Incidentalomas in Endocrinology

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DISCLOSURES

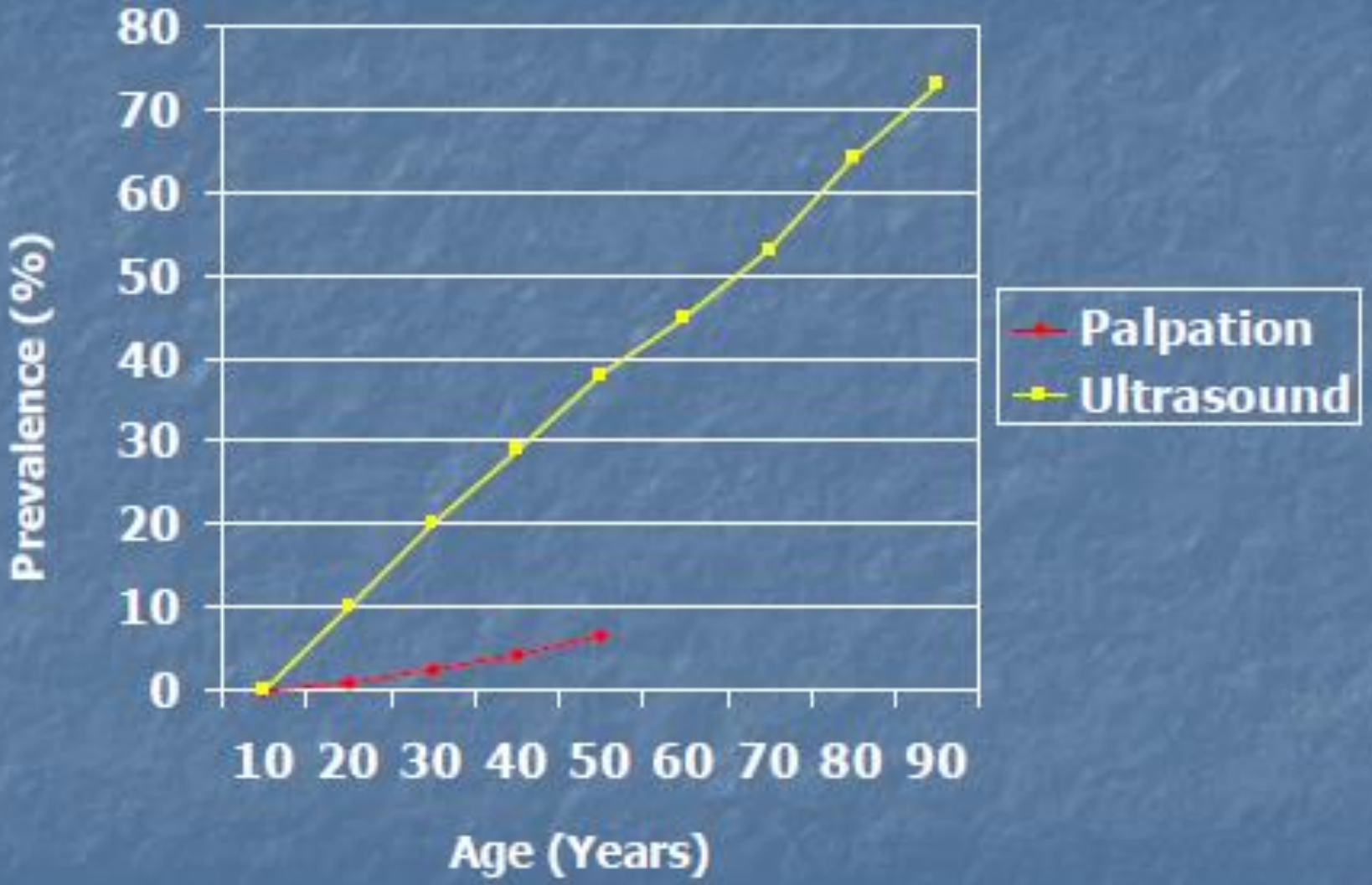
-None

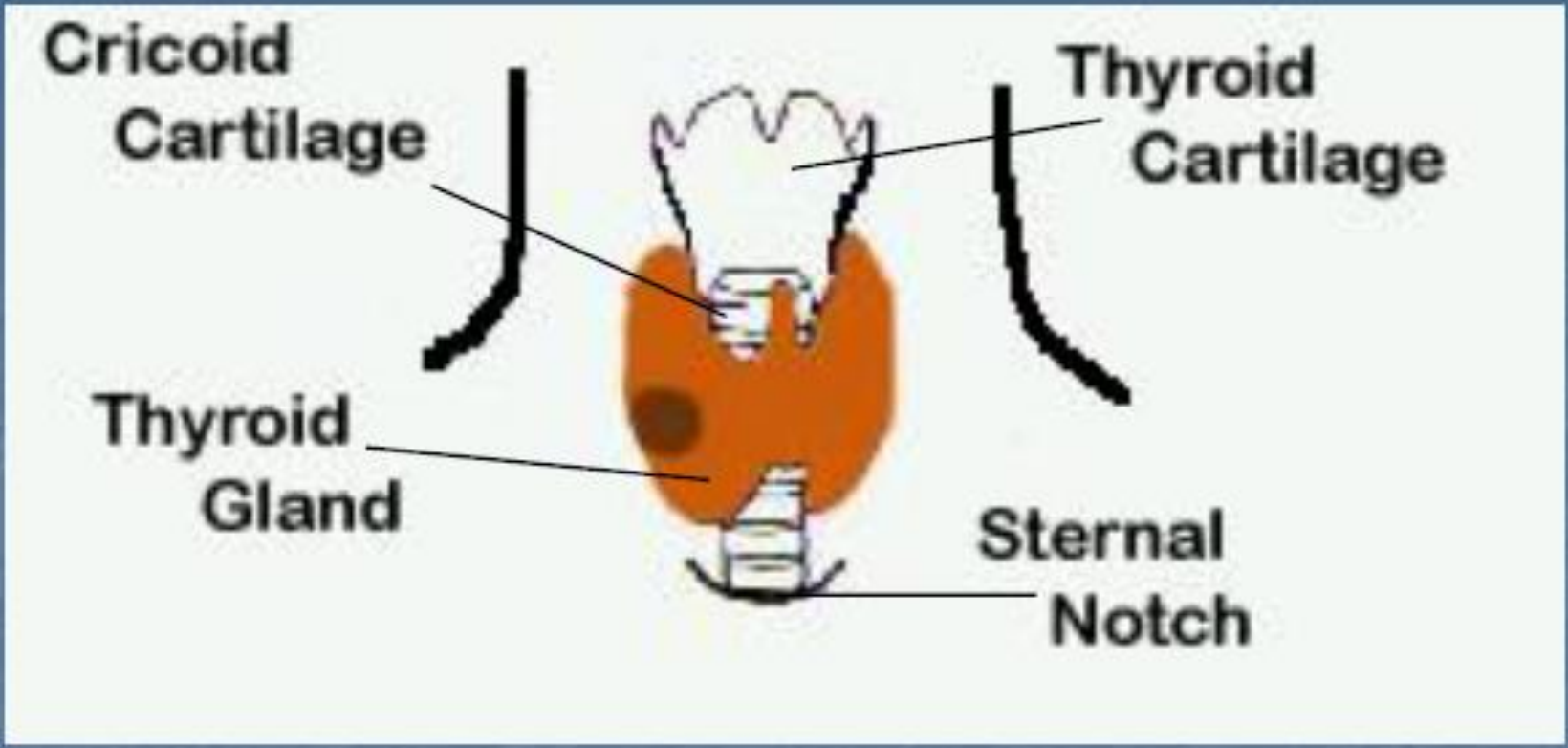
Thyroid Incidentalomas

Thyroid Nodules

- 63,000 new cases of thyroid cancer in the U.S. in 2016
- 300,000 new palpable thyroid nodules detected annually
- Incidental nodules noted on 13% of carotid doppler studies
- Discrete nodules identified on 67% of thyroid ultrasounds

Thyroid Nodules Detected Prevalence by Palpation and Ultrasonography





Benign Nodules 90-95%
Adenomatoid Nodules 85%
Adenomas 10-15%
Cysts < 1%

Malignant Nodules 5-10%
Papillary 80-85%
Follicular/Hürthle Cell 10%
Medullary 2-3%
Anaplastic ~1%
Lymphoma < 1%
Metastasis (another primary) < 1%

AACE/AME Thyroid Nodules Clinical Practice Guidelines

Table 3
Key Recommendations
Regarding History and Physical Examination
in Patients With a Thyroid Nodule*

- Remember that the vast majority of nodules are asymptomatic, and absence of symptoms does not rule out a malignant lesion (*grade C*)†
- Always obtain a biopsy specimen from solitary, firm, or hard nodules. The risk of cancer is similar in a solitary nodule and MNG (*grade B*)
- Record the following information (*grade C*):
  - Family history of thyroid disease
  - Previous neck disease or treatment
  - Growth of the neck mass
  - Hoarseness, dysphonia, dysphagia, or dyspnea
  - Location, consistency, and size of the nodule
  - Neck tenderness or pain
  - Cervical adenopathy
  - Symptoms of hyperthyroidism or hypothyroidism
- Factors suggesting increased risk of malignant potential (*grade C*):
  - History of head and neck irradiation
  - Family history of MTC or MEN2
  - Age <20 or >70 years
  - Male sex
  - Growing nodule
  - Firm or hard consistency
  - Cervical adenopathy
  - Fixed nodule
  - Persistent hoarseness, dysphonia, dysphagia, or dyspnea

*MEN2 = multiple endocrine neoplasia type 2; MNG = multinodular goiter; MTC = medullary thyroid carcinoma.
†See Table 1 for explanation of grades.

AACE/AME Thyroid Nodules Clinical Practice Guidelines

Table 10
Key Recommendations for Laboratory Evaluation of Thyroid Nodules*

- Serum TSH should be tested first, with a third-generation assay (*grade B*)†
- If TSH level is low (<0.5 μIU/mL), measure free T_4 and T_3; if TSH level is high (>5.0 μIU/mL), measure free T_4 and TPOAb (*grade C*)
- Routine assessment of serum thyroglobulin is not recommended for the diagnosis of thyroid nodules or nodular goiter (*grade C*)
- Serum calcitonin should be measured if FNA or family history suggests MTC (*grade B*)

*FNA = fine-needle aspiration; MTC = medullary thyroid carcinoma; T_3 = triiodothyronine; T_4 = thyroxine; TPOAb = thyroid peroxidase antibody; TSH = thyroid-stimulating hormone (thyrotropin).
†See Table 1 for explanation of grades.

Thyroid Nodules: Evaluation

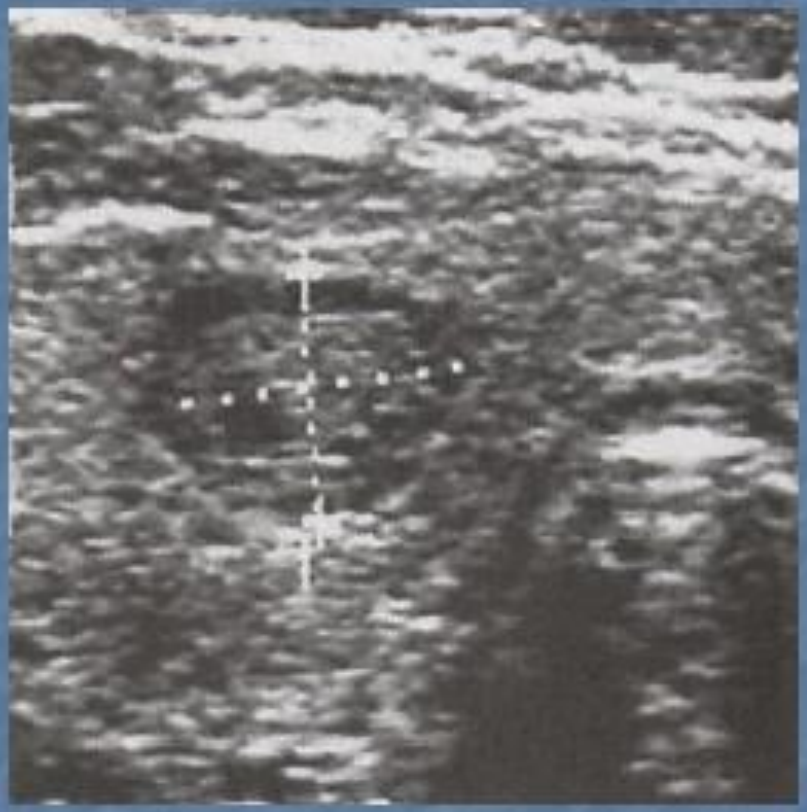
- TSH level
  - Assess functional status
- Thyroid ultrasound
  - Confirm presence
  - Characterize
  - Detect additional non-palpable nodules
  - Identify lymphadenopathy

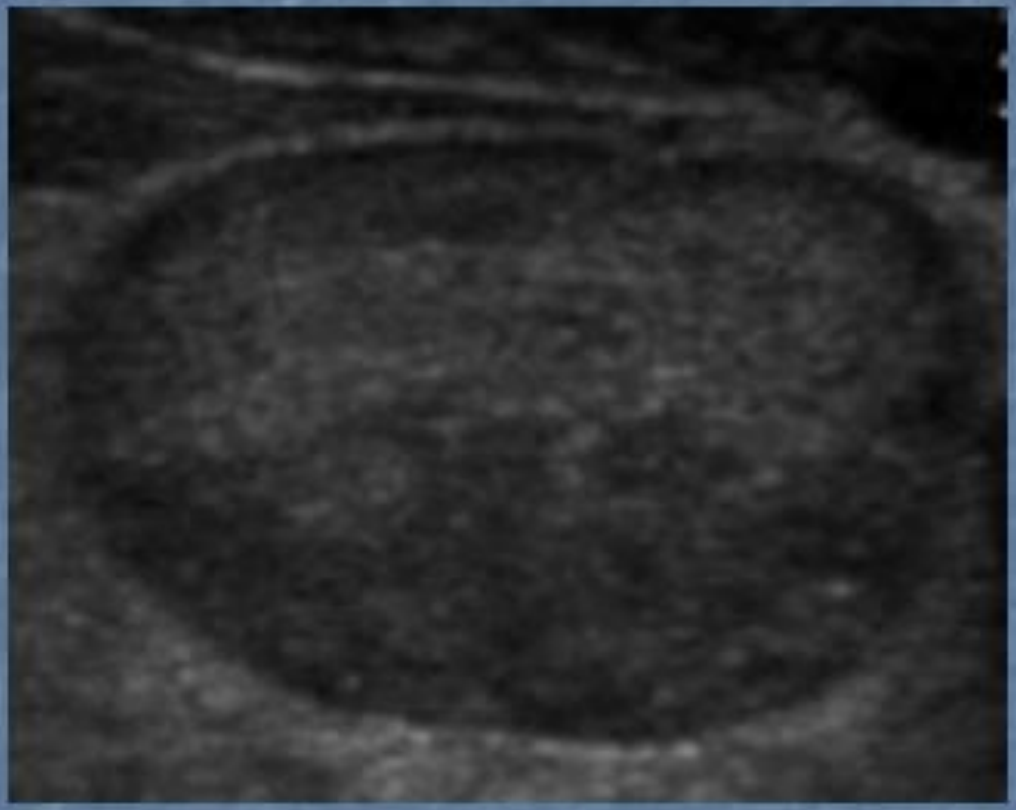
US Characteristics

US Feature	Sens (%)	Spec (%)	PPV Value (%)	NPV Value (%)
Microcalcifications	26- 59	85-95	24-71	42-94
Hypoechogenicity	26-87	43-94	11-68	74-94
Irregular margins	17-78	39-85	9-60	39-98
Solid	69-75	52-56	16-27	88-92
Intranodular Vascularity	54-74	79-81	24-42	86-97
Tall > Wide (Trans)	32	93	68	75

