Adrenal incidentaloma guideline for Northern Endocrine Network

Definition of adrenal incidentaloma
- Adrenal mass detected on an imaging study done for indications that are not related to an adrenal problem or hormonal excess.

Proceed to diagnostic work-up if adrenal mass is ≥1cm or clinical evidence of hormone excess (**Ignore if <1cm; EXCEPT in children, adolescents, pregnant women and adults <40 years of age**) 

Clinical assessment
- History and clinical examination for signs and symptoms of hormone excess (e.g. blood pressure, proximal myopathy, hirsutism or virilisation). History of diabetes mellitus. U&E, HbA1C.

Hormonal evaluation
(Unless the adrenal mass is an obvious myelolipoma with low CT attenuation of ≤ -10 HU)

A. Plasma metanephrines to exclude phaeochromocytoma, unless imaging clearly indicates otherwise.

B. Testosterone (include LH if male). If there is evidence of virilisation, hirsutism, gynaecomastia or imaging features suggestive of adrenocortical carcinoma, 17α-OHP, oestradiol (in male or post-menopausal female).

C. Plasma ACTH and DHEAS. If ACTH levels are suppressed (<15), and/or DHEAS<1, or there is clinical suspicion of cortisol excess, then proceed to 1.5mg O/NDST (See Appendix 1 for interpretation of O/NDST.)

D. Aldosterone: renin ratio in patients with arterial hypertension or hypokalaemia to exclude primary hyperaldosteronism (NB. K must be normal, sampled off B-blockers, diuretics, ACEI &AII RRs).

Radiological assessment
Establish the risk of adrenal malignancy with CT. **

Scanning should be performed with a non-contrast CT, followed by contrast and washout phase.

Decision making
- If the mass is homogenous, lipid-rich with HU unit ≤10 (benign) and less than 4cm in maximum diameter, no further imaging is required

- If the mass is indeterminate on non-contrast CT (30-40% of benign adenoma have an attenuation value of >10 HU) or SIZE >4cm despite HU<10 or there is clinical/biochemical evidence of hormone excess, refer to the multidisciplinary team meeting (MDT). Broadly, there are 3 options:
  a. Immediate additional imaging (MRI adrenal with washout phase, FDG-PET/CT)
b. Interval imaging in 6 to 12 months (non-contrast CT or MRI)

c. Surgery without delay

-If MRI with chemical shift has already been performed and the results are unambiguous, this radiology modality might be deemed adequate as judged by the MDT without subjecting an individual patient to non-contrast adrenal CT.

**Urgent assessment of an adrenal mass in children, adolescents, pregnant women and adults <40 years of age is required in view of higher likelihood of malignancy. MRI should be used instead of CT in these cases if dedicated adrenal imaging is required.

Management
All patients who meet the following criteria are to be discussed in the MDT:
- There is evidence of adrenal hormone excess
- Imaging is not consistent with a benign lesion (ie. is indeterminate or suggests malignancy)
- There is evidence of tumour growth on follow-up imaging
- When adrenal surgery is being considered
- The adrenal mass is >4cm

-Adrenal biopsy should NOT be performed unless the patient has a history of extra-adrenal malignancy (Provided phaeochromocytoma has been excluded and ACC is unlikely). In very rare instances, following MDT discussion, pathologic confirmation with CT-guided needle biopsy may be required for staging and planning of oncologic treatments.

-For frail older patients with poor general health and poor performance status, the management of adrenal incidentaloma should be weighed against the potential clinical gain.

Bilateral adrenal incidentalomas
- Establish radiological features using the same imaging protocol as for unilateral adrenal incidentaloma
- Perform clinical and hormonal assessments as for unilateral adrenal incidentaloma
- Exclude congenital adrenal hyperplasia by measuring 17α-hydroxyprogesterone
- If there is clinical evidence of adrenal insufficiency or imaging study in keeping with bilateral infiltrative disease or haemorrhage/ bilateral adrenal metastatic lesion; exclude adrenal insufficiency with 9am cortisol, ACTH +/- short synacthen test.
- Surgical indications (absolute) and follow-up recommendations are the same as for unilateral adrenal incidentaloma.
- Bilateral adrenalectomy should NOT be considered in ACTH-independent autonomous cortisol secretion unless there is clinical evidence of overt Cushing’s syndrome. A unilateral adrenalectomy of the dominant lesion might be considered in some patients using an individualised approach.
APPENDIX 1.

Interpretation of low-dose overnight dexamethasone suppression test (ONDST)

Following 1.5mg dexamethasone
- If cortisol <50nmol/L:
  - autonomous cortisol secretion excluded if patient is not on medications that prolong dexamethasone clearance: i.e liver enzyme inhibitor, ketoconazole etc (list 1)
- If cortisol between 51-140 nmo/L
  - possible autonomous cortisol secretion
  - Correlate with ACTH, DHEAS
  - Consider a 48hr low-dose dexamethasone suppression test, midnight serum or salivary cortisol level, or 24hr urinary free cortisol.

- To screen patient for type 2 diabetes and arterial hypertension
- To make sure patient is not on oestrogen/combined contraceptive pills or drugs that increase dexamethasone clearance (eg. carbamazepine)
- Individualised approach for consideration of surgery (younger patients with comorbidities from cortisol excess)
- No surgery required in patients without comorbidities related to cortisol excess
- To repeat the dexamethsone suppression test after 12 months unless indication for earlier testing (eg. poor BP control, deteriorating HbA1c).

If cortisol >140nmo/L
- ‘autonomous cortisol secretion’
- To screen for arterial hypertension, type 2 diabetes and asymptomatic vertebral fracture
- To make sure patient is not on oestrogen or combined contraceptive pills, carbamazepine or other drugs that increase dexamethasone clearance
- Consider a 48hr low-dose dexamethasone suppression test, 24hr urinary cortisol or midnight serum or salivary cortisol level.
- If basal morning plasma ACTH is normal or suppressed, with evidence or 2 or more comorbidities related to cortisol excess from adrenal adenoma, surgery can be offered to patient with individualised approach, taking patient’s age, preferences, comorbidities, degree of cortisol excess and general health into consideration.
References


2. ESE-ENSAT Guideline on Adrenal Incidentaloma 2016- under review