McGill ANNUAL REFRESHER COURSE FOR FAMILY PHYSICIANS | 2022

Incidentalomas - When to be concerned ?

Workshops B
15:30

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Potential Conflict of Interest:

None for this workshop

Objectives

- Review the definition of an incidentaloma
- Know its prevalence and possible associated pathologies
- Outline a biochemical work-up to assess functionality
- Consider a follow-up

Definition

“ An adrenal incidentaloma is an asymptomatic adrenal mass detected on imaging not performed for suspected adrenal disease”.

Fassnacht, Euro J Endo, 2016, Volume 175: Issue 2

Pre-test questions:

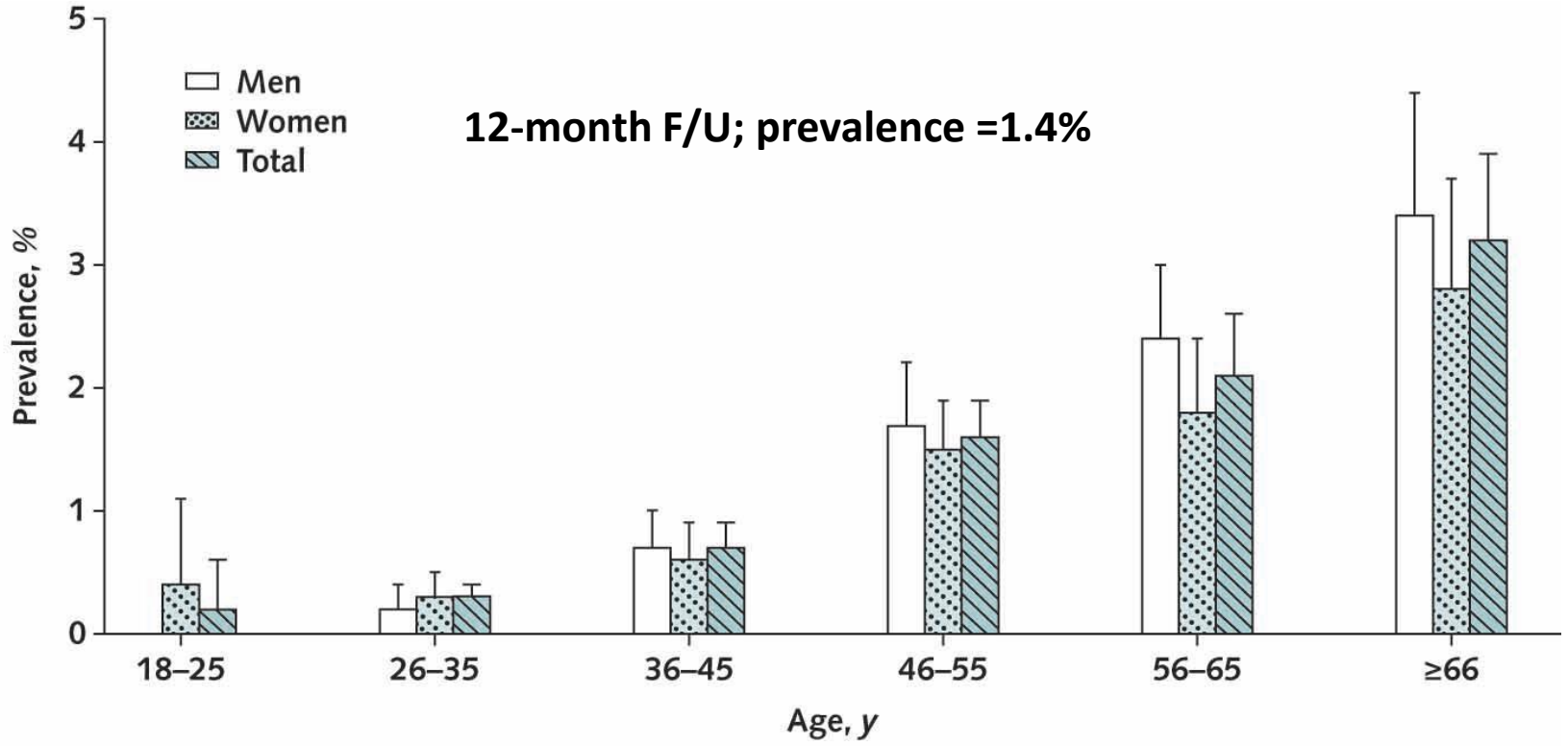
1- What is the prevalence in the general population?