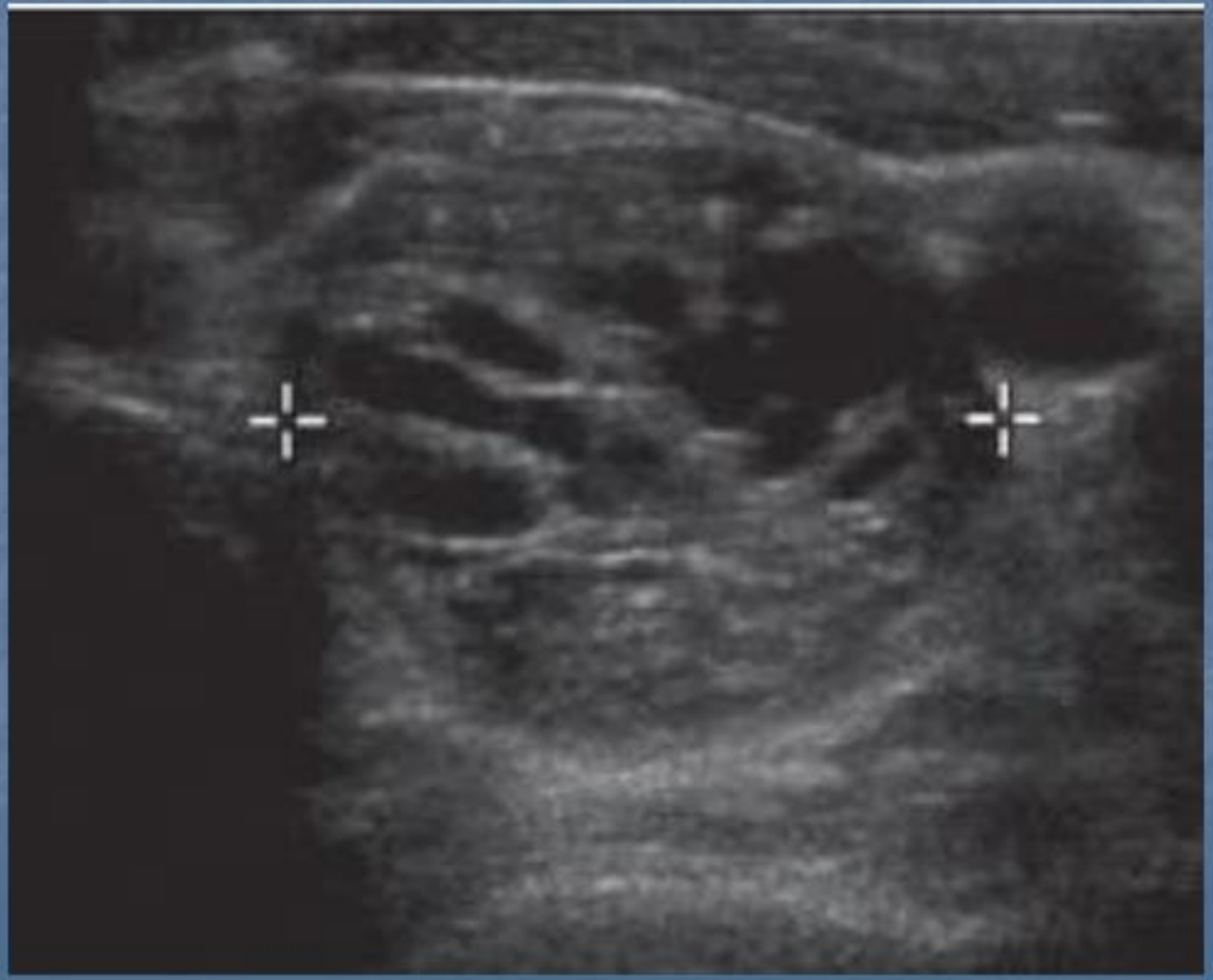
Frates et al. Radiology 2005; 237:794–800

Nodule Halo



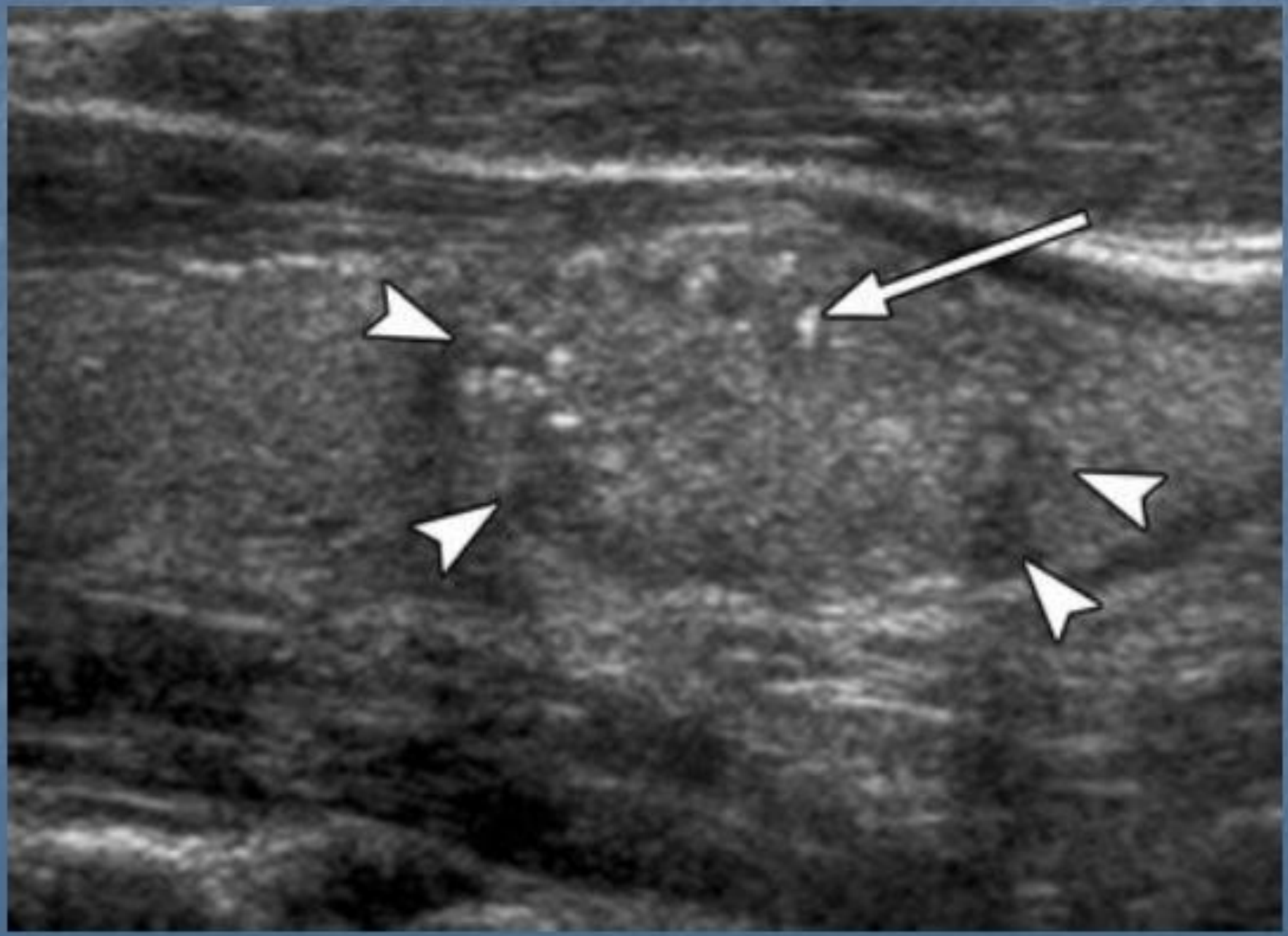


Spongiform Nodule

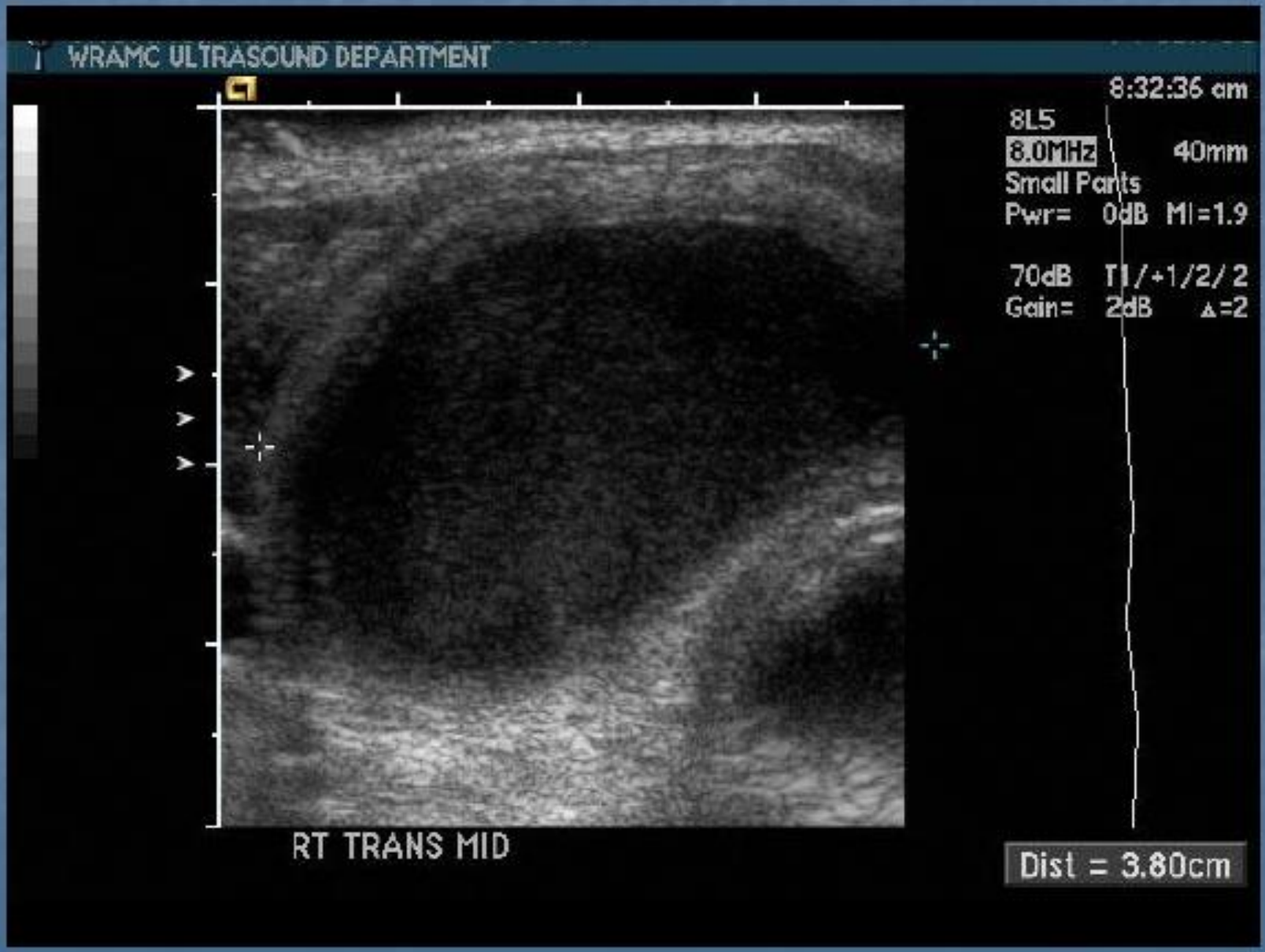


V. Bernet, FAES 2014

Microcalcifications

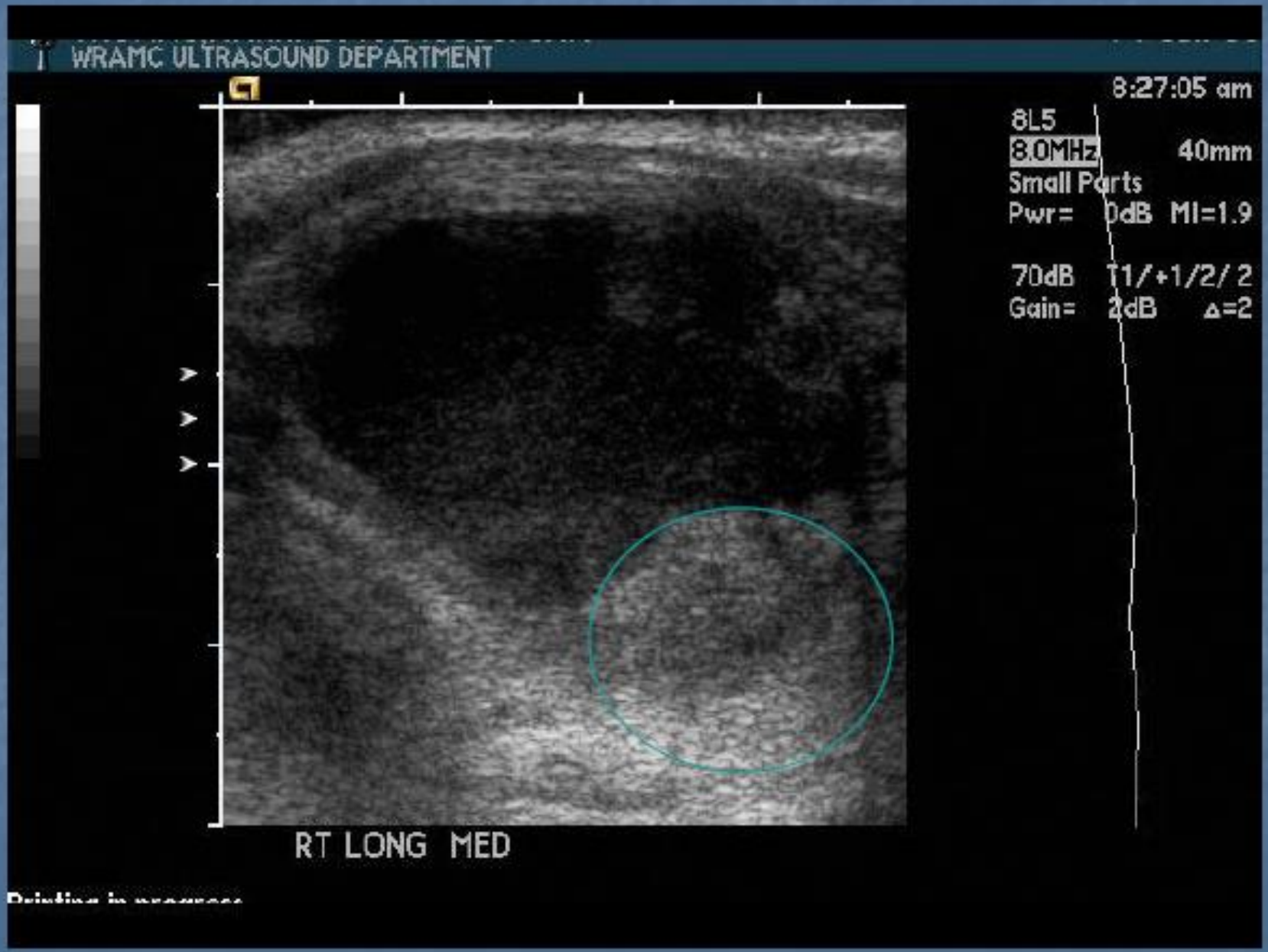


Simple Cyst ?



