

Differentiated Thyroid Carcinoma

The "GOOD" cancer?

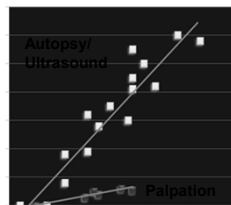
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Outline

- Thyroid Nodules
 - Epidemiology
 - High risk features
 - Indications for fine needle aspiration
- Thyroid Cancer
 - Epidemiology
 - Prognosis
 - Management

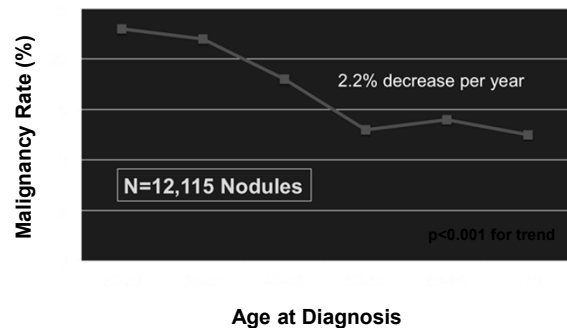
Epidemiology – thyroid nodules

- Common disorder
- More frequent in women
- Increase in frequency with age
- More common in areas of low iodine intake



Mazzaferri. N Engl J Med. 1993 Feb 25;328(8):553-9

Patient age and risk of malignancy



Kwong 2015 JCEM 100: 4434-40

Prevalence of Endocrine Disorders in U.S. Adults

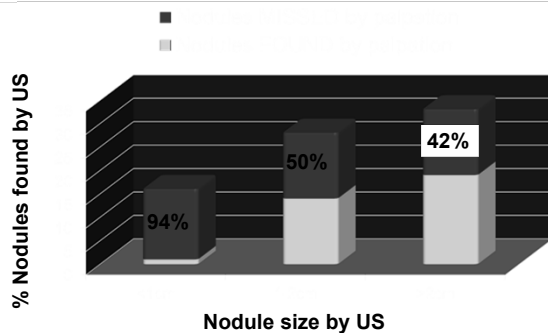
Endocrine Condition	Prevalence
Metabolic syndrome	35-40%
Obesity	25-50%
Diabetes	5-25%
Hyperlipidemia	15-20%
Osteoporosis	7%
Thyroid nodules	30-70%

Golden SH., et al. J Clin Endo Metab 2009; 94:1853-78
 Mazzaferri E. New England Journal Medicine 1993; 328:553-558
 Guth S., et al. Eur J Clin Invest 2009; 39:699-706

Causes of thyroid nodules

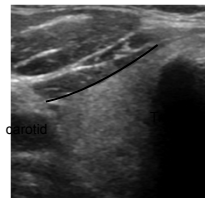
Benign	Malignant
Multinodular goiter (colloid adenoma)	Papillary carcinoma
Hashimoto's (chronic lymphocytic) thyroiditis	Follicular carcinoma
Cysts	Medullary carcinoma
Colloid	Anaplastic carcinoma
Simple	Primary thyroid lymphoma
Hemorrhagic	Metastatic carcinoma
Follicular adenomas	breast
Hurthle cell adenomas	melanoma
	renal cell