a) Less than 0.5%
b) 1.4%
c) 2.6%
d) 4.3%

2- When deemed functional, what type is most often encountered?

a) Pheochromocytoma
b) Elevated cortisol (Cushing)
c) Hyperaldosteronism

Prevalence of Adrenal Tumors in an Unselected Screening Population: Abdominal CT scans in 25,000 asymptomatic adults (age range, 18-78)



Prevalence, *n*/*N* (%)						
Men	0/212 (0)	4/1859 (0.22)	20/2846 (0.70)	67/3842 (1.74)	60/2475 (2.42)	48/1392 (3.45)
Women	1/272 (0.37)	9/2712 (0.33)	18/2882 (0.62)	51/3496 (1.46)	37/2101 (1.76)	36/1267 (2.84)
Total	1/484 (0.21)	13/4571 (0.28)	38/5728 (0.66)	118/7338 (1.61)	97/4576 (2.12)	84/2659 (3.16)

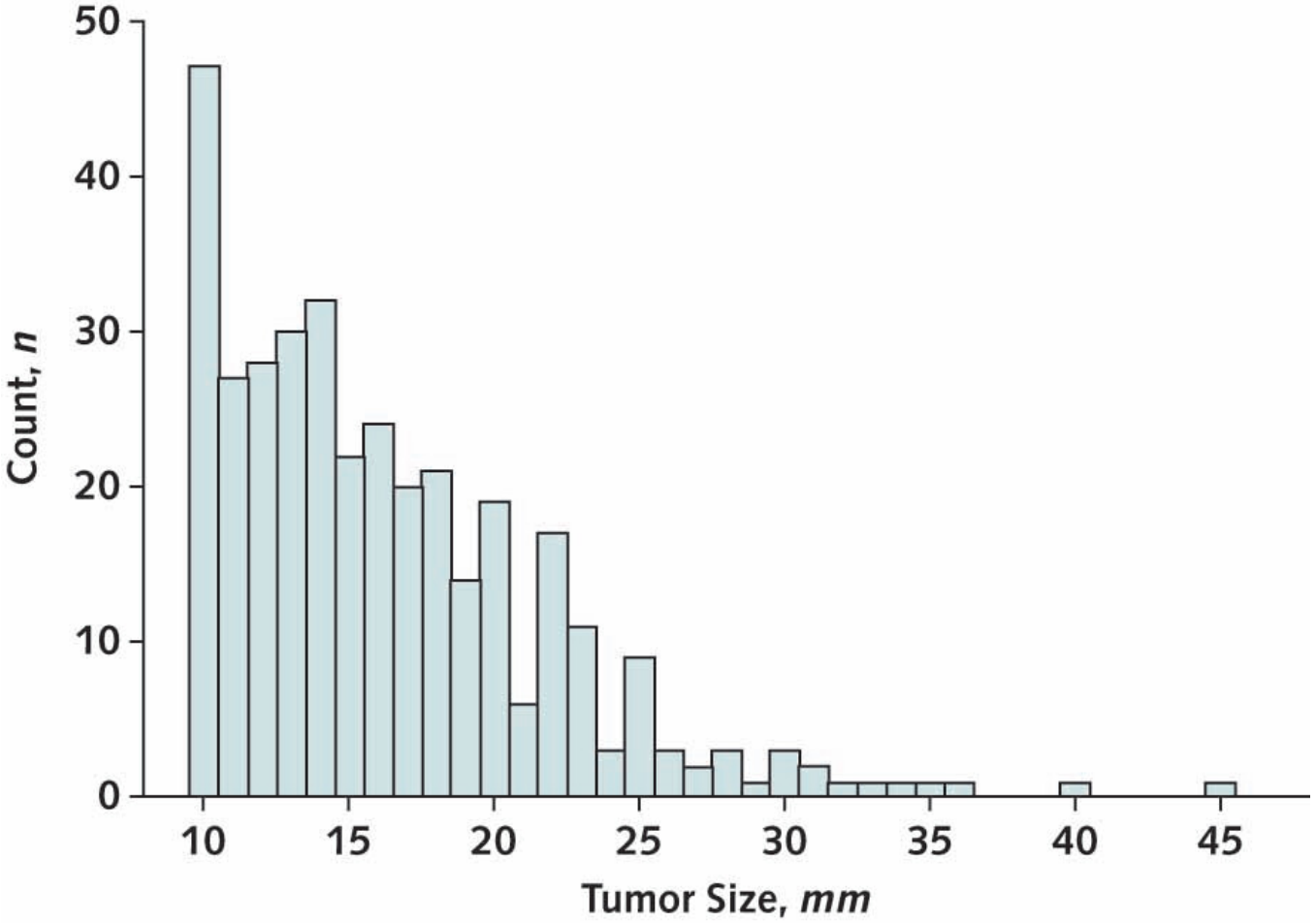
Ann Intern Med. 2022; 175(10):1383-1391.