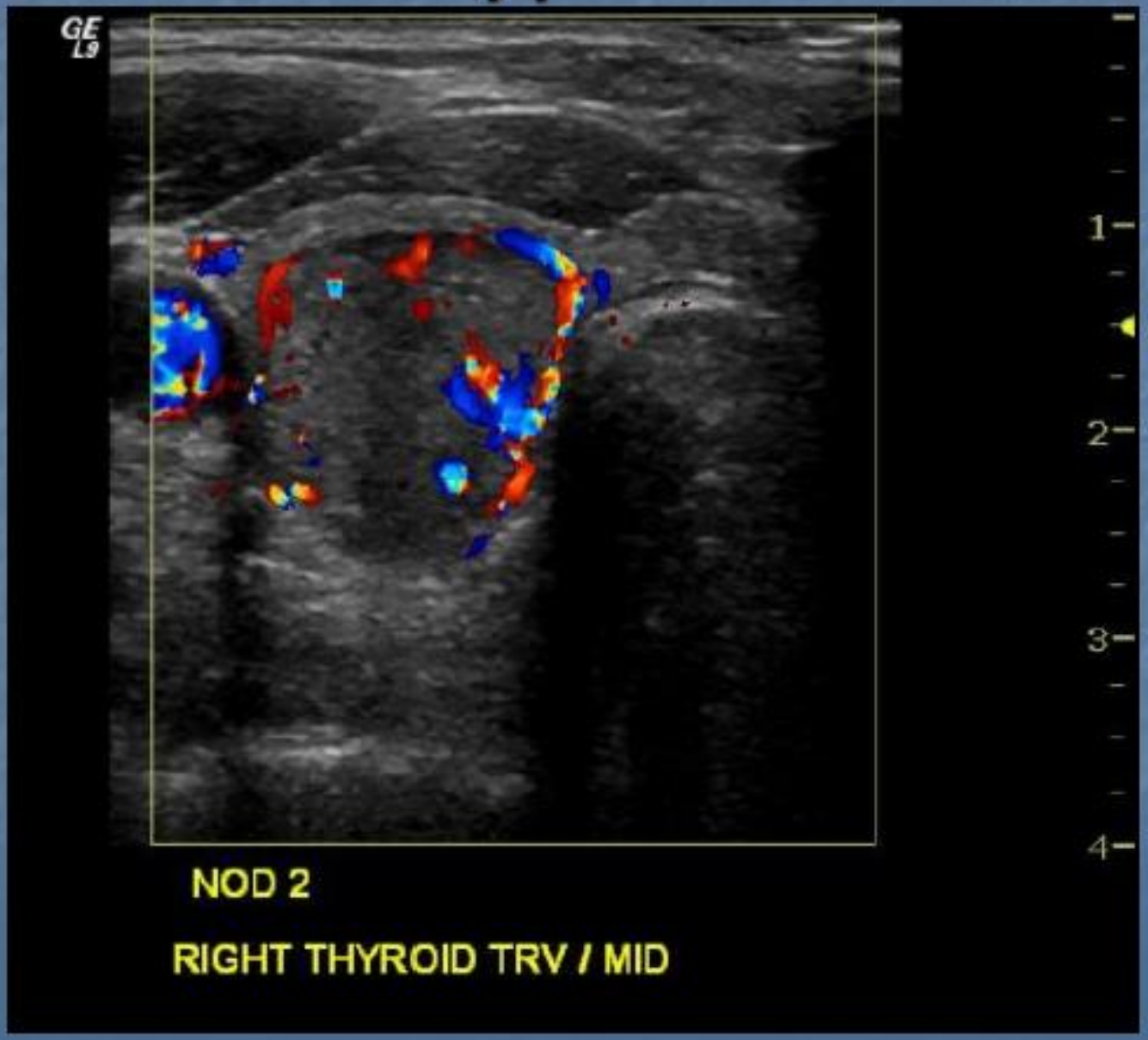
V. Bernet, FAES 2014

Complex Cyst



V. Bernet, FAES 2014

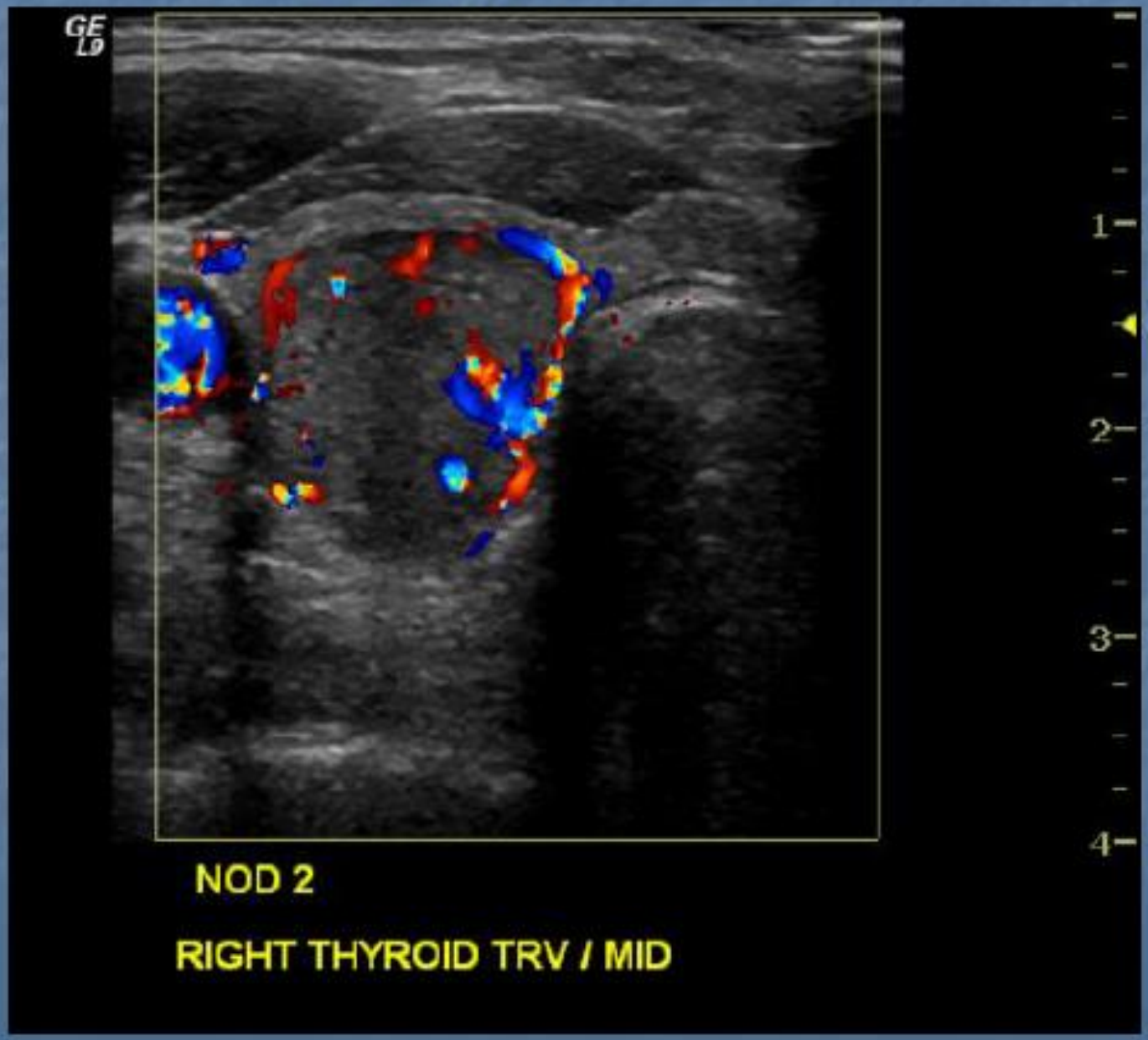
Vascularity
Type II



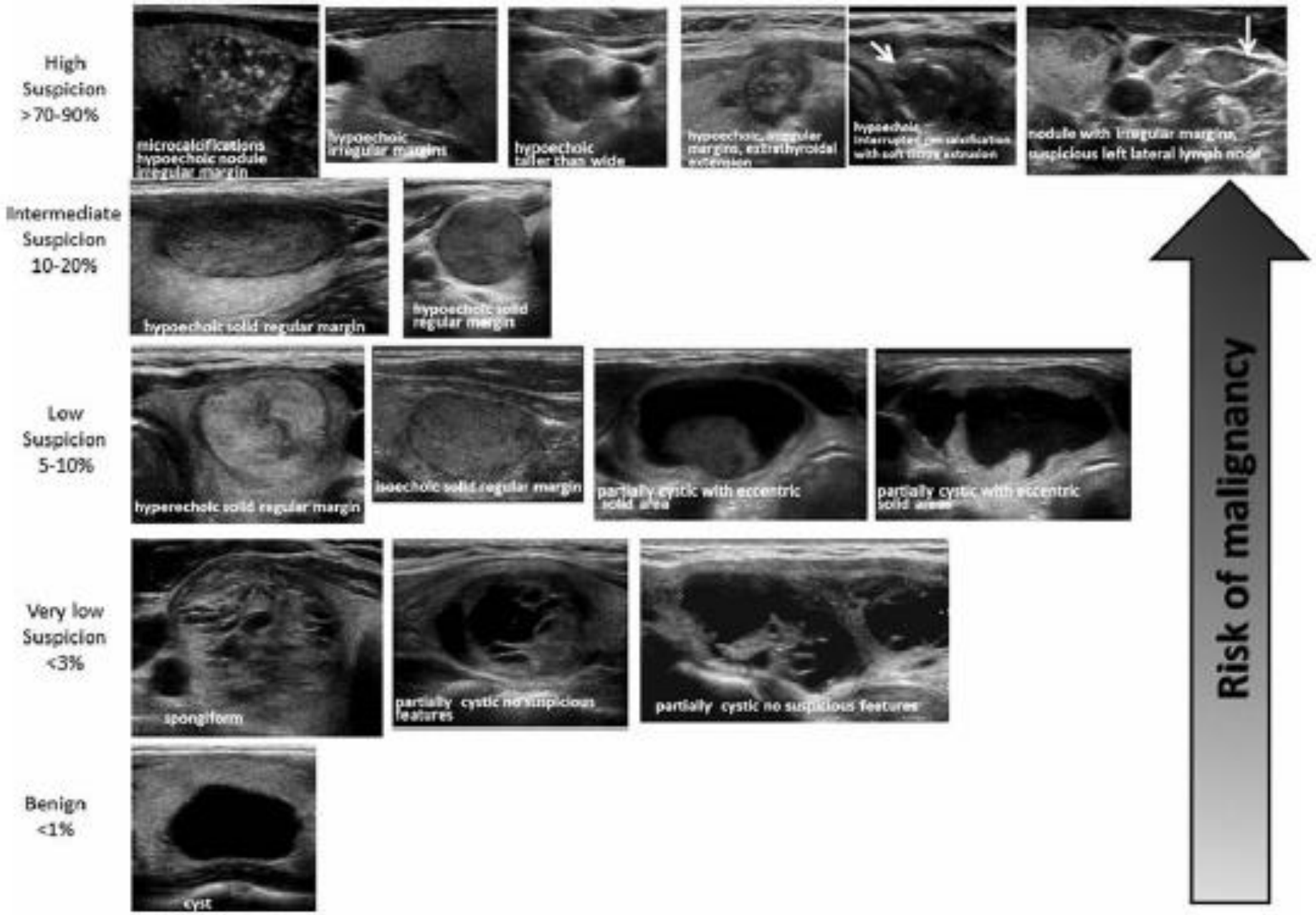
V. Bernet, FAES 2014

Tall > Wide
Trans

AP- 1.6 cm
Width- 1.3 cm

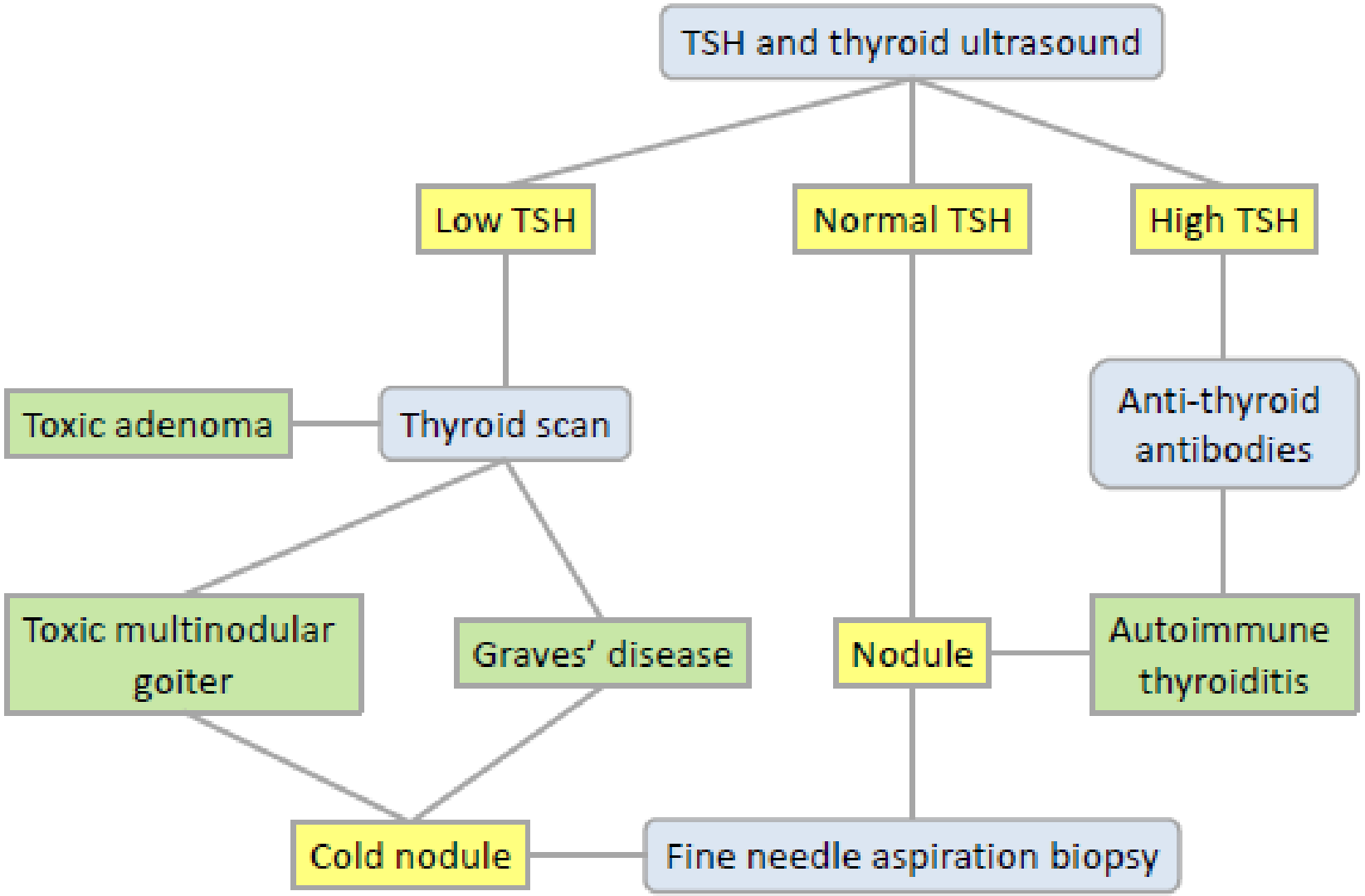


V. Bernet, FAES 2014


High Suspicion >70-90%
microcalcifications hypoechoic nodule regular margin
hypoechoic irregular margins
hypoechoic taller than wide
hypoechoic, irregular margins, extrathyroidal extension
hypoechoic interrupted rim calcification with soft tissue extension
nodule with irregular margins, suspicious left lateral lymph node
Intermediate Suspicion 10-20%
hypoechoic solid regular margin
hypoechoic solid regular margin
Low Suspicion 5-10%
hyperechoic solid regular margin
isoechoic solid regular margin
partially cystic with eccentric solid area
partially cystic with eccentric solid area
Very low Suspicion <3%
spongiform
partially cystic no suspicious features
partially cystic no suspicious features
Benign <1%
cyst
Risk of malignancy

