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Editorial

European recommendations for the management of adrenal incidentalomas: A debate on patients follow-up

Recommandations européennes pour la prise en charge des incidentalomes surrénaliens : un débat quant au suivi des patients

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New guidelines recommendations on the management of adrenal incidentalomas (AI) (nodules >1 cm) were published in 2016 by the European Society of Endocrinology (ESE) in partnership with the European Network for the Study of Adrenal Tumors (ENSAT) [1]. Other recommendations guidelines had been published previously as reviews [2] or as consensus of medical associations notably by the French Endocrine Society (SFE) in 2008 [3] and the American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons (AACE/AAES) in 2009 [4]. These new ESE recommendations have already received criticism [5], and differences with the previous recommendations need to be highlighted, which is the aim of this letter.

AI is defined as an adrenal mass detected on an imaging test ordered for a problem unrelated to adrenal disease. AI are found in 1% to 5% of abdominal CT scans and this frequency increases with age (< 1% before 30 years, 7% after 70 years) [6]. When an AI is discovered, two standard questions are asked: (1) is the AI functional? and (2) is the AI malignant? However, a third crucial question concerns the follow-up of these patients, taking into account the natural progression of AI. In this context, the new ESE recommendations have tried to address two other "practical" questions: (3) when does surgery need to be considered? and (4) how should patients who do not undergo surgery be followed?

Firstly, the decision tree for imaging proposed by ESE is presented in Fig. 1. A recent meta-analysis was done on 19 studies that evaluated different imaging modalities for initially diagnosing potential malignant features of AI. The results showed that a non-contrast CT scan is the preferred choice as first-line imaging to screen for malignancy of the mass. In patients with no known cancer history, a spontaneous density > 10 UH on the CT scan has a sensitivity of approximately 100% and a specificity of approximately 72% for diagnosing malignancy [7]. The first difference between the ESE and previous recommendations concerns the follow-up with imaging tests. If the AI is homogenous, < 4 cm and with a density ≤ 10 UH, no imaging follow-up is recommended by ECE, while SFE suggests a checkup after 6 months, 2 years and 5 years [3] and AACE/AAES after 6 months, 1 year and 2 years [4]. A review of the literature showed that with no history of cancer, the risk of developing a malignancy is very low (< 0.2%) [8] or is at least an exceptional random event [9]. The risk of complications related to radiation exposure from repeated CT scans, the psychological impact and the economic costs are arguments against the systematic use of imaging tests for AI follow-up [1,8]. It should be kept in mind, however, that the cut-off values are not absolute. For instance, 3 different CT scans over a 2-year follow-up period showed that 20% of adrenal nodules with a density of around 10 UH would at some point be reclassified from benign to indeterminate [10]. In addition, the determination of the 4 cm cut-off was not based on studies with a high level of proof [1], and a borderline AI, which may be very slow growing, could also be reclassified [5]. If the benign nature of an AI is uncertain, ESE suggests discussion amongst a multidisciplinary team the three following options: (1) immediate additional imaging with another method, (2) checkup at 6–12 months (via non-contrast CT scan or MRI) and (3) surgery [1]. As usually recommended, patients below 40 years and pregnant women should receive an urgent evaluation because of the higher likelihood of malignancy [2–4,6]. For these patients, imaging

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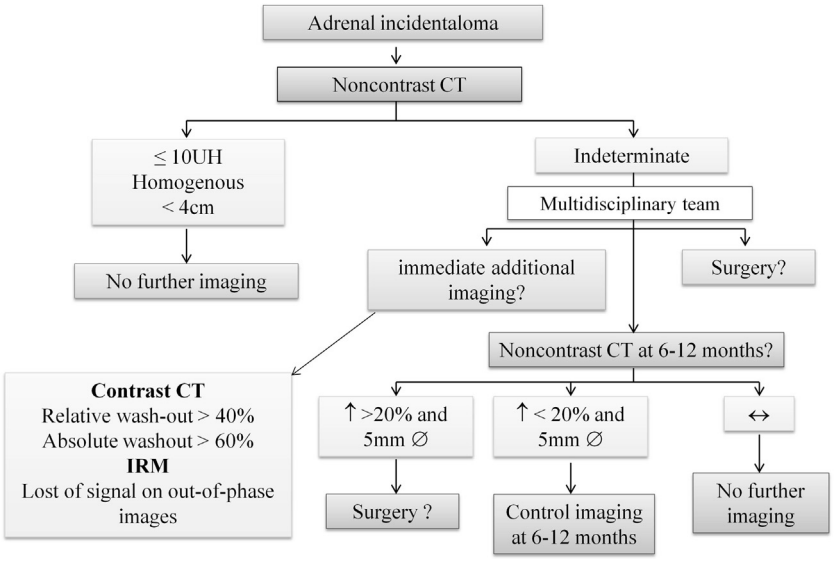