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

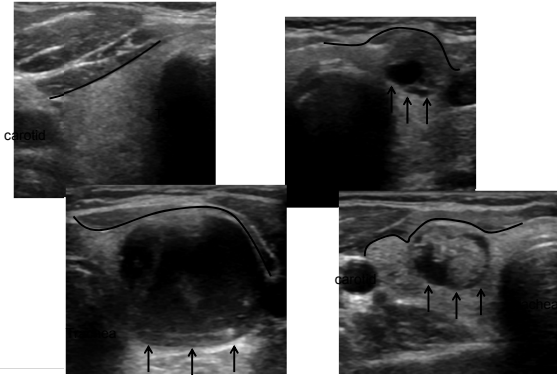


Brander 1992 J Clin Ultrasound 20: 37-42

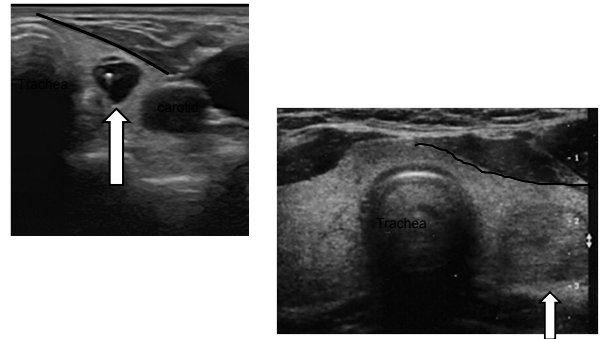
Palpable Thyroid Nodules



Palpable Thyroid Nodules



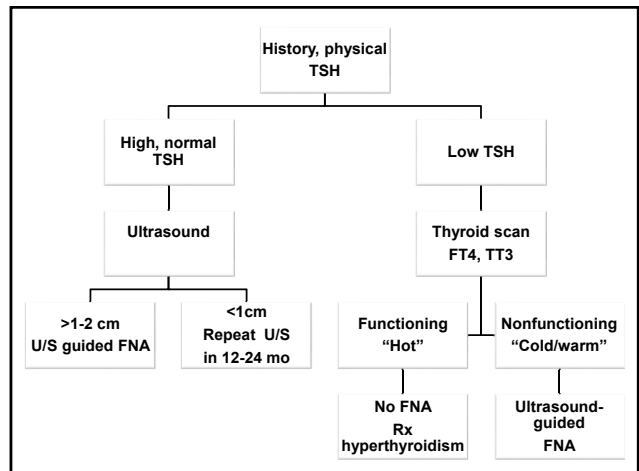
Nonpalpable Thyroid Nodules



American Thyroid Association Management Guidelines

Thyroid sonography should be performed in all patients with known or suspected thyroid nodules. Strong recommendation, high-quality evidence

Haugen 2016 Thyroid 26: 1-133



Concerning Clinical Features

High clinical suspicion

- Rapid tumor growth
- Very firm nodule (rock hard)
- Fixation to adjacent structures
- Vocal cord paresis
- Enlarged regional lymph nodes
- Family history of PTC or MEN 2
- Distant metastases
- History of radiation exposure to the head/neck

Hamming JF, et al. Arch Int Med 1990; 150:1088
Rago T., et al. Clin Endo 2007; 66:13

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Positive Predictive Value (PPV) – good (70-75%)

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Positive Predictive Value (PPV) – good (70-75%)

Negative Predictive Value (NPV) – unacceptable (85%)

Hamming JF, et al. Arch Int Med 1990; 150:1088
Rago T., et al. Clin Endo 2007; 66:13

Diagnostic yield of sequential aspirations in 120 patients with multiple nodules and cancer

FNA performed on	Number of nodules >1cm		
	2 (n = 73)	3 (n = 27)	≥ 4 (n = 20)
Largest nodule	86.3	51.8	55
Largest 2 nodules	100	81.5	85
Largest 3 nodules		100	95
Largest 4 nodules			100

FNA of only the largest nodule in a patient with 2 nodules would have missed 13.7% of cancers. In patients with 3 nodules, 48.2% of cancers would have been missed by performing a FNA on the largest nodule only.

