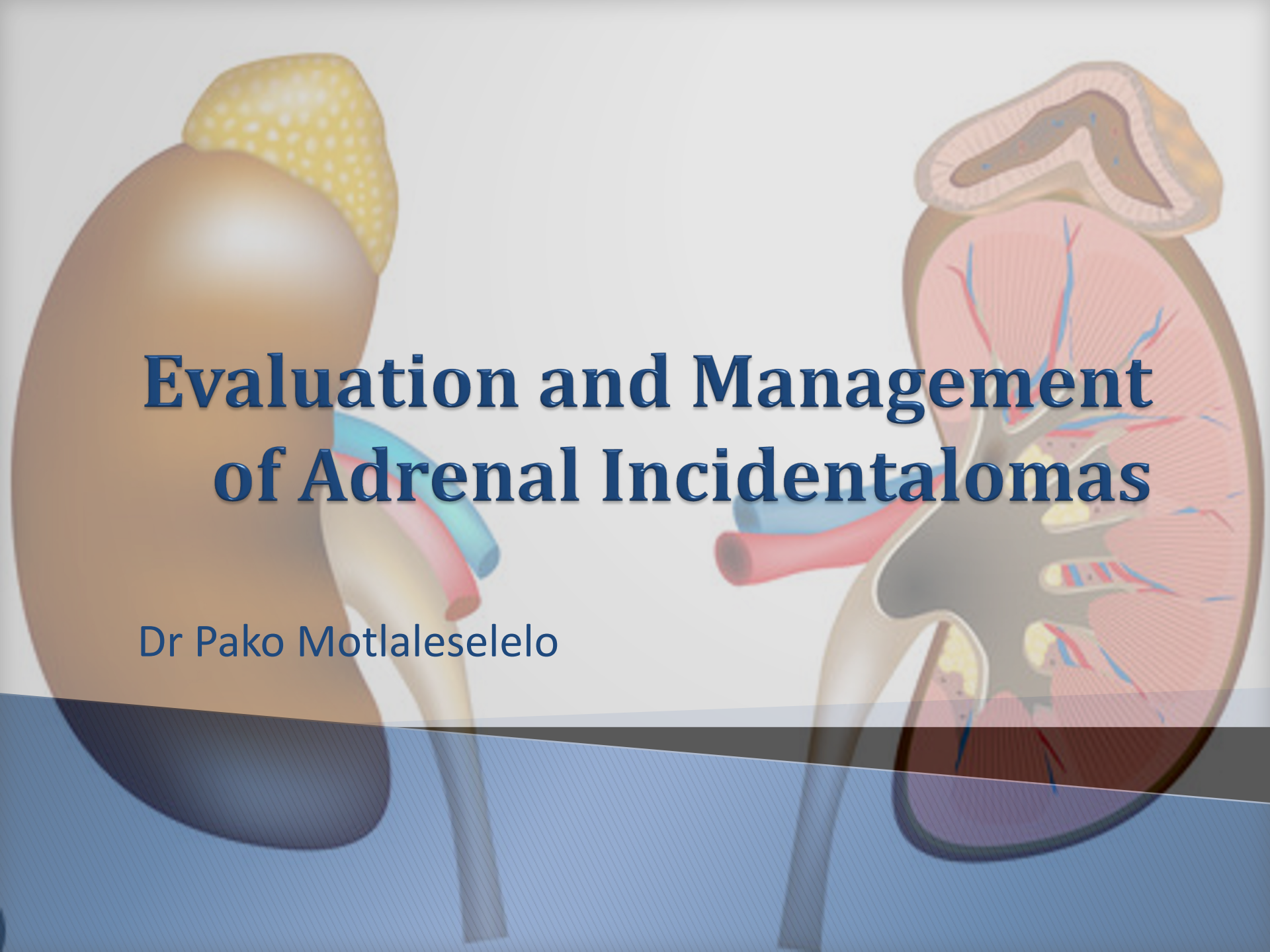

Evaluation and Management of Adrenal Incidentalomas

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Definition

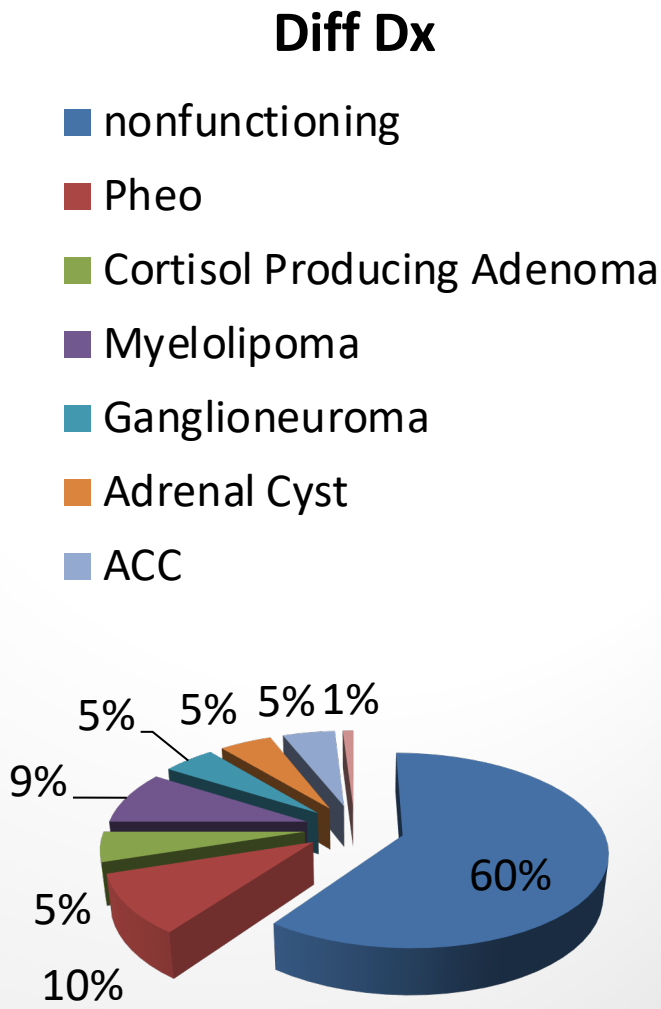
- Adrenal masses >1 cm in size that are detected on cross-sectional imaging performed for an unrelated indication
- Back pains, nonspecific abdominal pains, etc.
- Excludes staging imaging or follow-up in extra-adrenal malignancies
- An arbitrary work-up threshold of 1 cm, unless clinical signs and symptoms suggest adrenal hormone excess

Epidemiology

- They are not uncommon
- Estimated in **4%** of patients on **imaging** series and
- up to **10%** of the **elderly** population
- The differential diagnosis for an adrenal incidentaloma is broad**: nonfunctioning, functioning and malignant**
- Systematic review found that approximately **20%** of all adrenal incidentalomas were **potentia**l surgical lesions
- First question is whether it is **nonfunctional v functional** and **benign v malignant**

Table 2. Etiology of adrenal tumors presented as adrenal incidentaloma.

Etiology	Prevalence of the different entities among adrenal incidentalomas
Adrenocortical adenoma or macronodular bilateral adrenal hyperplasia	80%-85%
• Nonfunctioning	40%-70%
• Mild autonomous cortisol secretion	20%-50%
• Primary aldosteronism	2%-5%
• Overt Cushing's syndrome	1%-4%
Other benign mass	
• Myelolipoma	3%-6%
• Cyst and pseudocyst	1%
• Ganglioneuroma	1%
• Schwannoma	<1%
• Hemorrhage	<1%
Pheochromocytoma	1%-5%
Adrenocortical carcinoma	0.4%-4%
Other malignant mass (mostly adrenal metastases)	3%-7%



