Rate of Thyroid Cancer in the United States from 1973 to 2001
All Thyroid Cancers n=28979
Papillary Thyroid Cancer n=23803
Follicular Thyroid Cancers n= 3975
Rate per 100 000
2.4-fold increase
Sipos, Mazzaferri. 2010 Clinical Oncology 22: 395-404

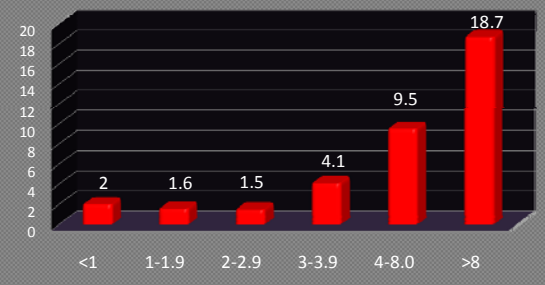

The Prevalence of PTMC in 11 Surgical Series with 6,942 Cases
17-fold difference among studies
Percent with thyroid cancer
1.3
1.8
2.2
3.8
5.1
7.1
7.2
10.5
16.4
16.7
21.6
Study Number
Adapted from: Pazaitou-Panayiotou, et al. 2007 Thyroid 17 (11): 1085-92


The prevalence of microcarcinoma in 24 autopsy series with 7,156 cases
18-fold difference among studies
Percent with thyroid cancer
Study Number
Adapted from: Pazaitou-Panayiotou, et al. 2007 Thyroid 17 (11): 1085-92


Incidence rates of PTC by tumor size
<1cm
1.1-2
2.1-5
>5cm
Rate per 100,000 population
Year Diagnosed
Cramer et al 2010 Surgery 148: 1147-52

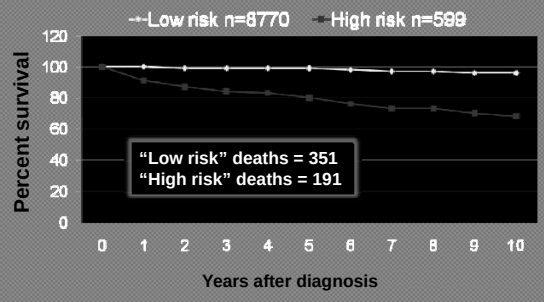
Mortality and Recurrence Rates for Thyroid Cancer

Ten year mortality by tumor size



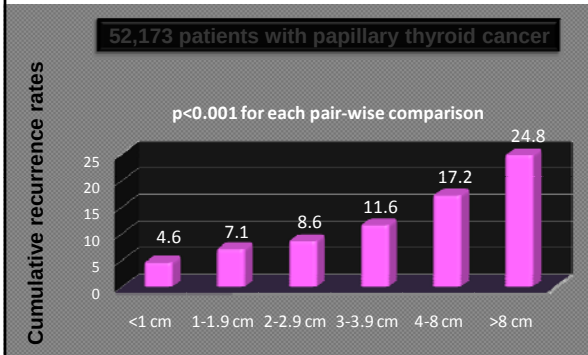
Bilimoria 2007. Annals Surg 207: 375-84

Relative survival of papillary thyroid carcinoma by AMES risk levels



Hundahl et al 1998 Cancer 83: 2638

10 Year recurrence rates by tumor size



Bilimoria 2007 Ann Surg 246: 375

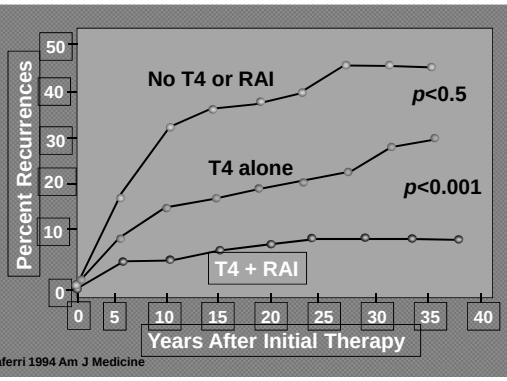
Initial Treatment and Long-Term Management