Prevalence of Adrenal Tumors in an Unselected Screening Population: Abdominal CT scans in 25,000 asymptomatic adults (age range, 18-78)

- 351 incidentaloma
- 337 were adenomas, 14 were other benign masses and none were malignant
- 2/3 underwent laboratory evaluation: - 69% non-functioning adenomas
  - 20% had autonomous cortisol secretion (usually mild)
  - 12% had primary aldosteronism
- No pheochromocytoma was identified

Ann Intern Med. 2022; 175(10):1383-1391.

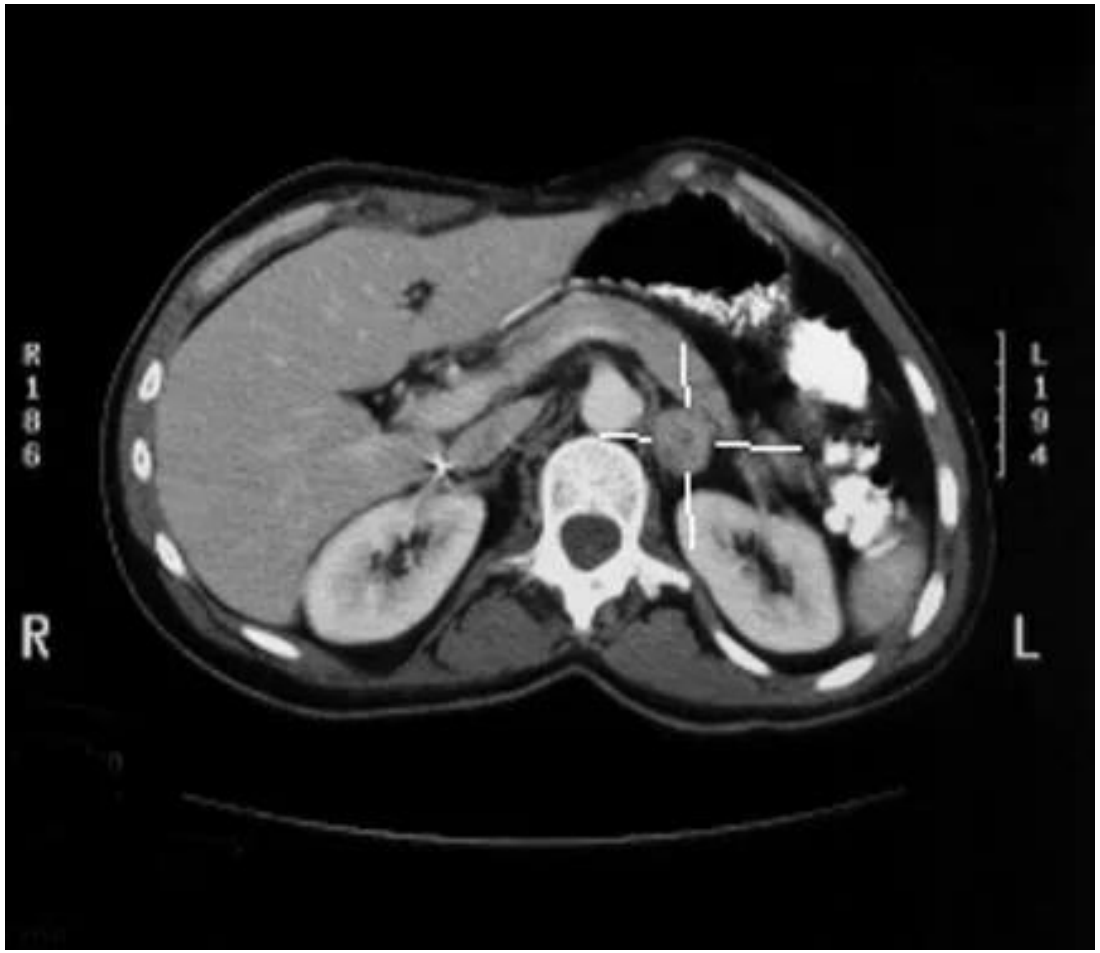
Prevalence and Characteristics of Adrenal Tumors in an Unselected Screening Population [A Cross-Sectional Study]