^{18}FDG PET and Incidental Nodule Summary

- Malignancy Risk ↑
  - Focal uptake
  - Euthyroid
  - SUV max > 5.0 max


TSH and thyroid ultrasound
Low TSH
Normal TSH
High TSH
Toxic adenoma
Thyroid scan
Anti-thyroid antibodies
Toxic multinodular goiter
Graves' disease
Nodule
Autoimmune thyroiditis
Cold nodule
Fine needle aspiration biopsy

Thyroid Nodules: FNA Criteria

- > 1.0 cm
  - Hypoechoic nodules
  - Nodules with suspicious features
- > 1.5 cm
  - Isoechoic nodules
  - Hyperechoic nodules
- > 2.0 cm
  - Spongiform nodules

Thyroid Nodules: FNA Criteria

- Suspicious features
  - Irregular margins
  - Microcalcifications
  - Coronal height > width
  - Extrathyroidal extension
  - Extrusion through a rim of calcification

Bethesda System for Reporting Thyroid Cytopathology

	Malignant
Benign	0 - 3%
Atypia of undetermined significance	20 - 25%
Suspicious for a follicular neoplasm	15 - 30%
Suspicious for malignancy	60 - 77%
Malignant	97 - 99%

Thyroid Nodules: Management

- Benign
  - Monitor with serial imaging
- Atypia of undetermined significance
  - Repeat biopsy +/- genetic profiling (Afirma®, ThyroSeq®)
- Suspicious for a follicular neoplasm
  - Repeat biopsy +/- genetic profiling
- Suspicious for malignancy
  - Hemithyroidectomy or total thyroidectomy
- Malignant
  - Total thyroidectomy

Question 1

A 33 year-old male is noted to have palpable enlargement of the right side of his thyroid. Ultrasound reveals a 3.1 cm nodule with smooth borders. Lab tests show TSH 0.1 mU/L (0.5 - 5.2 mU/L) and T4 11.5 µg/dL (4.6 - 10.7 µg/dL). He reports a history of symptomatic palpitations and weight loss of 5 lbs over the course of 3 months, despite an increase in his appetite. He is not taking any medications and has not noted any problems with dysphagia or dysphonia.

Question 1

What should you do next?

A. Perform a fine needle aspiration biopsy of the right sided nodule
B. Administer a 15 mCi dose of I-131
C. Refer the patient to a thyroid surgeon
D. Start Methimazole at a dose of 5 mg daily
E. Check a radioiodine scan and uptake

Question 1

What should you do next?

A. Perform a fine needle aspiration biopsy of the right sided nodule
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C. Refer the patient to a thyroid surgeon
D. Start Methimazole at a dose of 5 mg daily
E. Check a radioiodine scan and uptake

Thyroid Case

- 42 yo W for annual physical
- -feels well
- -no PMH, no meds
- -no FH
- On PE, vitals nl
- -palp possible R thyroid nodule, not mobile
- with swallowing
- -labs show TSH 1.7 uU/mL (0.5-5.0)

Thyroid Case

- -Thyroid US of neck shows R 1.5 cm hypoechoic nodule with internal microcalcifications
- **Which of the following is the most appropriate next step in management?**
- A. CT with contrast of neck
- B. Fine needle aspiration of the nodule
- C. Levothyroxine therapy
- D. Measurement of serum thyroglobulin
- E. Thyroid scan with technetium

Thyroid Case

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- **Which of the following is the most appropriate next step in management?**
- A. CT with contrast of neck
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- C. Levothyroxine therapy
- D. Measurement of serum thyroglobulin
- E. Thyroid scan with technetium

Adrenal Incidentalomas

Adrenal Incidentaloma

Prevalence

- Autopsy series: 1.4 – 2.9%
- Mayo Clinic series (>61,000 CTs/5 yrs): 0.4%
- Lung cancer patients: 4% (1/4 benign)

Mansmann, et. al. Endocrine Reviews, April 2004, 25(2): 309-340

Incidentally Disovered Adrenal Masses

- Adrenal tumors are incidentally discovered in 1-10% of adults.
- A minority represent malignant entities (primary adrenal malignancy or extra-adrenal metastasis)
- The majority are determined to be benign and "nonfunctional" and therefore are considered to pose *no* health risk.
- In contrast, ~10-15% of adrenal tumors autonomously secrete adrenal hormones. These "functional" tumors are associated with an increased risk for cardiometabolic outcomes, such as CV disease, diabetes, and osteoporosis/fracture.
- Therefore, all incidentally discovered adrenal tumors should be carefully evaluated to determine whether they are: 1) **malignant** and/or 2) **functional**.

Nieman LK. JCEM 2010; Young et al. NEJM 2007; Zeiger et al. Endocr Pract 2009; Fassnacht EJE 2016

Differential Diagnosis of Adrenal Mass

	NON-FUNCTIONAL	FUNCTIONAL
BENIGN		
MALIGNANT		

Differential Diagnosis of Adrenal Mass

	NON-FUNCTIONAL (85-95%)	FUNCTIONAL (5-15%)
BENIGN (~90-95%)	**Adrenocortical Adenoma** Myelolipoma Neuroblastoma Ganglioneuroma Cyst Hemorrhage Infection (fungal, tuberculous) Hemangioma	
MALIGNANT (~5%)		

Differential Diagnosis of Adrenal Mass

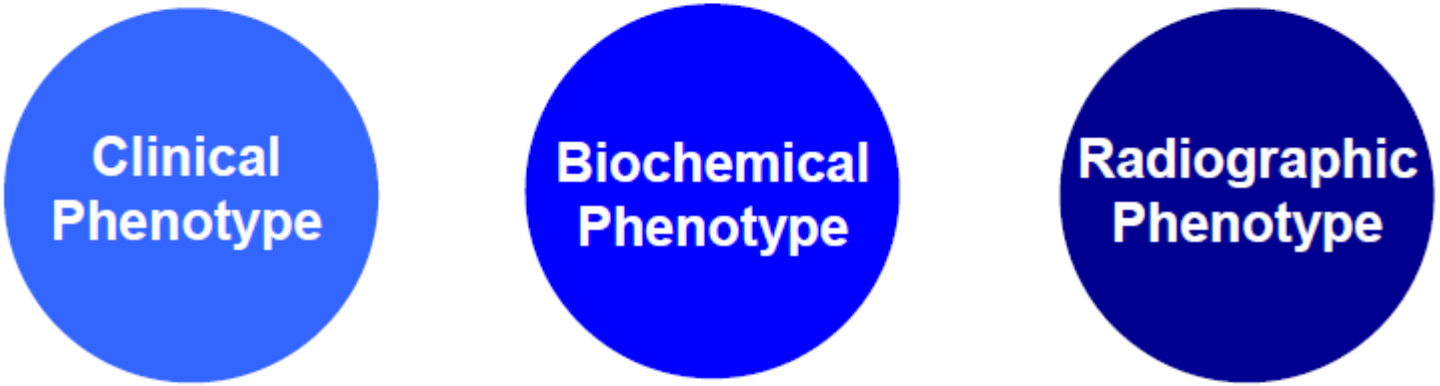
	NON-FUNCTIONAL (85-95%)	FUNCTIONAL (5-15%)
BENIGN (~90-95%)	**Adrenocortical Adenoma**	**Adrenocortical Adenoma**
	Myelolipoma	*Aldosterone producing*
	Neuroblastoma	*Cortisol producing*
	Ganglioneuroma	Micro- or Macro-nodular Disease
	Cyst	*Aldosterone producing*
	Hemorrhage	*Cortisol producing*
	Infection (fungal, tuberculous)	Pheochromocytoma
	Hemangioma	
MALIGNANT (~5%)		

Differential Diagnosis of Adrenal Mass

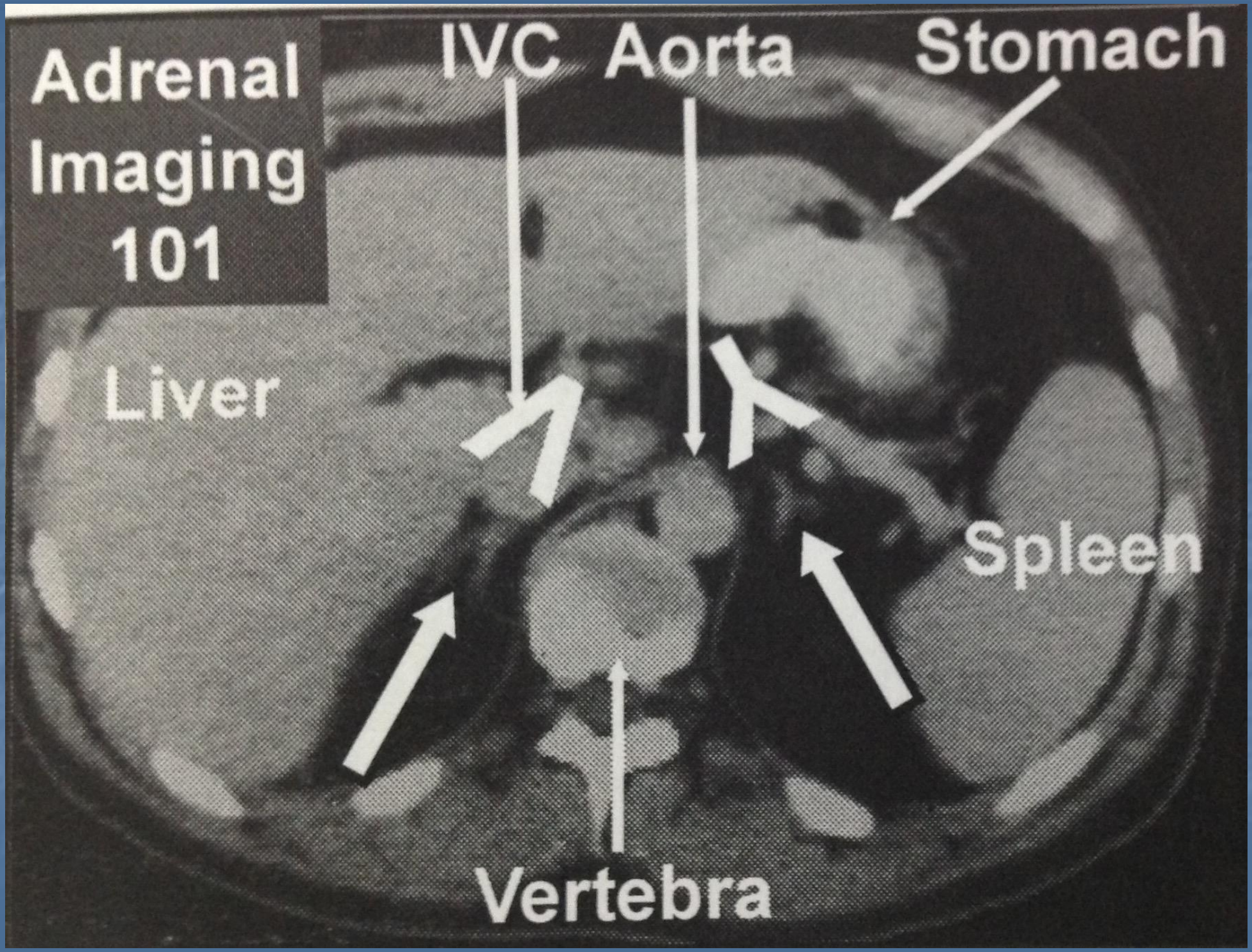
	NON-FUNCTIONAL (85-95%)	FUNCTIONAL (5-15%)
BENIGN (~90-95%)	**Adrenocortical Adenoma**	**Adrenocortical Adenoma**
	Myelolipoma	*Aldosterone producing*
	Neuroblastoma	*Cortisol producing*
	Ganglioneuroma	Micro- or Macro-nodular Disease
	Cyst	*Aldosterone producing*
	Hemorrhage	*Cortisol producing*
	Infection (fungal, tuberculous)	Pheochromocytoma
	Hemangioma	
MALIGNANT (~5%)	Adrenocortical carcinoma	Adrenocortical carcinoma
	Metastatic cancer from a non-adrenal primary	Pheochromocytoma

General Diagnostic Approach

1. *Is there evidence for malignancy?*
2. *Is there adrenal hormone excess?*

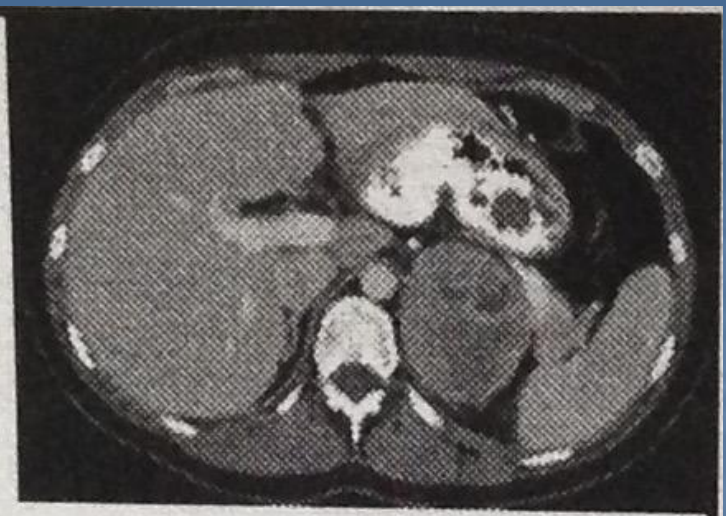


Clinical Phenotype	Biochemical Phenotype	Radiographic Phenotype
History and physical exam for evidence of hormone excess or malignancy	Laboratory evaluation for evidence of adrenal hormone excess	Radiographic evidence supportive of a benign or malignant mass



W Young, CEU 2012

Hounsfield Unit (HU) Density



+60 HU

More lipid

Benign

-20 HU

Less lipid

Pheo

ACC

Met

Lipid-poor adenoma

Characteristics of Adrenal Incidentalomas on Imaging (Imaging Phenotype)

Table 3. Characteristics of Adrenal Incidentalomas on Imaging (Imaging Phenotype).*