Frates et al 2006 JCEM 91: 3411-17

Size and risk of malignancy

Characteristic	No. benign	No. malignant	% Malignant	p Value
Size (mm)				0.48
11-14.9	135	15	10	
15-19.9	167	16	8.7	
20-24.9	149	19	11.3	
25-29.9	112	11	8.9	
>30	208	33	13.7	

Frates et al 2006 JCEM 91: 3411-17

Nodule composition and malignancy risk

Characteristic	No. benign	No. malignant	% Malignant	p Value
Composition				<0.01
Completely solid	330	55	14.3	
Predominantly solid	209	24	10.3	
Mixed solid and cystic	129	8	5.8	
Predominantly cystic	85	2	2.3	
Completely cystic	7	0	0	

Frates et al 2006 JCEM 91: 3411-17

Indications for FNA

Nodule Type	Threshold for FNA
Solid Nodule	
With suspicious US features	≥1.0 cm
Without suspicious US features	≥1.5 cm
Mixed cystic-solid nodule	
With suspicious US features	Solid component >1 cm
Without suspicious US features	Solid component >1.5 cm
Spongiform nodule	≥2.0 cm
Simple cyst	Not indicated
Suspicious cervical lymph node	FNA node ± FNA-associated thyroid nodule(s)

Suspicious US features: hypoechoic, microcalcifications, increased central vascularity, infiltrative margins, taller than wide in transverse plane

NCCN 2016 Clinical Practice Guidelines in Oncology, Thyroid Carcinoma. V.1.2016: 1-75

Thyroid FNA Cytology

NCI Classification	% Malignant
Benign	<1%
FLUS/Atypia (indeterminate)	5-10%
Neoplasm	20-30%
Suspicious	50-75%
Malignant	98-100%
Non-diagnostic	

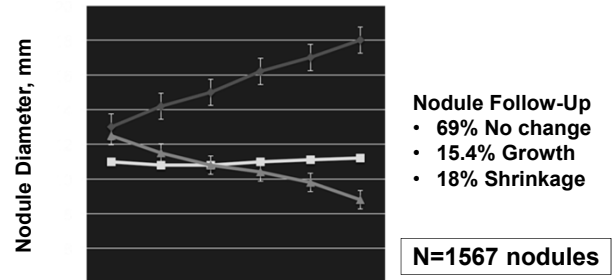
Baloch ZW., et al. Diag Cytopath 2008; 36:425-437

Follicular neoplasm

- Cannot determine if malignant by cytology
- At surgery, malignancy is determined if there is capsular or vascular invasion
- Only 20-30% are malignant
- Molecular markers are being investigated for assistance in determination of malignancy

Natural history

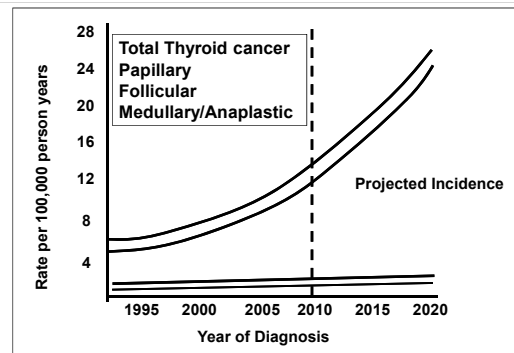
5-year follow up of cytologically benign nodules