Fig. 1. Imaging in adrenal incidentalomas: decision tree proposed by the European Society of Endocrinology.

can be repeated and MRI is a good compromise to avoid the radiation risk from additional imaging. For patients with a known history of cancer, FDG-PET/CT could replace other imaging and indeterminate lesions could be followed-up at the same interval and with the same method as primary malignancies. ESE suggests that nodules with a density below10 UH and smaller than 4 cm do not need follow-up [1]. However, in the meta-analysis cited above, if patients had an extra-adrenal malignancy, 7% of AI with a density below 10 UH corresponded to metastasis [7]. We therefore think that every patient with a history of cancer should keep having an imaging follow-up. Finally, follow-up should be individualized to the patient, especially for nodules with borderline characteristics.

Secondly, the decision tree proposed for laboratory screening is presented in Figs. 2 and 3. The first steps are basically similar to those previously proposed [2–4,6]. Tests to be done at diagnosis include the routine measurement of metanephrines, screening for hypokalemia and hyperglycemia, a mineralocorticoid evaluation in case of hypertension or hypokalemia history and screening for hypercortisolism using the 1 mg overnight dexamethasone suppression test (DST). The threshold for diagnosing subclinical hypercortisolism remains at 1.8 μg/dL (50 nmol/L), with 95% sensitivity and 80% specificity [11]. The use of this 1.8 μg/dL threshold is now supported due to the strong demonstration of increased morbidity and mortality in patients with a post-DST cortisol greater than 1.8 μg/dL [12,13]. If there is evidence of hormonal hypersecretion, management should be discussed by a multidisciplinary team. With regard to follow-up, while it was previously recommended a regular reevaluation of the DST for 5 years [3,4], ESE does not recommend repeating the DST in patients with a cortisol at the first DST ≤ 1.8 μg/dL without comorbidities (diabetes or glucose intolerance, hypertension, obesity, dyslipidemia, osteoporosis) [1]. Reassessment of excess cortisol and comorbidities, i.e. follow-up by an

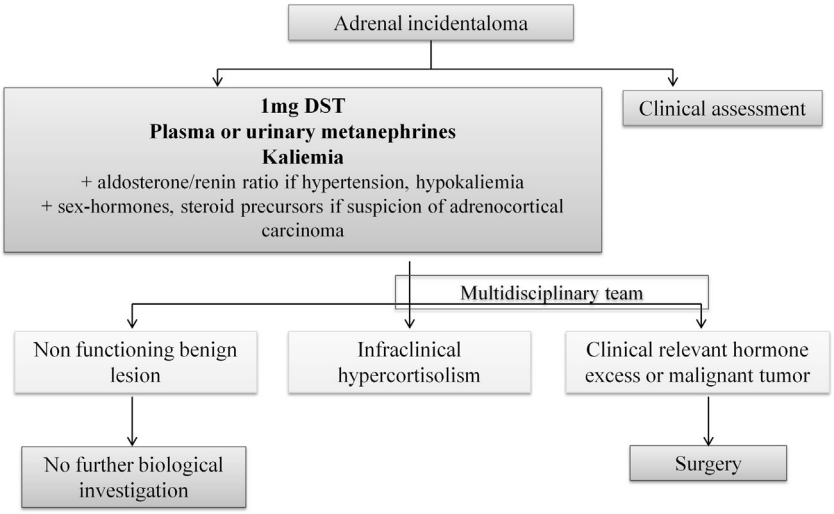

Fig. 2. Biochemical investigations in adrenal incidentalomas: decision tree proposed by the European Society of Endocrinology.

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