Variable	Adrenocortical Adenoma	Adrenocortical Carcinoma	Pheochromocytoma	Metastasis
Size	Small, usually ≤3 cm in diameter	Large, usually >4 cm in diameter	Large, usually >3 cm in diameter	Variable, frequently <3 cm
Shape	Round or oval, with smooth margins	Irregular, with unclear margins	Round or oval, with clear margins	Oval or irregular, with unclear margins
Texture	Homogeneous	Heterogeneous, with mixed densities	Heterogeneous, with cystic areas	Heterogeneous, with mixed densities
Laterality	Usually solitary, unilateral	Usually solitary, unilateral	Usually solitary, unilateral	Often bilateral
Attenuation (density) on unenhanced CT	≤10 Hounsfield units	>10 Hounsfield units (usually >25)	>10 Hounsfield units (usually >25)	>10 Hounsfield units (usually >25)
Vascularity on contrast-enhanced CT	Not highly vascular	Usually vascular	Usually vascular	Usually vascular
Rapidity of washout of contrast medium	≥50% at 10 minutes	<50% at 10 minutes	<50% at 10 minutes	<50% at 10 minutes
Appearance on MRI†	Isointense in relation to liver on T_2-weighted image	Hyperintense in relation to liver on T_2-weighted image	Markedly hyperintense in relation to liver on T_2-weighted image	Hyperintense in relation to liver on T_2-weighted image
Necrosis, hemorrhage, or calcifications	Rare	Common	Hemorrhage and cystic areas common	Occasional hemorrhage and cystic areas
Growth rate	Usually stable over time or very slow (<1 cm per year)	Usually rapid (>2 cm per year)	Usually slow (0.5 cm to 1.0 cm per year)	Variable, slow to rapid

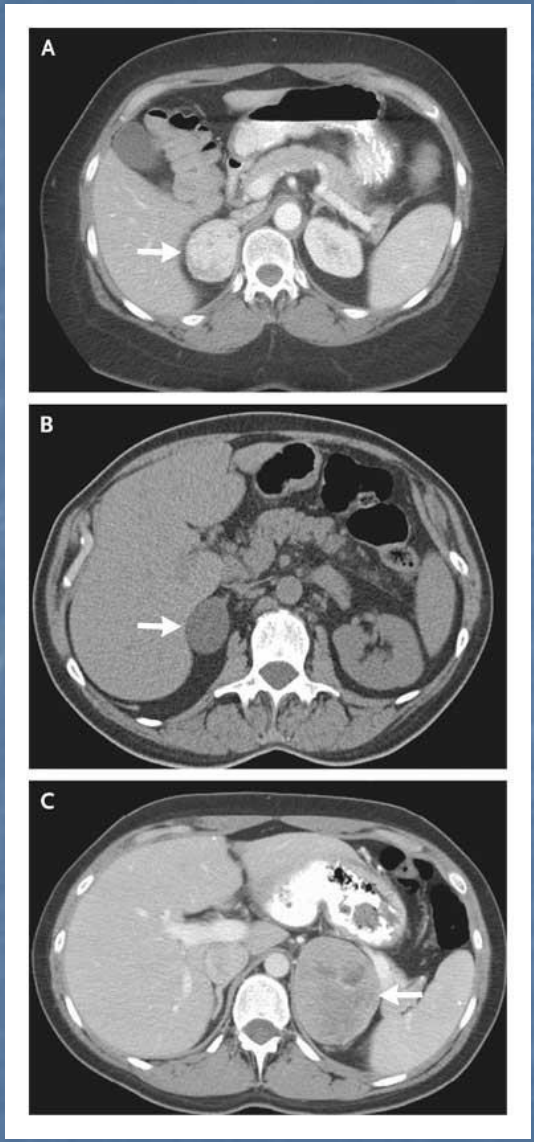
* Adrenal hemorrhage and myelolipoma are usually easily characterized because of their distinctive imaging characteristics.[24,25] Myelolipomas are composed of myeloid, erythroid, and adipose tissue. On imaging, they have low attenuation on unenhanced CT, and they are hyperintense on T_1-weighted in-phase MRI. The presence of pure fat within an adrenal lesion on CT is consistent with the presence of a myelolipoma. Acute adrenal hemorrhage has increased attenuation on unenhanced CT, and on T_1-weighted MRI, there is hyperintensity secondary to methemoglobin. In a chronic adrenal hemorrhage, a dark rim develops along the periphery of the mass on the T_2-weighted image because of the hemosiderin-laden macrophages.

† If the imaging characteristics are indeterminate on both unenhanced and enhanced CT, MRI may be considered to clarify the imaging phenotype.

Young W. N Engl J Med 2007;356:601-610

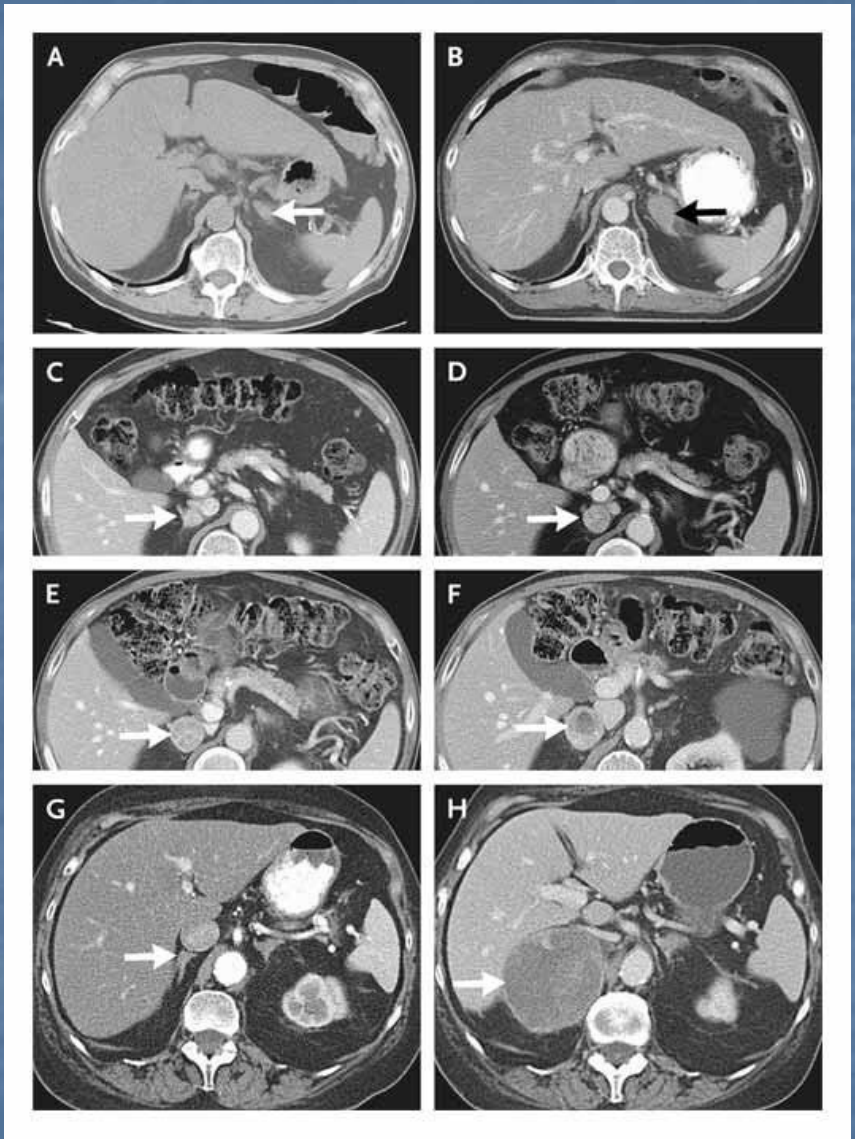
The NEW ENGLAND JOURNAL of MEDICINE

Pheochromocytoma (Panel A), Benign Cortical Adenoma (Panel B), and Adrenocortical Carcinoma (Panel C)



Young W. N Engl J Med 2007;356:601-610

Serial CT Scans Showing Metastatic Disease to the Adrenal Gland (Panels A and B), a Benign Pheochromocytoma (Panels C through F), and Adrenocortical Carcinoma (Panels G and H)



Young W. N Engl J Med 2007;356:601-610

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Clinical Phenotype

Overt Cortisol Excess

- Obesity/weight gain
- Lipodystrophy
  - Central adiposity
  - Supraclavicular fat pads
  - Dorsocervical fat pad
  - Rounded face
- Hyperglycemia/Diabetes
- Hypertension
- Insomnia
- Mood disorder/Psychosis
- Osteoporosis
- Immunesuppression
- Platelet dysfunction
- Hypercoagulable state
- Myopathy
- Atrophic skin

Overt Catecholamine Excess

- Episodic symptoms
  - Hypertension
  - Palpitations
  - Anxiety/Panic
  - Sweats/Tremors
  - Headache
  - Arrhythmia

Overt Aldosterone Excess

- Hypertension
- Hypokalemia

Adrenal Incidentaloma

Evaluation for Malignancy

- Size
- Radiographic findings
- FNA biopsy (first exclude pheo)

Adrenal Incidentaloma Management

- Indications for surgery
  - Functional, clinically apparent cortical lesions
  - Pheochromocytoma
  - Lesions > 6cm
- Indications for clinical follow-up
- Dilemma: Subclinical hypercortisolism

Mansmann, et. al. Endocrine Reviews, April 2004, 25(2): 309-340

Case 2

- 46 year old pre-menopausal woman was in a car accident.

- No known medical conditions

- Brought to ER and complained of some abdominal pain. Had a rapid unenhanced Abdominal CT that revealed no hemorrhage or other injuries

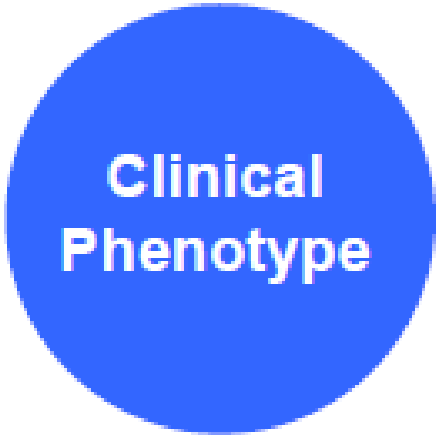
- Incidental discovery of a 2.2 cm R adrenal mass, with 5 HU unenhanced density

What, if anything, do you tell her about the incidental adrenal mass??

Case 2 – Clinical Phenotype

- No symptoms
- No signs to suggest hypercortisolism, pheochromocytoma, hyperaldosteronism, or hirsutism.

- No evidence of weight loss, abdominal distention, or androgen excess, to suggest metastatic cancer or hyperfunctioning adrenocortical carcinoma



Unrevealing

Question 2

A 2.2 cm adrenal nodule with an unenhanced density of 5 HU on CT is most suggestive of:

A)Myelolipoma
B)Adrenocortical adenoma
C)Pheochromocytoma
D)Metastatic lung cancer to the adrenal gland
E)Adrenocortical carcinoma

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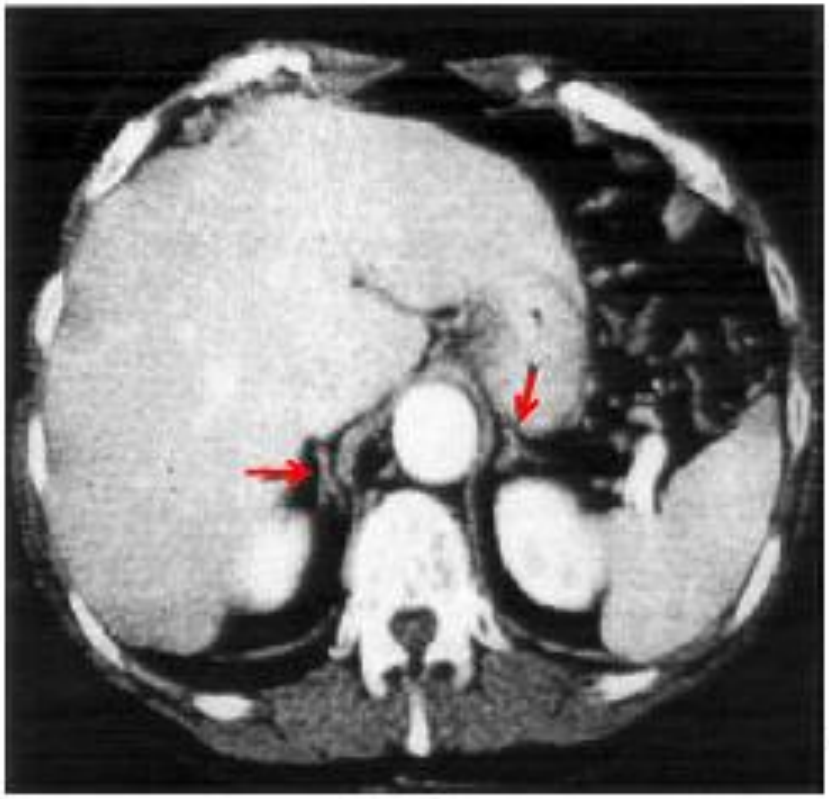
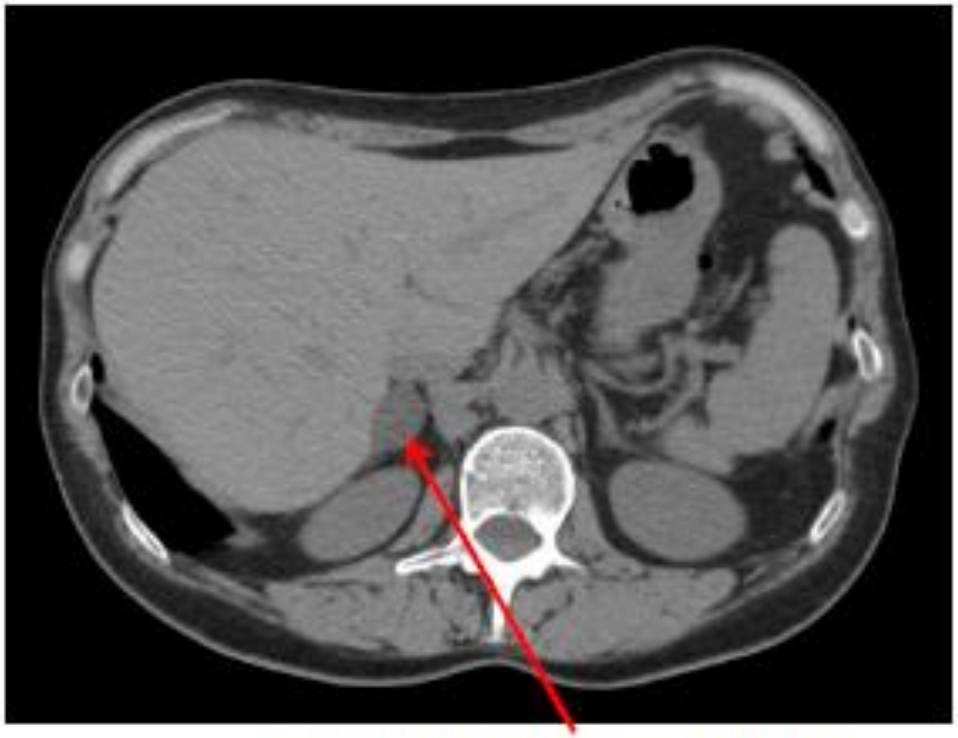
Case 2 – Radiographic Phenotype

Normal comparison



Patient's non-contrast CT



2.2cm right adrenal mass
5 Hounsfield units
Round, homogenous

Case 2 – Radiographic Phenotype

Characteristic	Likely Benign	Potentially Malignant
Size	< 4 cm	> 4-6 cm
Attenuation on unenhanced CT	< 10 HU	> 10 HU
Contrast washout on CT protocol at 15 minutes	>50-60%	<50%
MRI chemical shift suggestive of lipid-rich content	Yes	No
FDG avidity on PET	No	Yes
Irregular Borders	No	Yes
Heterogeneous content	No	Yes
Necrosis	No	Yes
Calcifications	No	Yes
Rate of Growth	< 1cm/y	> 1cm/y

Radiographic Phenotype

BENIGN: Suggestive of adrenocortical adenoma

Miller. Nature Rev Endo 2014
Validya. Scientific American Medicine 2015

Case 2 – Biochemical Phenotype

*Suggested **screening biochemical evaluation** for adrenal masses:*

Condition	Patients	Test	Abnormal Value
Autonomous cortisol secretion	ALL	1 mg Dexamethasone Suppression Test	Nonfunctional: ≤1.8 mcg/dL Possible: 1.9-5.0 mcg/dL Autonomous: 5.0 mcg/dL
Primary Aldosteronism	HTN and/or hypokalemia	Serum aldosterone to plasma renin activity ratio (ARR)	• Suppressed PRA • ARR>20-25
Pheochromocytoma	ALL (almost)	Plasma (or urinary) fractionated metanephrines	>2-4x ULRR
Adrenal androgen excess	Hirsutism or virilization	DHEAS Total Testosterone	Higher than ULN

Fassnacht EJE 2016

Case 2 – Biochemical Phenotype

- 1mg DST #1 => cortisol: **8.0** µg/dL
- 1mg DST #2 => **7.8** µg/dL, ACTH<5 pg/mL
- 8mg DST => **8.1** µg/dL, ACTH<5 pg/mL

- 24h Urine Free Cortisol: **45** µg/24h (<45)

- Midnight Salivary Cortisol:
  3.7, 3.9, **4.6**, **4.3** nmol/L (<4.3)

- Random ACTH: 5 pg/mL
- Plasma metanephrines: normal
- Aldosterone/PRA: not suggestive
- DHEAS: normal

Biochemical Phenotype

Autonomous cortisol secretion?