European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors

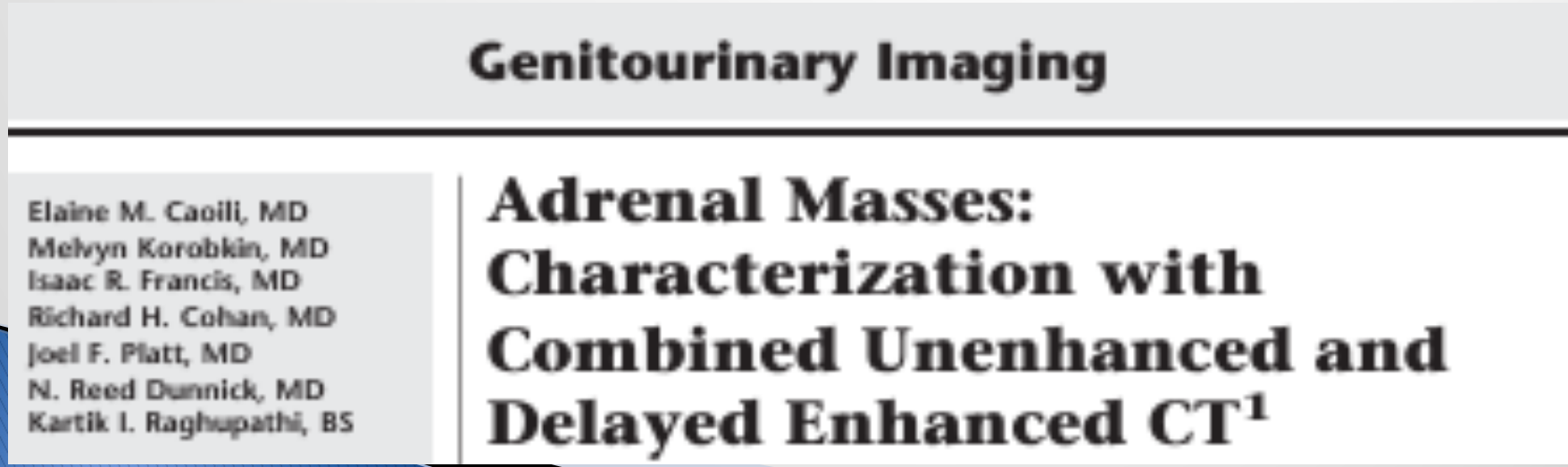
Martin Fassnacht,[1,2,*] Stylianos Tsagarakis,[3] Massimo Terzolo,[4] Antoine Tabarin,[5] Anju Sahdev,[6] John Newell-Price,[7,8] Iris Pelsma,[9] Ljiljana Marina,[10] Kerstin Lorenz,[11] Irina Bancos,[12] Wiebke Arlt,[13,14] and Olaf M. Dekkers[9,15]

Assessment of Malignancy Risk

- The actual frequency of primary adrenal carcinoma in patients with adrenal incidentaloma is approximately 2-5%, another 0.7-2.5% have non-adrenal metastases to the adrenal gland
- HPE to identify signs/symptoms of adrenal malignancy and/or extra-adrenal malignancy
- CT and MRI are the primary imaging modalities
- CS-MRI is slightly more sensitive in detecting lipid rich adenomas but less so for indeterminate adenomas and CT might still be needed, however MRI is used in patients with iodinated contrast allergies. The disadvantages are availability, patient convenience for a single examination, and cost, which usually favor CT.

NC-CT

- Noncontrast CT is performed as the first imaging modality if not yet performed
- If noncontrast CT is consistent with a benign adrenal mass (homogenous, round with smooth contour and Hounsfield units ***[HU] <10***), no further imaging is required
- In a retrospective review of 216 patients who underwent adrenalectomy, 143/143 (100%) patients who had benign features on CT had benign final pathology