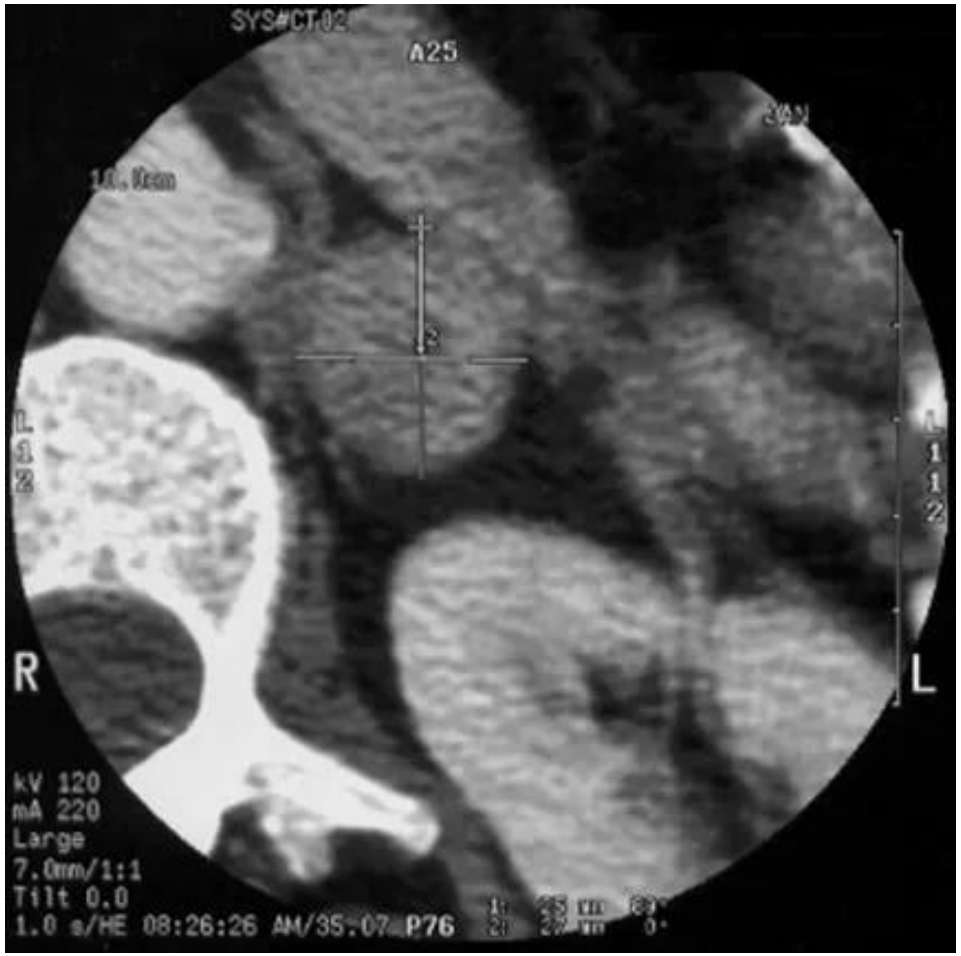


The size distribution of adrenal tumors

Ann Intern Med. 2022; 175(10):1383-1391

Adrenal Incidentaloma

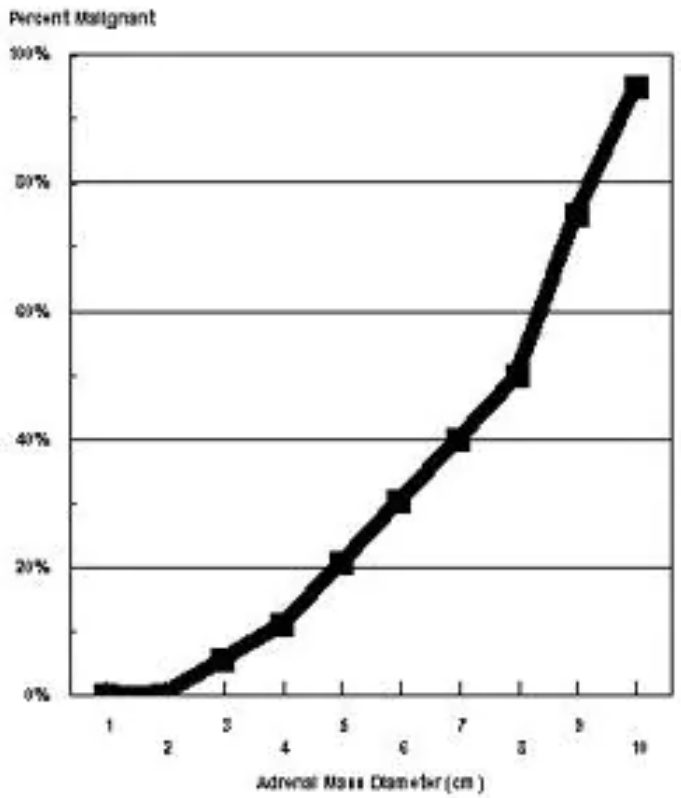




Medscape, George T Griffing, MD, Jan 12, 2022

Adrenal Mass Characteristics & Malignant Potential