Durante et al 2015 JAMA 313: 926-35

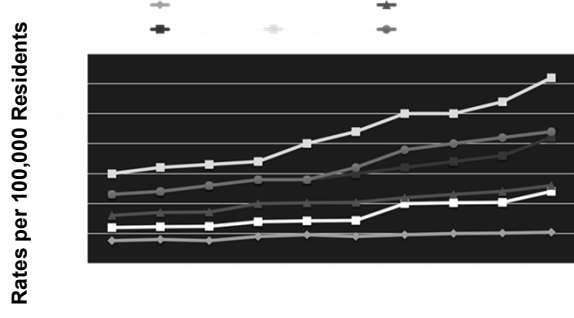
Thyroid Cancer

Epidemiology – thyroid cancer



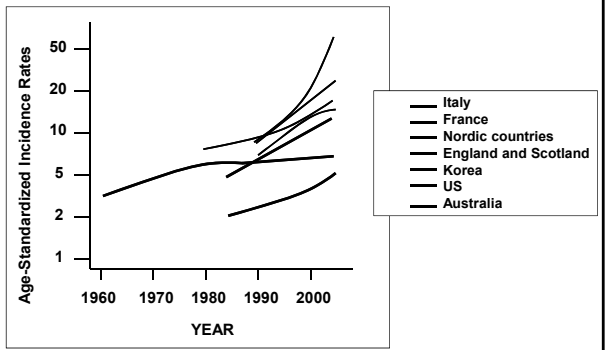
Aschebrook-Kilfoy 2013 Cancer Epidemiol Biomark Prev 22: 1252-9

Thyroid cancer incidence trend Age and Gender



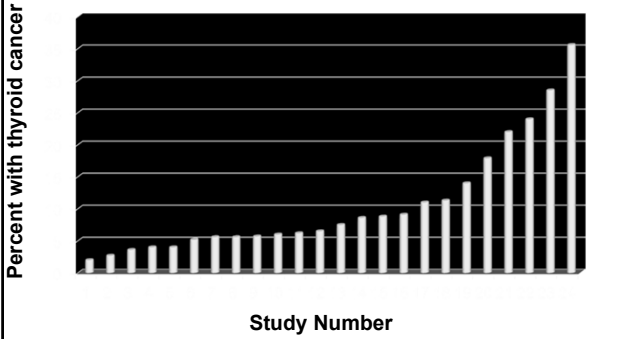
Pellegriti 2013 J Cancer Epidemiol ID 965212

Age-standardized incidence rates of thyroid cancer by sex and country



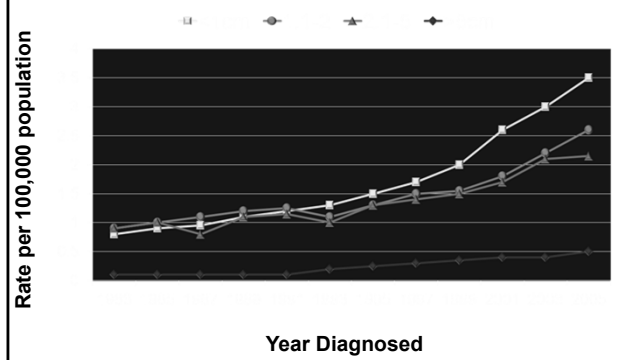
Vaccarella 2015 Thyroid 25: 1127-36

Prevalence of microcarcinoma of the thyroid 24 autopsy series with 7,156 cases



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

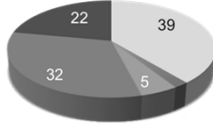
Incidence rates of PTC by tumor size



Cramer et al 2010 Surgery 148: 1147-52

Financial Impact of Thyroid Cancer United States 2013

Percent of total cost



Cost Category	Estimated Price
Initial Treatment	\$623,367,851
Surgical Deaths	\$7,907,800
Surgical Complications	\$27,302,922
Recurrences	\$74,677,703
Surveillance	\$520,511,027
Thyroid Cancer Deaths	\$351,011,185
TOTAL	\$1,604,778,489

Lubitz, et al 2014 Cancer 120: 1345-52

Bankruptcy Rates—Cancer Patients

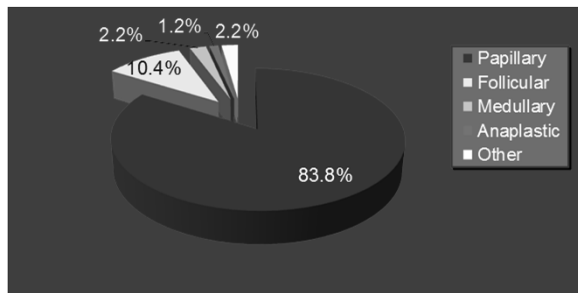
Cancer Type	Hazard Ratio
Lung	3.80
Thyroid	3.46
Colorectal	3.02
Leukemia/Lymphoma	3.0
Breast	2.41
Prostate	2.32
ALL	2.65

