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Management of Adrenal Incidentalomas

European Society of Endocrinology (ESE) Clinical Practice Guideline with The European Network for the Study of Adrenal Tumors (ENSAT)

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The aim of this new clinical guideline is to issue a practical guidance in line with the system GRADE (Grading of Recommendation Assessment, Development and Evaluation). The guidelines have been developed around four main predefined clinical questions of relevance for the management of patients with adrenal incidentaloma (AI).

DEFINITION and EPIDEMIOLOGY

By definition, an AI is an asymptomatic adrenal mass detected on imaging not performed for suspected adrenal disease. As in previous guidelines, in the absence of signs and symptoms suggestive of a hormonally active lesion, a diagnostic work-up is recommended only for AI ≥ 1 cm. The definition of AI embraces benign and malignant lesions originating from the adrenal cortex or medulla, or from tumor tissue elsewhere in the body. The relative frequency of these causes is related to the clinical context and to the size of the lesion. Most AIs are adenomas: 55% in surgical case series vs 80% in radiological series. The prevalence in postmortem studies is about 2% and it tends to increase with age. In radiological series the prevalence is about 3% in patients of about 50 years of age, and over 10% in older individuals. AIs are rare in pediatric practice. In the current guidelines the term «subclinical Cushing» has been replaced with «autonomous cortisol secretion» to stress that these patients do not present the typical signs of the syndrome despite the detection of excess cortisol.

Recommendation (R) 1.1. Patients with adrenal incidentaloma should be discussed in a multidisciplinary team meeting if at least one of the following criteria is met:

- Imaging not consistent with a benign lesion
- Evidence of hormone excess (including «autonomous cortisol secretion»)
- Evidence of significant tumor growth during follow-up imaging
- Consideration of adrenal surgery

Comment*: The multidisciplinary team should include at least a radiologist, an endocrinologist and a surgeon, all with significant experience in adrenal tumors.*

QUESTION 1: HOW TO ASSESS THE RISK OF MALIGNANCY?

R 2.1. The aim at the time of initial detection should be to establish if an adrenal mass is benign or malignant. Malignant lesions may require urgent surgical intervention and a diagnostic delay has the potential for harm (recommendation: strong).

R 2.2. All AI should undergo an imaging procedure to establish whether the mass is homogeneous and lipid rich and therefore benign. For this purpose, a non contrast-enhanced CT is the exam recommended (recommendation: strong; evidence: very low).

R 2.3. If the non-contrast CT is consistent with an adenoma (HU ≤10) smaller than 4 cm, no further imaging is required (recommendation: strong, evidence: very low).

Comment*: The non-contrast CT value is reflective of tissue density expressed in Hounsfield units. A value of HU ≤10 is the threshold most commonly used for the diagnosis of a lipid rich adenoma. 30% of adenomas, however, present a density >10 HU, overlapping with the values of malignant lesions and pheochromocytomas.*

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R 2.4. If the adrenal mass is indeterminate on non-contrast CT and the results of the hormonal work-up do not indicate significant hormone excess, three options should be considered by a multidisciplinary team acknowledging the patient's clinical context:

- Immediate additional imaging with another modality
- Interval imaging in 6-12 months (non-contrast CT or MRI)
- Surgery without delay

***Comment**: Evidence of targeted evaluation for «second or third line» imaging in patients with indeterminate adrenal mass is very poor. However, the panel considered it important to provide some guidance for daily clinical practice. The role of MRI in ruling out malignancy in an AI is poorly standardized, and this exam should be chosen only when the CT is better avoided (e.g. pregnancy or children). However, if an MRI is already performed and the results are unambiguous, a multidisciplinary team might judge this sufficient for the individual patient. The contrast enhanced CT allows evaluation of contrast wash-out: adenomas show a rapid wash-out, quite different from the pattern observable in cancer. There is however a huge variability in the protocols applied, and contrast wash-out is supported by very limited and low-quality evidence. FDG-PET/CT has a low risk of false negative results (namely, missing a malignant adrenal tumors) but it is expensive, not always easily available and burdened by false positives (e.g. functional adenomas or benign pheochromocytoma).*

R 2.5. Adrenal biopsy is not recommended in the diagnostic work-up of patients with AI, unless there is a history of extra-adrenal malignancy.

***Comment**: An adrenal biopsy should be especially avoided if an AI is suspected to be an adrenocortical carcinoma, because of the high risk of dissemination. The only exception might be if a formal confirmation of the diagnosis is needed in an inoperable tumor to inform oncological management.*

REFERENCE

Fassnacht M, Arlt W, Bancos I, et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol 2016, 175: G1-34.