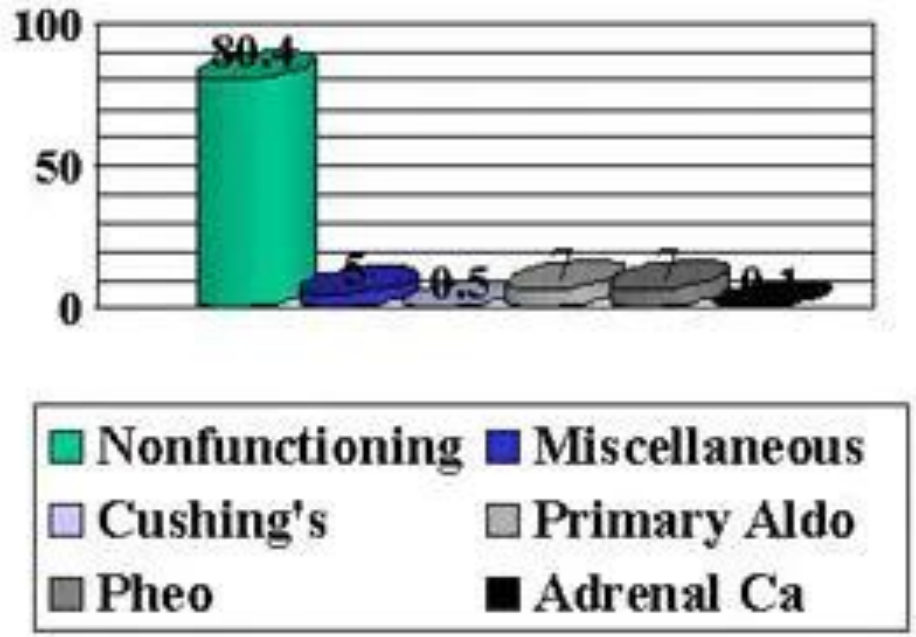
- Qualitative
  - Irregular margin
  - Inhomogeneous
  - Contrast Enhancement
  - Intermediate T2 Intensity
  - Lymph Nodes enlarged
  - Soft tissue density CT



At times, usually in patients with a known malignancy, there could be bilateral metastases