Age-Adjusted Bankruptcy Rates in Cancer and Non-cancer Patients

	20-34		35-49		50-64		65-79	
	Cancer	Control	Cancer	Control	Cancer	Control	Cancer	Control
Thyroid	11.37	3.92	9.05	2.06	6.01	2.91	4.05	1.83

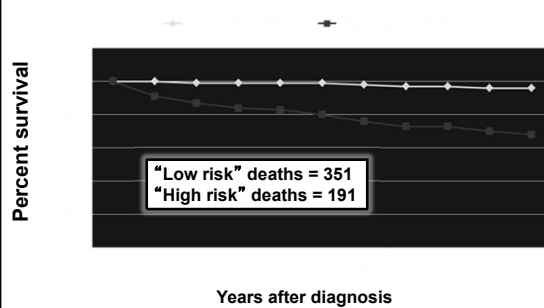
Ramsey et al 2013 Health Affairs 32: 1143-52

Thyroid Cancer Histologic Subtypes SEER Database 1992-2006




Aschebrook-Kilfoy 2011 Thyroid 21: 125-34

Relative survival of papillary thyroid carcinoma by AMES risk levels

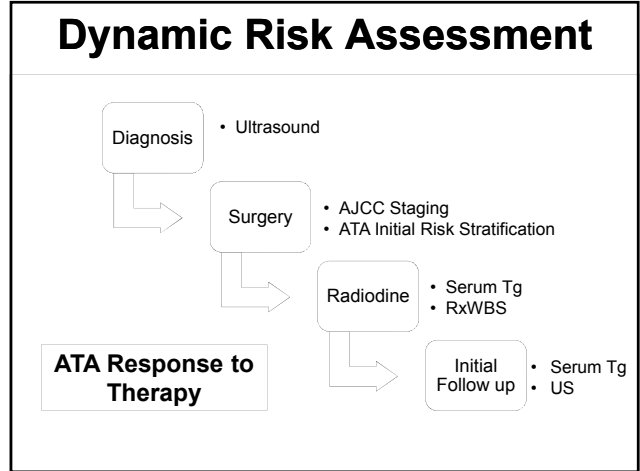


Hundahl et al 1998 Cancer 83: 2638

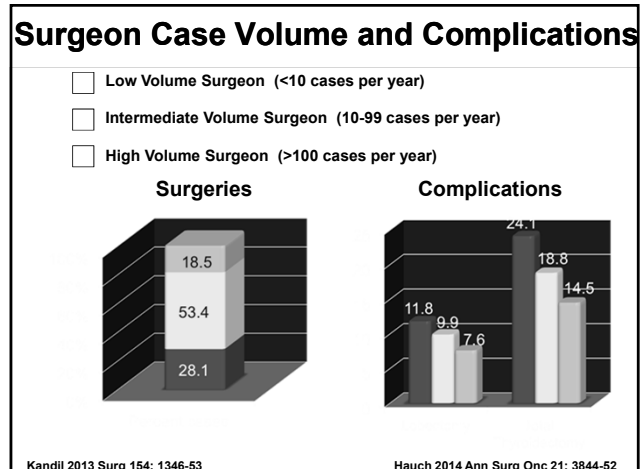
Risk of Structural Disease Recurrence

High Risk	 <ul style="list-style-type: none"> FTC, extensive vascular invasion (30-55%) pT4a gross extrathyroidal extension (30-40%) pN1 with extranodal extension, >3 LN involved (40%) pN1, any LN >3cm (30%) PTC, Vascular invasion (15-30%) pN1, >5 LN involved (20%)
Intermediate Risk	<ul style="list-style-type: none"> pT3 minor extrathyroidal extension (3-8%) pN1, ≤5 lymph nodes involved (5%) Intrathyroidal PTC, 2-4cm (5%) Multifocal Papillary Microcarcinoma (4-6%)
Low Risk	<ul style="list-style-type: none"> Minimally invasive FTC (2-3%) Unifocal Papillary microcarcinoma(1-2%)