Case 2 – Clinical Diagnosis

Benign adrenocorticol adenoma

Autonomous cortisol secretion

No clinical signs of hypercortisolism

Should surgery be recommended?

Case 2 – Outcome

- BP = 122/75 mmHg
- Fasting Blood Glucose = 99 mg/dL
- HbA1c = 5.8%
- Bone Mineral Density:
  - Spine T= **-3.2**
  - Femoral Neck T= **-2.2**
  - Total Hip T= **-2.0**

- ***INDIVIDUALIZED DECISION:*** Laparoscopic R adrenalectomy
- Peri-operative IV hydrocortisone considered, but not given
- Pathology revealed 2.5 cm adrenal cortical adenoma
- Post-op AM cortisol 4 mcg/dL, ACTH<10 pg/mL (asymptomatic)
- 1 week post-op, morning cortisol = 17 µg/dL

Comorbidities associated with adrenal tumors with autonomous and "subclinical" cortisol secretion

Comorbidities
Hypertension
Glucose intolerance/type 2 diabetes
Obesity
Dyslipidemia
Osteoporosis/Vertebral Fracture

Fassnacht et al. EJE 2016

Autonomous Cortisol Secretion

Prediction of Vertebral Fractures in Patients With Monolateral Adrenal Incidentalomas

Valentina Morelli,* Cristina Eller-Vainicher,* Serena Palmieri, Elisa Cairoli, Antonio Stefano Salcuni, Alfredo Scillitani, Vincenzo Carnevale, Sabrina Corbetta, Maura Arosio, Silvia Della Casa, Giovanna Muscogiuri, Anna Spada, and Iacopo Chiodini

- Participants with adrenal incidentalomas who developed incident subclinical vertebral fractures detected on BMD and higher 1mg DST (2.7 vs 2.0 mcg/dL).
- Autnomous cortisol secretion associated with ~10-fold higher risk of incident (~3y follow-up) vertebral fracture.

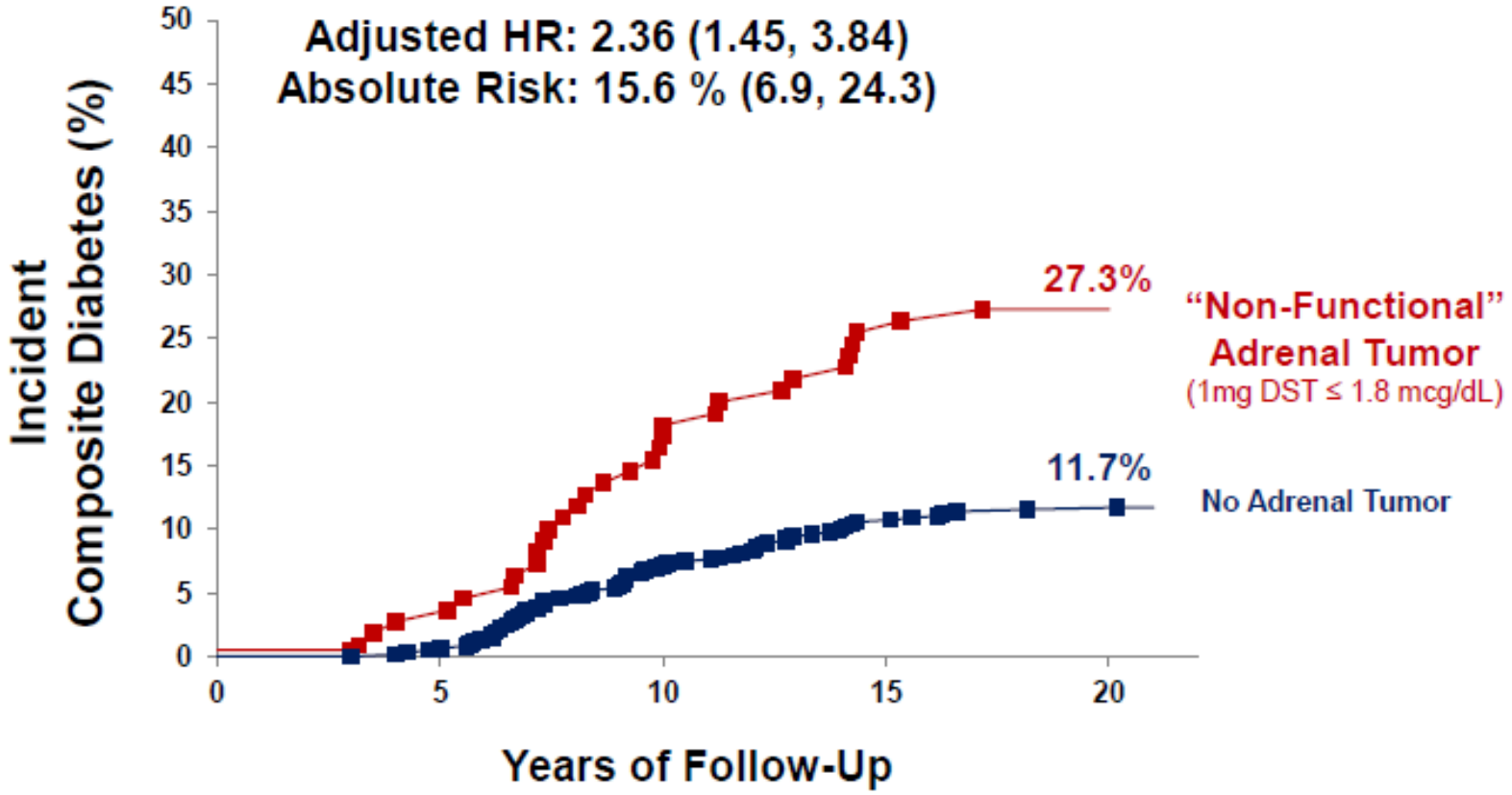
DeBone et al. JCEM 2014
Morelli et al. JCEM 2015

Annals of Internal Medicine ORIGINAL RESEARCH

"Nonfunctional" Adrenal Tumors and the Risk for Incident Diabetes and Cardiovascular Outcomes

A Cohort Study

Diana Lopez, MD; Miguel Angel Luque-Fernandez, PhD, MPH, MSc; Amy Steele, BA; Gail K. Adler, MD, PhD; Alexander Turchin, MD, MS; and Anand Vaidya, MD, MMSc



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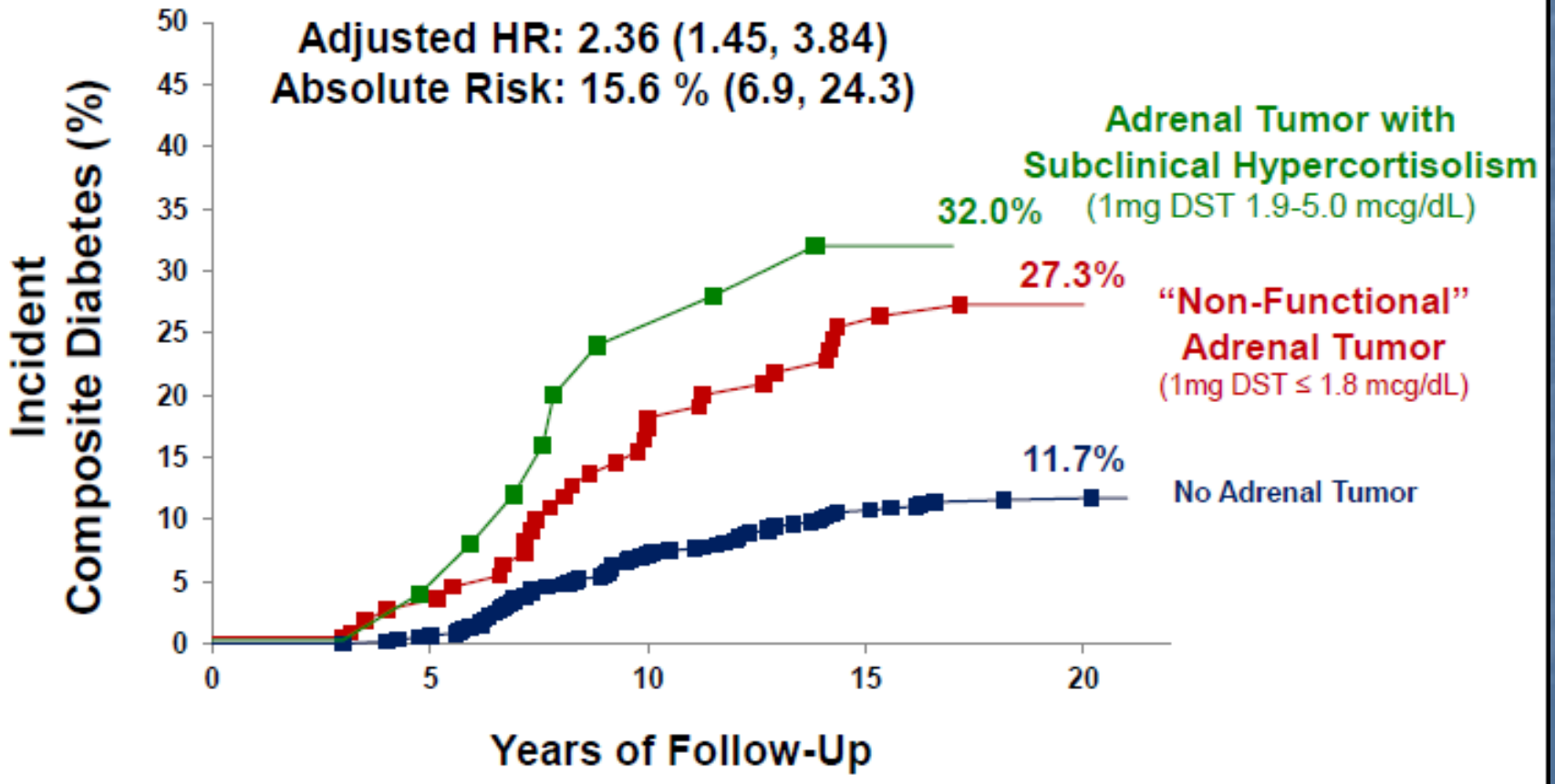
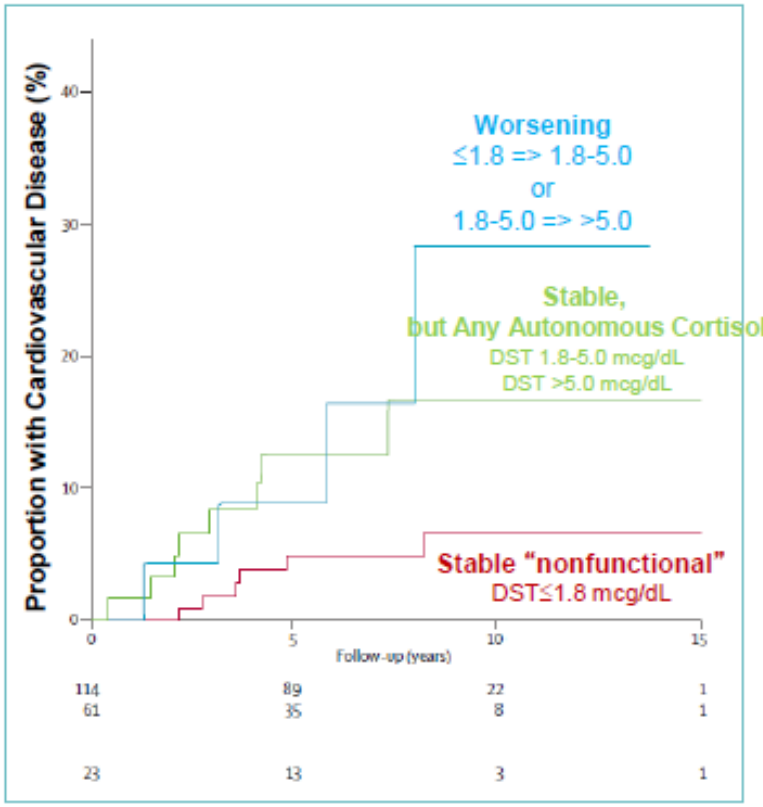
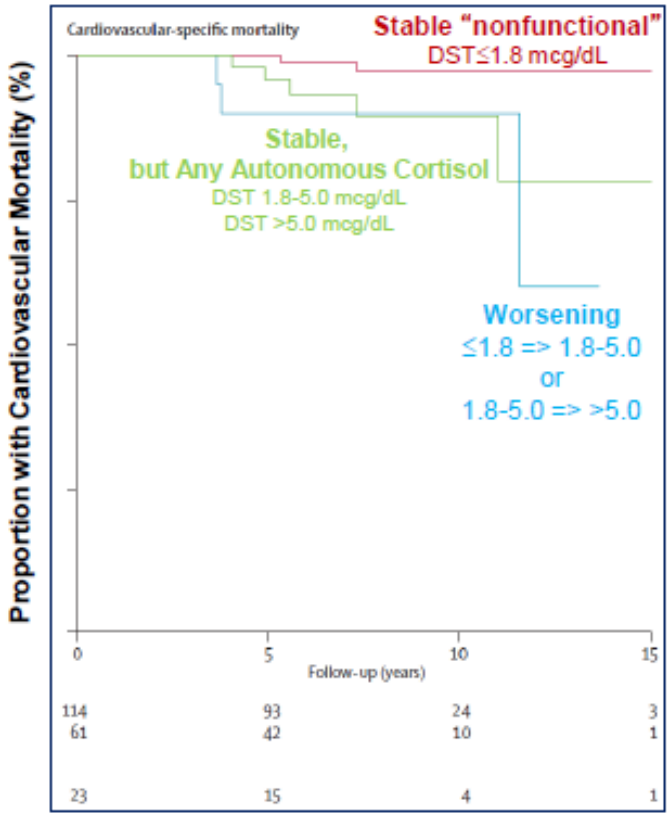