Medscape, George T Griffing, MD, Jan 12, 2022

Adrenal Incidentaloma by Disease type



Trivia: pheochromocytomas are present in 1 out of 1000 autopsies

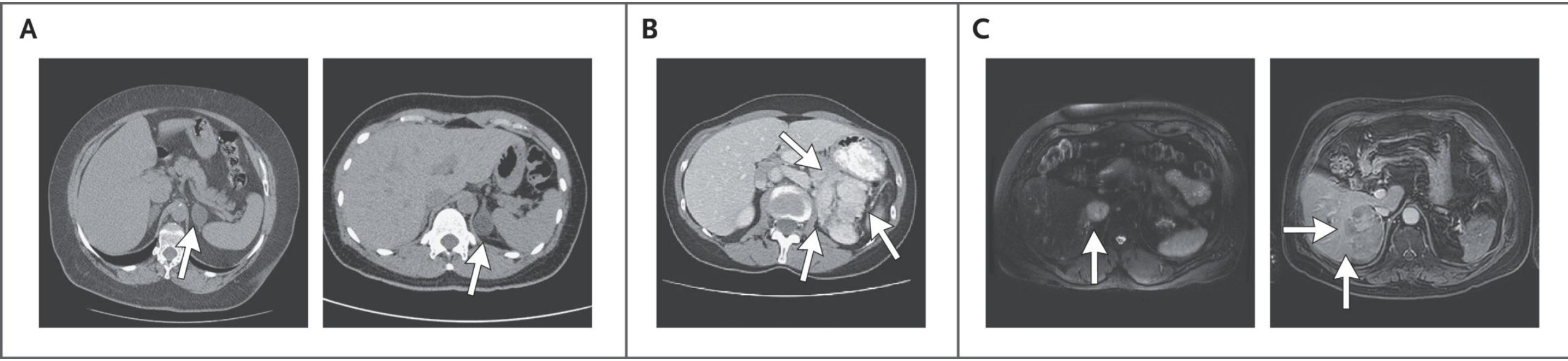
Medscape, George T Griffing, MD, Jan 12, 2022

Adrenal Mass Differential Diagnosis

- **Adrenal Cortex**
  - Adenoma
  - Nodular Hyperplasia
  - Carcinoma
- **Adrenal Medulla**
  - Pheochromocytoma
  - Ganglioneuroma
  - Ganglioneuroblastoma
- **Metastases**
  - Breast, Lung, Lymphoma
  - Leukemia, other
- **Technical Artifacts**
- **Other**
  - Myelolipoma
  - Neurofibroma
  - Hamartoma
  - Teratoma
  - Xanthomatosis
  - Amyloidosis
  - Cyst
  - Hematoma
  - Granulomatosis
- **Pseudoadrenal**
  - Renal, Pancreas, Spleen etc

Medscape, George T Griffing, MD, Jan 12, 2022

Imaging Features of Adrenal Masses



A. Probable pheochromocytoma on left (high attenuation) and probable adenoma on right (low attenuation)

B. Large adrenal mass with heterogeneous content, irregular borders and areas of necrosis

C. Right pheochromocytoma on left and right adrenocortical carcinoma on right

NEJM, 2021; 384:1542-51

Biochemical work-up to assess functionality (1)

- Usually the patient has no signs of hormonal excess or obvious malignancy
- Cushing syndrome and hyperaldosteronism can present as bilateral adrenal disease

1. Cushing syndrome includes weight gain, weakness (more pronounced in limbs), depression and bruising. May have features of metabolic syndrome and reduced bone density
2. Primary aldosteronism includes hypertension (often resistant) and unprovoked hypokalemia in 40% of patients.
3. Pheochromocytoma symptoms include palpitations, headaches, abdominal pain, shakiness, pale face and labile hypertension.

Biochemical work-up to assess functionality (2)

Cushing syndrome:
→Plasma cortisol (to do fasting at 08:00). Variable results.
→Better: overnight 1 mg dexamethasone suppression test (one tablet at 23:00 and plasma cortisol the following morning at 08:00)

Pheochromocytoma:
→ Urine-free catecholamines and plasma-free catecholamines (avoid coffee, tea, bananas, cocoa, vanilla)

Primary aldosteronism:
→ Plasma aldosterone-to-renin ratio (off diuretics and RAAS inhibitors)

If CT scan results are uncertain…

- Repeat CT scan in 3-6 months (better with contrast)
- MRI with gadolinium
- PET scan if possibly malignant (Nuclear Medicine)
- MIBG scan for pheochromocytoma (Nuclear Medicine)
- Refer to Radiology for CT guided if features of malignancy or recommended by the radiologist

Prognosis

- Prognosis is excellent; incidentalomas do not transform in cancer
- 85% are non-functional (no hormone secretion)
- Most adrenal lesions remain unchanged or decrease in size over time
- For those who do not require surgery (see below), repeat CT scan in 6-12 months if hormone level still high.