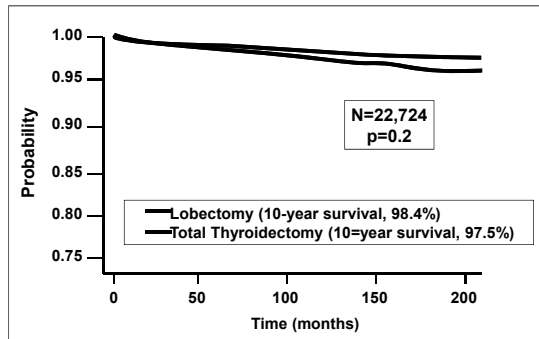
Haugen et al 2016 Thyroid 26: 1-133



- ## Treatment decisions
- Extent of surgery
 - Radioiodine ablation
 - TSH suppression
 - Follow-up algorithm
 - Serum thyroglobulin
 - Diagnostic WBS
 - Ultrasonography



Lobectomy vs Total Thyroidectomy Disease-Specific Survival



Mendelsohn 2010 Arch Otolaryngol Head Neck 136: 1055-1061

Surgical Approach—ATA Guidelines

R35. For patients with thyroid cancer >1cm and <4cm, or without extrathyroidal extension and without clinical evidence of any lymph node metastases (cN0), the initial surgical procedure can be either a bilateral procedure (near-total or total thyroidectomy) or unilateral procedure (lobectomy). Thyroid lobectomy alone may be sufficient initial treatment for low risk PTC and FTC; however, the treatment team may choose total thyroidectomy to enable RAI therapy or to enhance follow-up based upon disease features and/or patient preferences—Strong recommendation, Moderate-quality evidence.

Haugen et al 2016 Thyroid 26: 1-133

Surgical Approach—ATA Guidelines

R35. For patients with thyroid cancer >4cm, or with gross extrathyroidal extension (clinical T4), or clinically apparent metastatic disease to nodes (clinical N1) or distant sites (clinical M1), the initial surgical procedure should include a near-total or total thyroidectomy and gross removal of all primary tumor unless there are contraindications to this procedure—Strong recommendation, Moderate-quality evidence.

Haugen et al 2016 Thyroid 26: 1-133

TSH targets for long-term thyroid hormone therapy

Risk of LT4 therapy	Response to cancer therapy			
	Excellent	Indeterminate	Biochemical incomplete	Structural incomplete
Minimal	0.5-2.0	0.1-0.5	<0.1	<0.1
Moderate	0.5-2.0	0.5-2.0	0.1-0.5	<0.1
High	0.5-2.0	0.5-2.0	0.5-2.0	0.1-0.5

Haugen et al 2016 Thyroid 26: 1-133

Thyroglobulin

- **Thyroglobulin is a protein secreted by thyroid tissue only**
- **Tumor marker for differentiated thyroid cancers**
- **Thyroglobulin should be measured in:**
 - **The same laboratory**
 - **Always with a quantitative TgAb level**
 - **Always with a serum TSH level**

Haugen et al 2016 Thyroid 26: 1-133

Summary

Revised ATA Management Guidelines for Patients with Thyroid Nodules

- **Measure TSH in all patients with thyroid nodules**

Haugen 2016 Thyroid 26: 1-133.

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Haugen 2016 Thyroid 26: 1-133.

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Haugen 2016 Thyroid 26: 1-133.

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Haugen 2016 Thyroid 26: 1-133.

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- **Hemithyroidectomy for most low risk cancers**
- **TSH replacement dosing in cancer dependent on response to therapy and risk of TSH suppression**
- **Serum thyroglobulin for follow up of cancer patients at same lab**

Haugen 2016 Thyroid 26: 1-133.