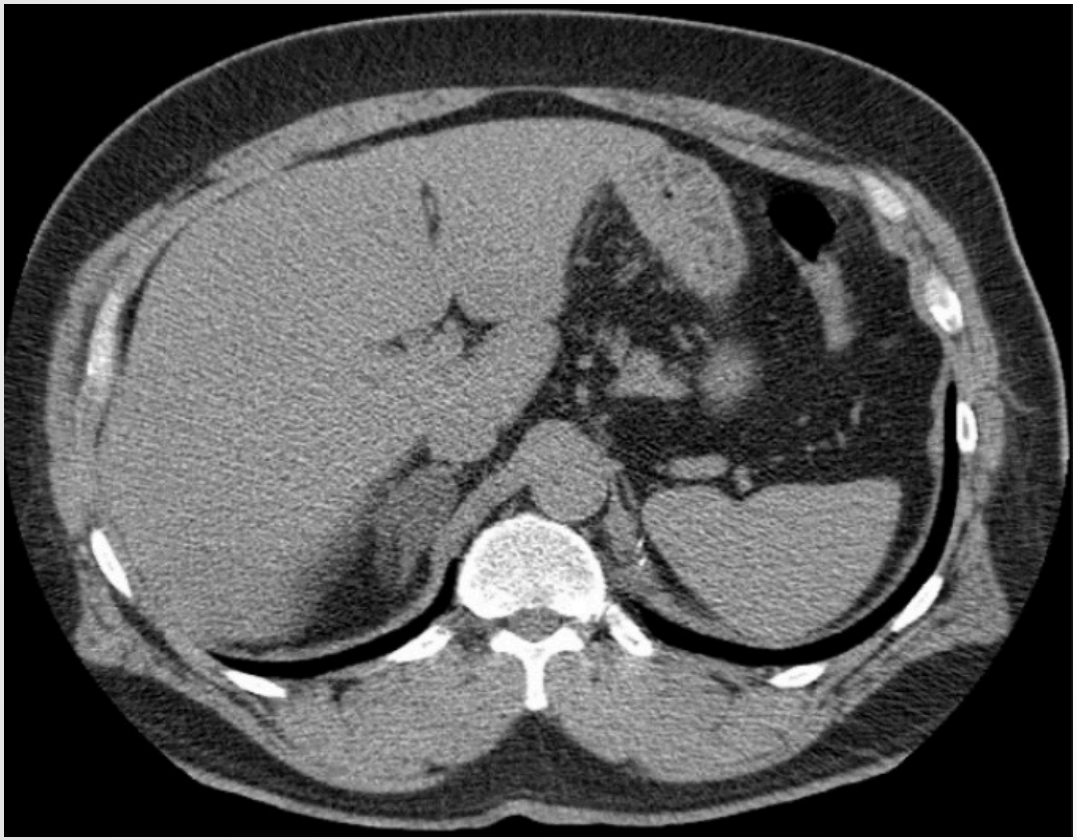


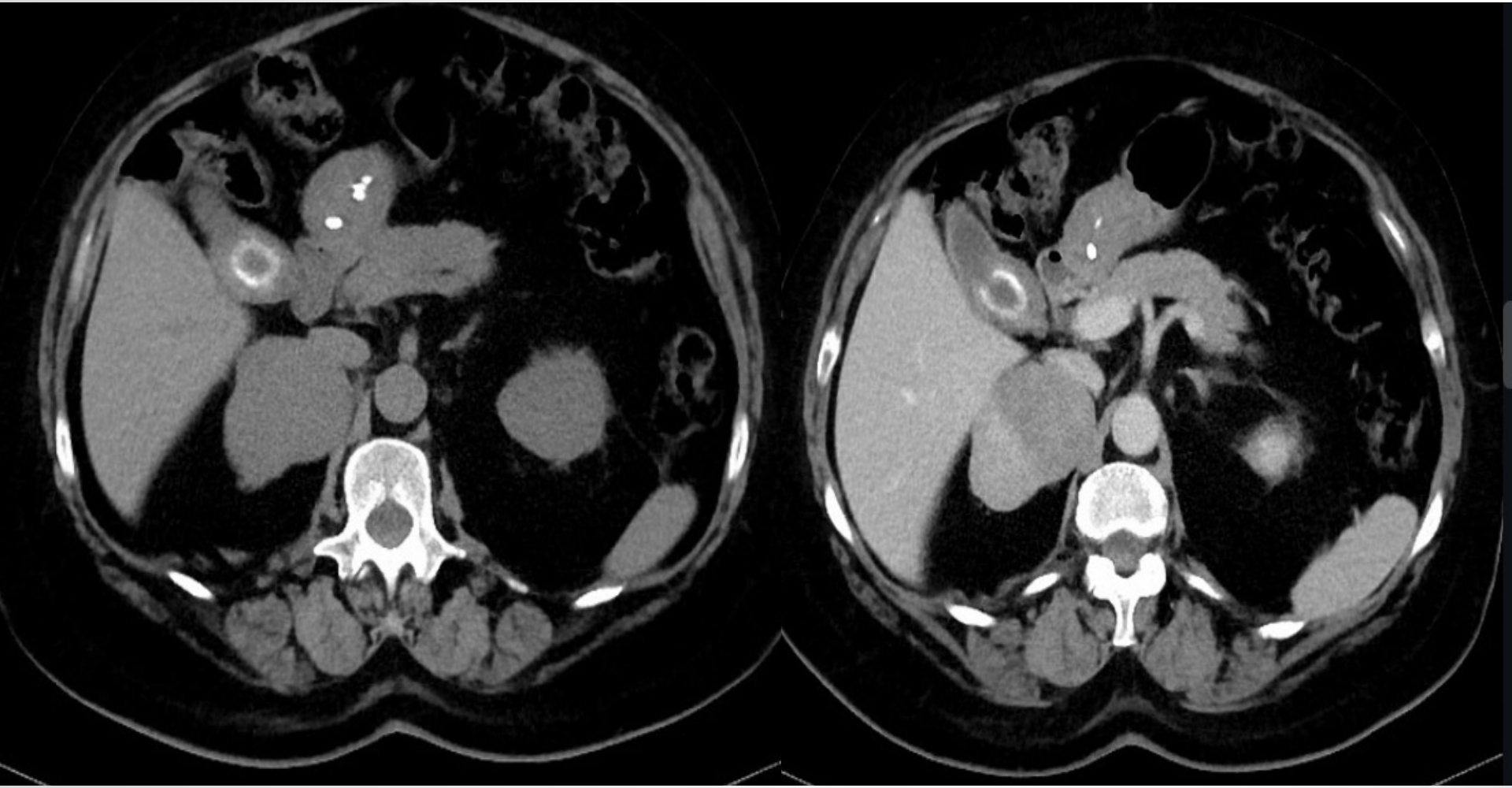
CECT

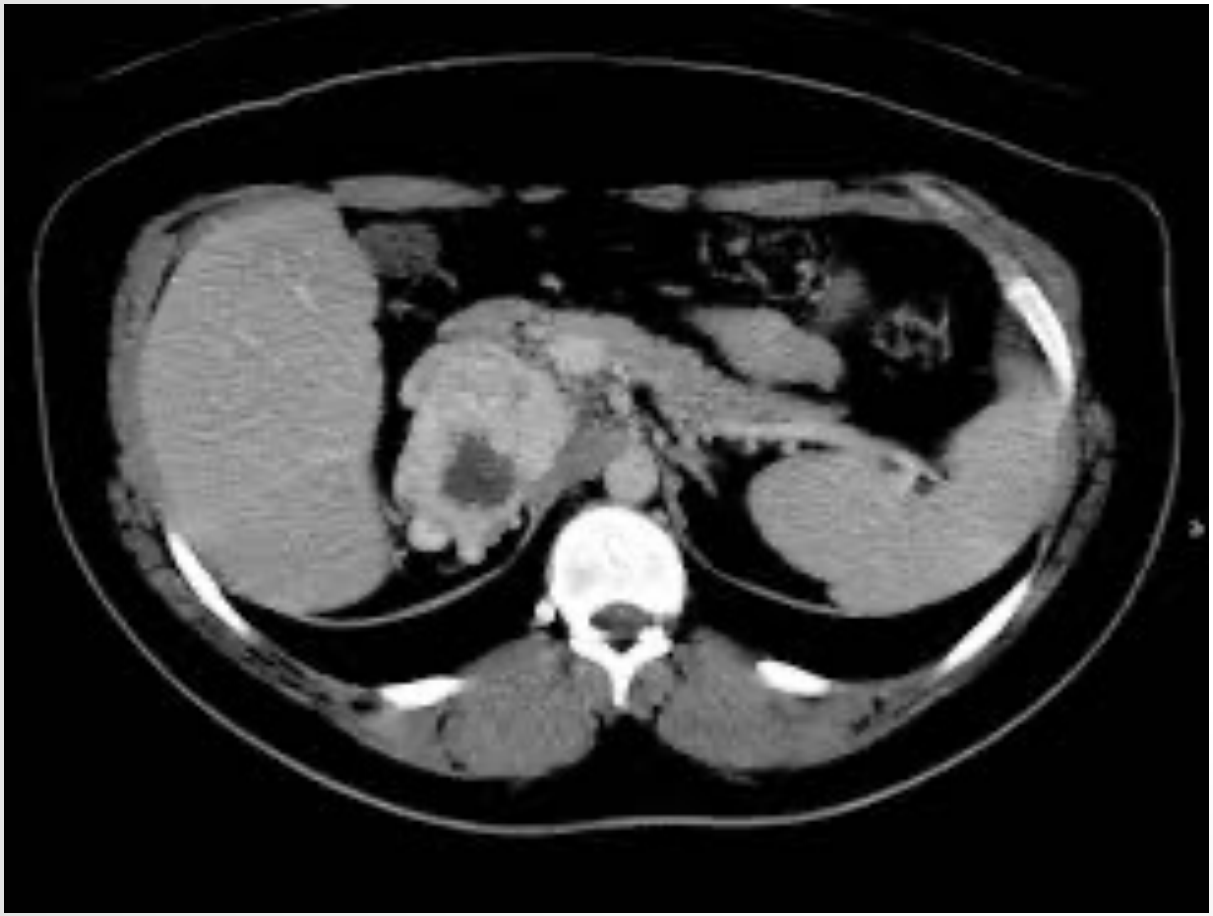
- The recommended collimation for an adrenal CT is 3 mm with reconstructions in the axial and coronal planes
- consists of an unenhanced CT acquisition through the upper abdomen with a reduced dose followed by a dynamic contrast-enhanced CT (60-90s after IV contrast) and a 15-min delayed acquisition are performed
- Absolute percentage washout values are calculated using the formula (enhanced HU-15min delayed HU)/(enhanced HU-unenhanced HU)X 100% or
- relative percentage washout with the formula (enhanced HU-15min delayed HU)/(enhanced HU-unenhanced HU)X100%
- APW>60% or RPW>40% is diagnostic of an adenoma with 98% sensitivity and 92% specificity