Treatment

- Please refer to a specialized Clinic
- Cushing: ketoconazole, mitotane, and metyrapone
- Primary aldosteronism: surgery in venous sampling positive from an adenoma. Medical tx: mineralocorticoid receptor antagonists
- Pheochromocytoma: surgical removal. Otherwise, chemotherapy, radiotherapy. Medications to control symptoms (α- then β blockers)

Adrenal Incidentalomas – Frequency of the different underlying tumor types

Tumor entity	Median (%)	Range (%)
Series including all patients with an adrenal mass*		
Adenoma	80	33–96
Nonfunctioning	75	71–84
Autonomously cortisol-secreting	12	1.0–29
Aldosterone-secreting	2.5	1.6–3.3
Pheochromocytoma	7.0	1.5–14
Adrenocortical carcinoma	8.0	1.2–11
Metastasis	5.0	0–18
Surgical series**		
Adenoma	55	49–69
Nonfunctioning	69	52–75
Cortisol-secreting	10	1.0–15
Aldosterone-secreting	6.0	2.0–7.0
Pheochromocytoma	10	11–23
Adrenocortical carcinoma	11	1.2–12
Myelolipoma	8.0	7.0–15
Cyst	5.0	4.0–22
Ganglioneuroma	4.0	0–8.0
Metastasis	7.0	0–21

Fassnacht, Euro J Endo, Volume 175: Issue 2

Other Incidentalomas

- Pituitary
- Thyroid
- Pulmonary
- Hepatic
- Pancreatic
- Ovarian

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Pituitary

- Pituitary incidentalomas are found in at least one in 10 persons
- Clinically significant in one in 1,000.
- Solid lesions ≥ 1 cm are more likely to grow and cause symptoms (visual, hormonal deficits, prolactin increase)
- Preferred imaging: MRI
- Treatment: surgery if visual deficit. Medical treatment most often.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Thyroid

- Often discovered on CT , MRI or PET scan performed for other reasons. One half of patients undergoing imaging have thyroid nodules; most are 1 cm or smaller.
- Cysts are benign
- Cancerous nodules found in less than 2%
- History should include exposure to radiation, positive family history
- On physical exam, check for neck lymph nodes, hoarseness
- Basic investigation includes thyroid gland U/S and dosage of TSH
- Low TSH is associated with a hyperfunctioning benign nodule
- High TSH level have a greater risk of malignancy
- Fine needle biopsy is recommended for nodules $>$ 2 cm and microcalcifications, hypoechogenicity or intramodular vascularity.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Pulmonary

- Most nodules are low-risk
- Risk of malignancy if history of extrathoracic malignancy, age, smoking history, asbestos exposure, family history
- Worrisome nodules are $>$ 8 mm, have irregular borders, eccentric calcifications, absence of calcification, and low density
- Repeat CT scan in 6-24 months, except in high risk patients: annually for 3 years.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Hepatic

- Found in up to 15% of CT studies; most often: hemangiomas
- No work-up if $<$ 5 mm or lesions with low attenuation (20 HU), benign features
- Suspicious lesions are ≥ 5 mm, ill-defined margins, enhancement greater than 20 HU, heterogenous appearance or interval growth
- Cysts are benign; cystadenomas warrant F/U
- Adenomas become suspicious if large. Stop BCP as they can enlarge them.
- Multi-phasic CT or MRI is preferred for F/U.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Pancreatic

- Cysts are found in more than 2% of patients undergoing abdominal CT or MRI; can be neoplastic if larger (>3 cm), mucinous cystic, intraductal papillary and mucinous and solid pseudo papillary.
- MRI recommended for best characterization.
- Surgery recommended for cysts larger than 3 cm and suspicious features (mural nodules, lymphadenopathy and invasion of bile or pancreatic ducts).
- Radiologic monitoring is suggested for lesions 1 to 3 cm in size.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

Ovarian

- Most ovarian incidentalomas are benign and are often functional cysts in premenopausal women and cystadenomas in post menopausal women.
- Normal size of cysts is $\leq$ 3 cm in pre menopause and $\leq$ 1 cm in post menopause
- Risk of malignancy is greater in postmenopausal women with complex cysts and masses. Intravaginal U/S is the preferred imaging.
- Red flags characteristics for adnexal lesions include thickened walls/septa and solid components with blood flow.
- Antigen 125 (CA-125) have little predictive value in pre menopause, but may indicate malignancy in postmenopausal women.

Hitzeman, Am Fam Physician. Volume 175: 2014;90(11)

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Thank you !