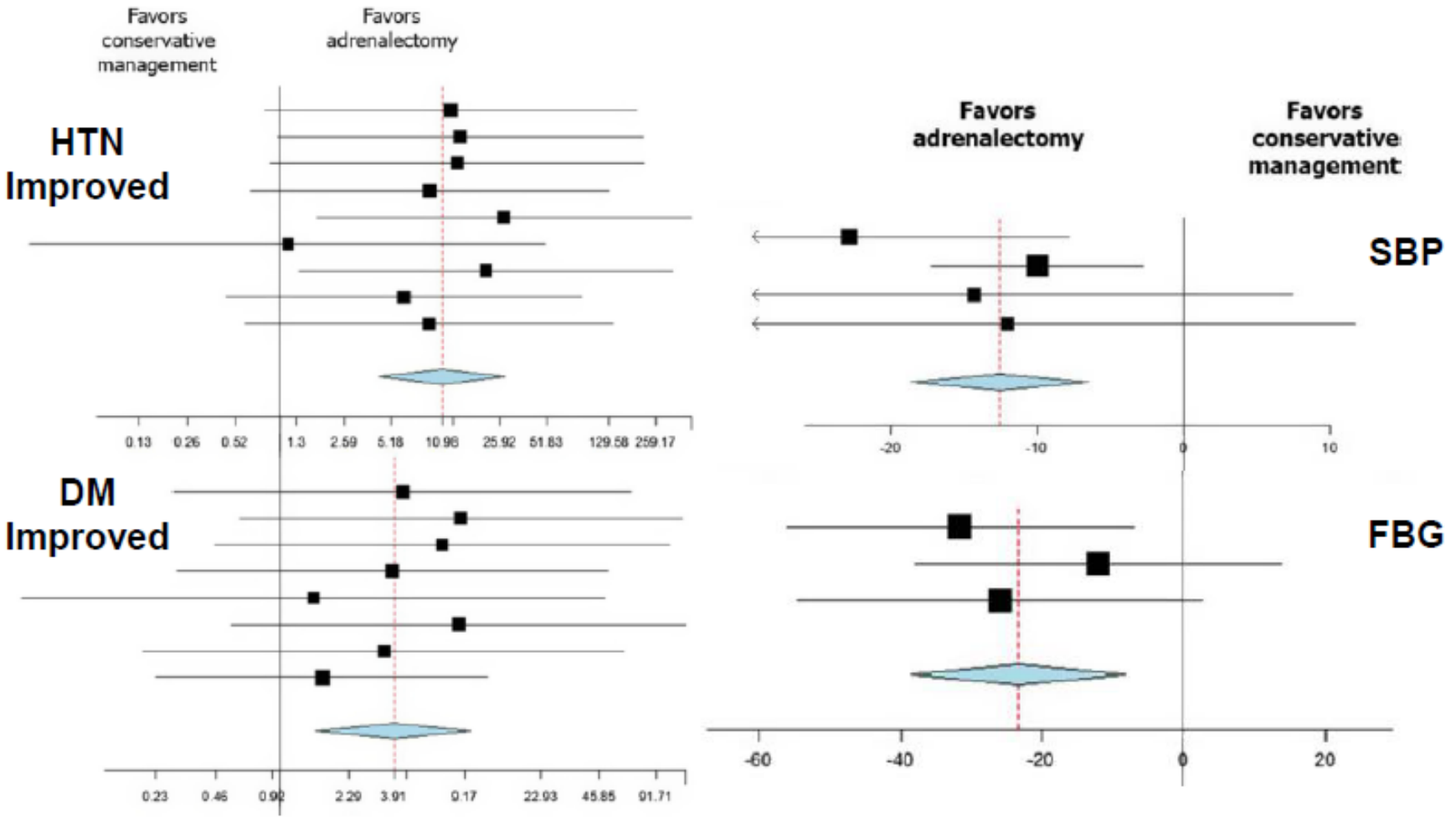
Autonomous Cortisol Secretion





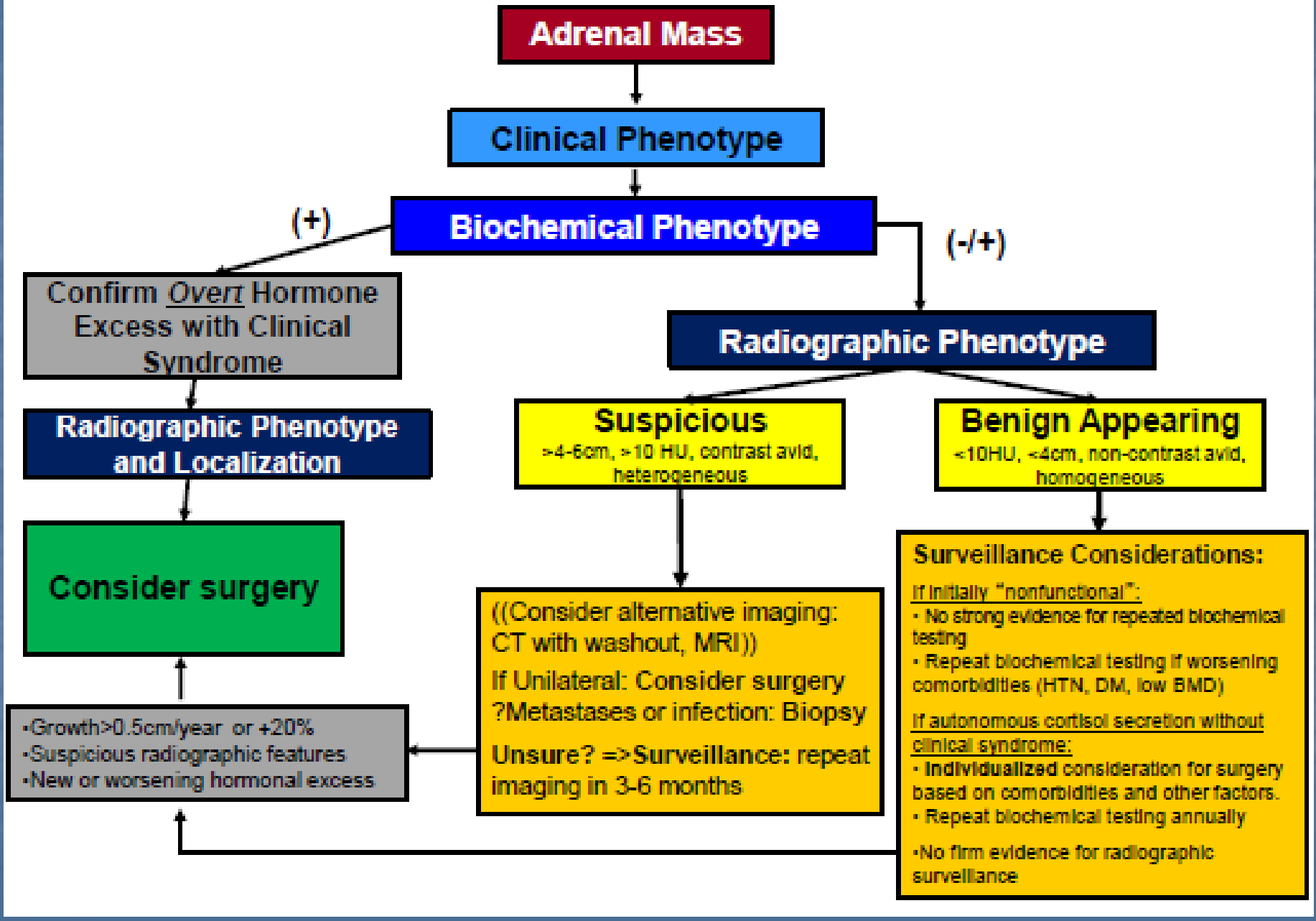
Di Dalmazi et al. Lancet Diabetes & Endo 2014

Should Intervention be Performed?



Bancos et al. EJE 2016

Suggested Diagnostic Algorithm for Incidentally Discovered Adrenal Mass



Adrenal Case

- A 47 yo W is evaluated for an incidentally discovered R adrenal mass.
- On PE, BP 120/80 mmHg both arms and HR 84/min
- -Abd nontender and no palpable masses
- -Remainder unremarkable
- -Noncontrast CT abd demonstrates 3.2 cm, well circumscribed, partially cystic R adrenal lesion with density 30 HU. Low dose DST is negative for evidence of cortisol hypersecretion.

Adrenal Case

- **Which of the following is the most appropriate next step in management**?
- A. Adrenalectomy
- B. CT guided transcutaneous biopsy
- C. Plasma aldosterone to plasma renin ratio
- D. Plasma free metanephrines
- E. No additional testing is indicated

Adrenal Case

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- E. No additional testing is indicated

Pituitary Incidentalomas

Differential Diagnosis of Sellar/Parasellar Lesions

Benign Tumors
- **Pituitary adenoma** (carcinoma)
- Meningioma

Cell Rest Tumors
- Craniopharyngioma
- Rathke's cleft cyst
- Epidermoid
- Chordoma
- Lipoma
- Colloid cyst

Primitive Germ Cell Tumors
- Germinoma
- Teratoma
- Dysgerminoma
- Oligodendroglioma
- Ependymoma
- Astrocytoma

Granulomatous, Infectious, and Inflammatory
- Lymphocytic hypophysitis
- Abscess
- Sarcoidosis
- Tuberculosis
- Eosinophilic granulomatosis
- Mycoses

Metastatic Tumors

Vascular Lesions

Hematologic Malignancies

Miscellaneous
- Empty sella syndrome
- Arachnoid cyst

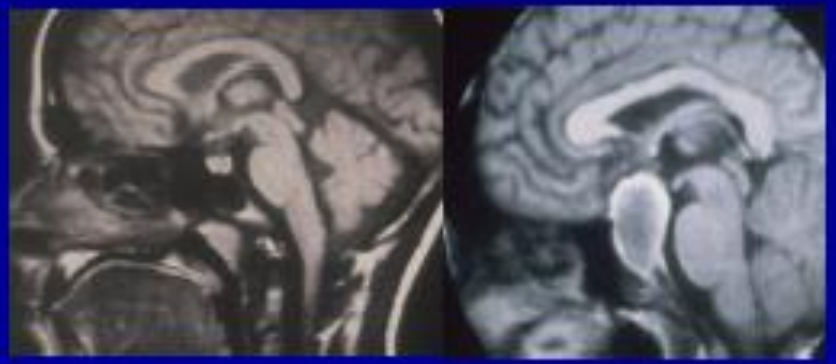
Frequency of Pituitary Adenomas Found at Autopsy

- 19,387 unselected pituitaries examined at autopsy in 30 series
  - 2,084 (10.7%) had pituitary adenomas
    - (range 1.5 – 27.0%)
    - All but 7 were < 10 mm
  - ~40% stained positively for prolactin

Molitch. Neurosurg Clin N Amer 2012;23:543

Pituitary Adenomas: Epidemiology

- Pituitary adenomas are the 3rd most common brain tumor.
- They account for 10-15% of all intracranial tumors.
  - MRI studies 14.4%
  - Autopsy series 12-22.5%
- They are classified according to size.
  - Microadenomas - < 10mm
  - Macroadenomas - > 10 mm

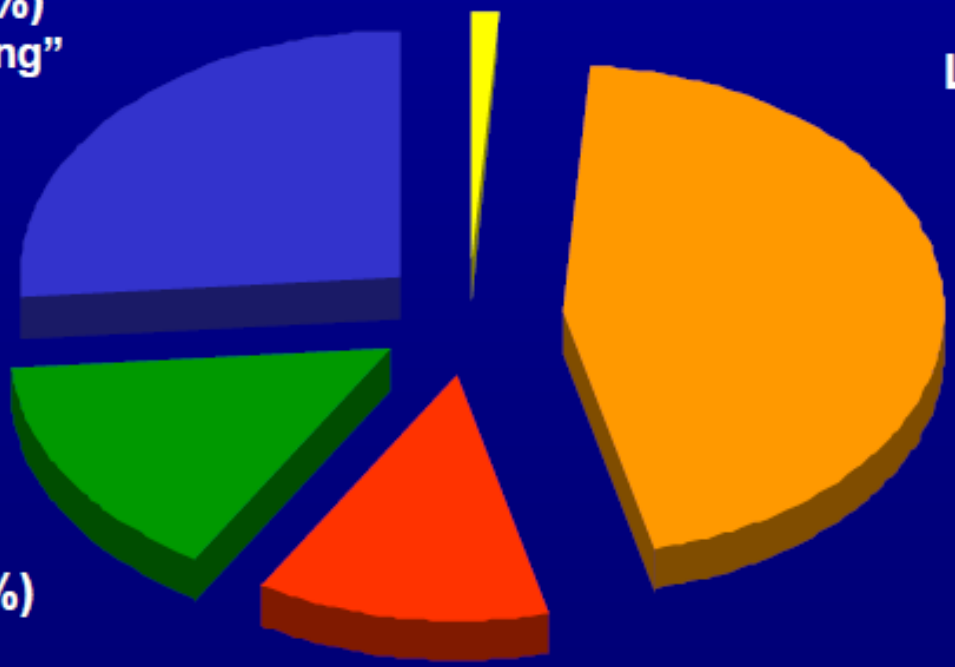


Ezzat Cancer 101: 613, 2004
Daly JCEM 91: 4769, 2006

Pituitary Disorders

- ***Anterior Pituitary***
  - Sellar Masses
    - Pituitary Adenoma
      - Mass effect
      - Hyperfunction
      - Hypofunction
  - Apoplexy
  - Hypopituitarism
- ***Posterior Pituitary***
  - Overproduction of AVP
    - Syndrome of Inappropriate Antiduretic Hormone Secretion (SIADH)
  - Underproduction of AVP
    - Diabetes Insipidus
      - Central (pituitary)
      - Nephrogenic

Pituitary Tumor Subtypes



Thyrotroph (1%)
Hyperthyroidism

Gonadotroph (15-40%)
"Clinically nonfunctioning"
Visual field loss
Hypopituitarism

Lactotroph (40-50%)
Hyperprolactinemia

Somatotroph (10-20%)
Acromegaly

Corticotroph (10-15%)
Cushings Disease

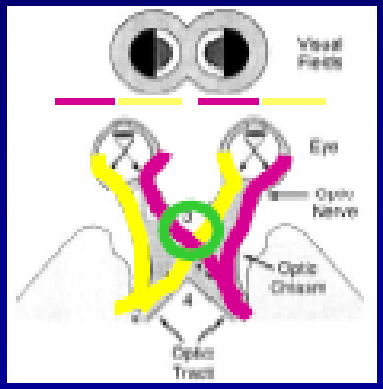
Patient Evaluation

History:

- Question regarding endocrine hypo or hyper function. Think of anterior & posterior pituitary function.

- **Hypofunction:**
  - Hypothyroidism
  - Hypogonadism
  - Adrenal insufficiency
  - GH Deficiency

  Hyperfunction:
  - Hyperthyroidism
  - Prolactin excess
  - Cushings' syndrome
  - GH excess



- Neurological symptoms: headache, visual disturbance.