Levels of TSH Suppression

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

Derived from: Cooper et al. 2009 Thyroid 12: 1-48

Recurrence Rates as a Function of Treatment



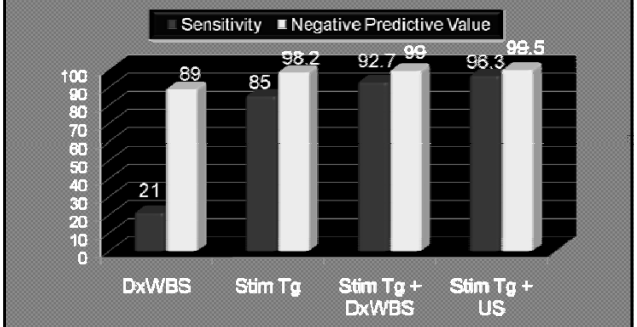
Mazzaferri 1994 Am J Medicine

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

Cooper, D. S., et. al. 2009 Thyroid 19(12) 1-48.

Diagnostic value of standard testing



Pacini 2003. JCEM 88 (8): 3668-3673.

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

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.**

Cooper, et al 2009 Thyroid 12: 1-48

Outline

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

Preoperative Assessment

Risk Stratification

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

<u>High Risk Features</u>

>4 cm

Atypical features or suspicious on FNA

Family history

Radiation exposure

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

Surgical Goals

Extent of Surgery (lobectomy versus total)

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

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

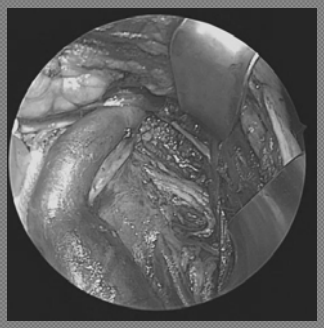
+/-

Central **Lateral**

Adopted from Gray's Anatomy, Wikipedia Commons

Neck Dissection (central +/- lateral)

Post-ND Anatomy



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

- 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.
Zaydfudium et al 2008 133: 1070-1077

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

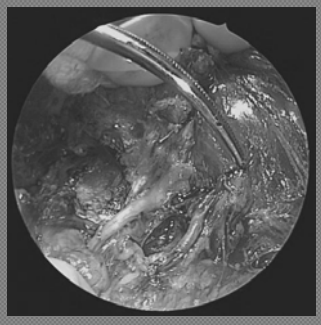
- Total thyroidectomy without prophylatic central neck dissection for T1 or T2, node-negative PTCs, and most follicular cancers: Rating C

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

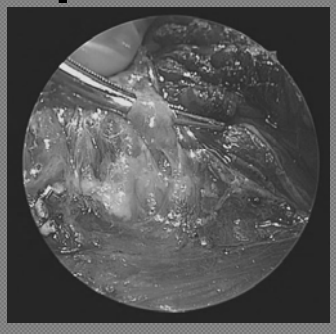
Minimizing Risks + Maximizing Outcome

- 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

Case1 –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

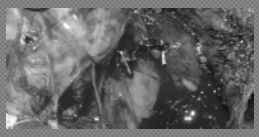
Case 2

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

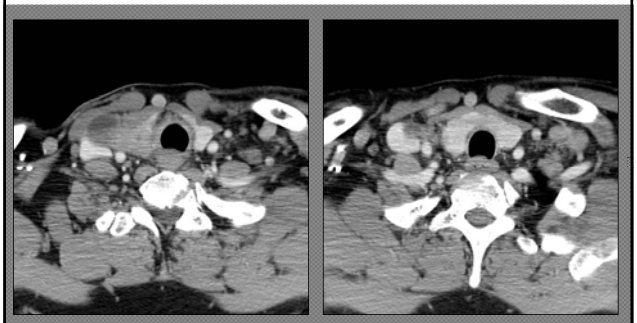
Path: 2 cm angioinvasive unencapsulated follicular thyroid carcinoma

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/ deep neck muscular invasion; 15/79 nodes positive with ECS