CECT…2

- If the adrenal mass is >4 cm and heterogeneous or has unenhanced HU>20, there is a relevant risk that this lesion is malignant. Therefore such cases require MDT discussion, in most cases, immediate surgery will be the management of choice, but in some patients, additional imaging might be an option
- Adrenal masses with 11-20HU, tumor size <4 cm and negative hormonal work-up immediate additional imaging or interval imaging in 12 months by noncontrast CT (or MRI) could be performed
- In adrenal masses that do not fall in one of the categories above (eg, tumor size >4 cm with unenhanced HU 11-20; or tumor size <4 cm with unenhanced HU>20; or tumor size <4 cm with heterogeneous appearance), an individualized approach in a MDT meeting is performed, and usually immediate additional imaging is the preferred option as the risk is still low
- If the tumor is still judged as indeterminate mass on CECT and surgery is not performed, interval imaging in 6-12 months should be performed







Role of Biopsy

- Not indicated unless there is a history of extra-adrenal malignancy to confirm suspected mets or the tumor is deemed unresectable
- 3 key criteria should be fulfilled before adrenal biopsy is considered:
  - the lesion is hormonally inactive (in particular, exclude a pheochromocytoma)
  - the lesion has not been conclusively characterized as benign by imaging
  - the histology will alter clinical management of the patient

Evaluation of Hormone Excess

- There are some controversies
  - When to send tests for hormonal excess
  - What is the clinical significance of MACS

- Evaluate for clinical signs or symptoms of a hyperfunctioning/adrenal hormone excess (e.g. pheochromocytoma, Cushing's or Conn's syndrome)

ACS

- **All patients with adrenal incidentalomas** should undergo a **1-mg overnight DST** to exclude autonomous cortisol secretion
- In frail patients with limited life expectancy, this test may not be warranted
- In patients without signs and symptoms of overt Cushing's syndrome a post DST serum cortisol concentration **>50 nmol/L (> 1.8 µg/dL)** should be considered as **MACS**
- ACTH-independency should be confirmed

- In patients with **concomitant hypertension or unexplained hypokalemia** determine aldosterone/renin ratio to evaluate primary aldosteronism
- Exclude pheochromocytoma by measurement of plasma free metanephrines or urinary fractionated metanephrines in all patients with adrenal **lesions with features not typical for a benign adenoma**
- in patients with imaging or clinical features suspicious of an **adrenocortical carcinoma** measurement **of sex steroids and precursors of steroidogenesis** is highly accurate(PPV:76.4%, NPV:99.7%)

Surgery

- Indicated for patients with hormonally active adrenal incidentalomas
- Pts with MACS; treatment is individualized based on age, general condition, degree of cortisol autonomy and comorbidities
- Indeterminate adrenal mass enlarging > 20% or 5mm on repeat imaging
- If surgery is indicated for a benign adrenal mass causing hormone excess (including MACS) a minimally invasive approach is used
- In patients with unilateral adrenal masses with radiological findings suspicious of malignancy and a diameter $\leq$6 cm but without evidence of local invasion, minimally invasive adrenalectomy can be performed
- open adrenalectomy for unilateral adrenal masses with radiological findings suspicious of malignancy and signs of local invasion

Follow-up

- Clear benign features on imaging studies = no follow up
- Indeterminate adrenal mass- repeat noncontrast CT or MRI after 6-12 months to exclude significant growth, if stable discharge, if there is minimal growth repeat imaging in 6-12mo.
- patients with normal hormonal work-up at initial evaluation do not need repeat work-up unless new clinical signs of endocrine activity appear or there is worsening of comorbidities (e.g., hypertension, type 2 diabetes)
- MACS patients can be discharged from specialized endocrine and follow-up of comorbidities by local CHC

Thank You