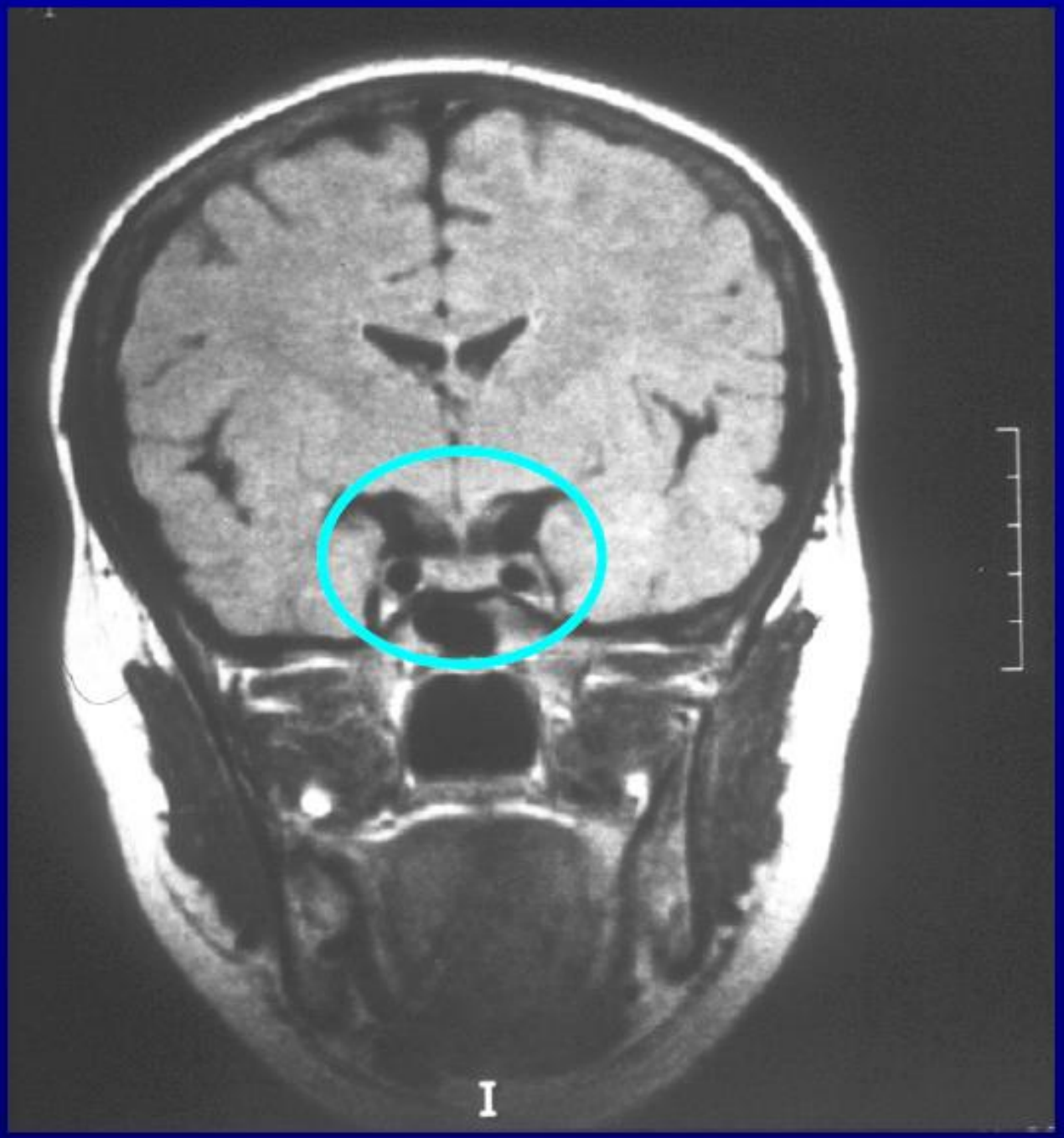
Standard Pituitary Laboratory Tests

- Thyroid
  - TSH, Free T4 (sometimes need Total T4, T3RU)
- Reproductive
  - Prolactin (with dilution if macroadenoma)
  - FSH, LH, testosterone (men) or estradiol (women)
- GH
  - IGF-I, GH
- Adrenal
  - ACTH, Cortisol

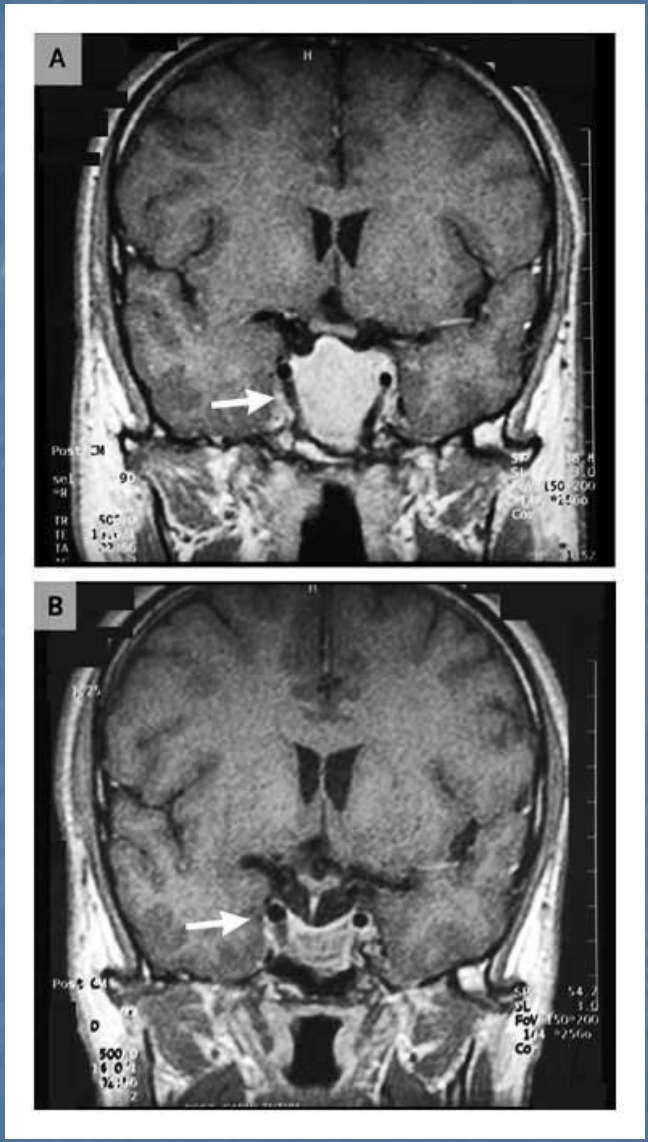
Critical to assess prolactin prior proceeding to surgery

Extra tests required if GH or ACTH excess is suspected

Normal head MRI



MRI Scans Showing Tumor Shrinkage after Treatment with a Dopamine Agonist in a Patient with a Macroprolactinoma



Klibanski A. N Engl J Med 2010;362:1219-1226

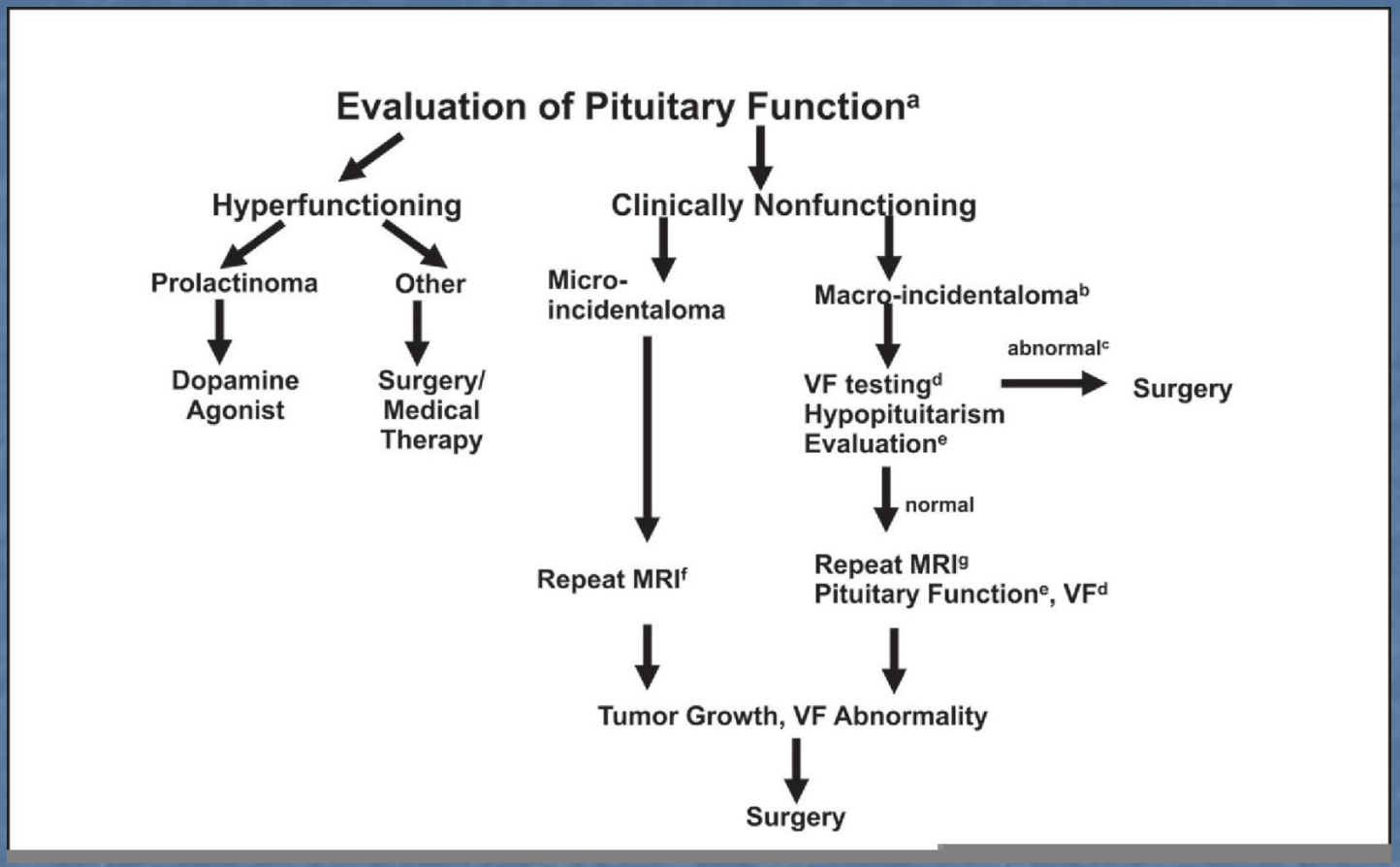
The NEW ENGLAND JOURNAL of MEDICINE

Indications for Therapy in Patients with Prolactinomas

Table 1. Indications for Therapy in Patients with Prolactinomas.

Macroadenoma
Enlarging microadenoma
Infertility
Bothersome galactorrhea
Gynecomastia
Testosterone deficiency
Oligomenorrhea or amenorrhea
Acne and hirsutism

Klibanski A. N Engl J Med 2010;362:1219-1226



Published in: R. Michael Tuttle; Published in: Laurence Katznelson; Published in: Hall WA; Luciano MG; Doppman JL; Patronas NJ; Oldfield EH; Published in: Molitch ME; Published in: Freda PU; Post KD; Published in: Zada G; Lin N; Ojerholm E; Ramkissoon S; Laws ER; Published in: Black PM; Hsu DW; Klibanski A; Kliman B; Jameson JL; Ridgway EC; Hedley-Whyte ET; Zervas NT; Published in: Feldkamp J; Santen R; Harms E; Aulich A; Modder U; Scherbaum WA; Published in: Freda PU; Beckers AM; Katznelson L; Molitch ME; Montori VM; Post KD; Vance ML; Published in: Yuen KC; Cook DM; Sahasranam P; Patel P; Ghods DE; Shahinian HK; Friedman TC; Published in: Arita K; Tominaga A; Sugiyama K; Eguchi K; Iida K; Sumida M; Migita K; Kurisu K; Published in: Donovan LE; Corenblum B;
DOI: 10.1210/MTP2.9781936704637.ch44

Pituitary Case

- 64 yo W seen for f/u exam
- -2 wks ago in car accident and an incidental pituitary adenoma found on cervical spine CT scan
- -No residual injuries from the car accident
- -Otherwise healthy and takes no meds
- -Menopausal since age 51
- -Has night sweats 2-3x/mth and occ hot flushes which have improved over the past decade, not bothersome
- -Not sexually active, never took HRT
- -No change in vision, HA or galactorrhea

Pituitary Case

- On PE, temp 37.5C(99.5F), BP 110/63 mmHg, Pulse 82/min, RR 14/min. BMI 26
- -has axillary & pubic hair loss
- -VF intact
- -No signs suggestive of Cushing syndrome or Acromegaly

Pituitary Case

- LABS
- -Estradiol <20 pg/mL (<20)
- -FSH 6.4 mU/mL (>35)
- -LH 3.2 mU/mL (>30)
- -Prolactin 53 ng/mL (<20)
- -TSH 3.2 uU/mL (0.5-5.0)
- -FT4 1.1 ng/dL (0.9-2.4)

Pituitary Case

- Pituitary MRI shows a 7 mm adenoma in the anterior sella. Tumor is not invasive. It does not approximate the optic chiasm. Pituitary stalk is mid-line.
- **Which of the following is the most appropriate management?**
- A. Begin Dopamine agonist
- B. Gamma knife stereotactic radiosurgery
- C. Repeat testing in 12 mths
- D. Transsphenoidal resection

Pituitary Case

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Take Home Points

- For patients with pituitary adenomas, evaluate:
- -Mass effects(headache, visual dysfunction)
- -Pituitary hyperfunction
- -Pituitary hypofunction-all hormonal systems

Treatment aimed at restoring normal pituitary function and can include surgery, medications, hormonal replacement

Take Home Points

1. All patients with an incidentaloma should have a 1-mg dexamethasone suppression test and measurement of plasma free metanephrines.
2. Patients with hypertension should also undergo measurement of serum potassium and plasma aldosterone concentration-plasma renin activity ratio.
3. A homogeneous mass with a low attenuation value (<10 HU) on computed tomography is probably a benign adenoma.
4. Surgery should be considered in all patients with functional adrenal cortical tumors that are clinically apparent.
5. All patients with biochemical evidence of pheochromocytoma should undergo surgery.
6. Data are insufficient to indicate the superiority of a surgical or nonsurgical approach to manage patients with subclinical hyperfunctioning adrenal cortical adenomas.
7. Recommendations for surgery based on tumor size are derived from studies not standardized for inclusion criteria, length of follow-up, or methods of estimating the risk for carcinoma. Nevertheless, patients with tumors >6 cm usually are treated surgically, while those with tumors <4 cm are generally monitored. In patients with tumors between *4* and 6 cm, criteria in addition to size should be considered in the decision to monitor or proceed to adrenalectomy.
8. The literature on adrenal incidentaloma has proliferated in the last several years. Unfortunately, the lack of controlled studies makes formulating diagnostic and treatment strategies difficult. Because of the complexity of the problem, the management of patients with adrenal incidentalomas will be optimized by a multidisciplinary team approach involving physicians with expertise in endocrinology, radiology, surgery, and pathology. The paucity of evidence-based data highlights the need for well-designed prospective studies.
9. Open or laparoscopic adrenalectomy is an acceptable procedure for resection of an adrenal mass. The procedure choice will depend on the likelihood of an invasive adrenal cortical carcinoma, technical issues, and the experience of the surgical team.
10. In patients with tumors that remain stable on two imaging studies done at least 6 months apart and do not exhibit hormonal hypersection over 4 years, further follow-up may not be warranted.

Grumbach, M. M. et. al. Ann Intern Med 2003;138:424-429

Take Home Points

- The TSH is the most sensitive index of thyroid function
- Thyroid ultrasound is preferred to identify and characterize nodules
- Fine needle aspiration is the most informative approach to the evaluation of thyroid nodules

- THANK YOU!