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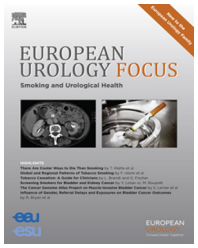

Review – Adrenal Glands

Work-up of the Incidental Adrenal Mass

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Abstract

Context: Incidental adrenal masses (or adrenal incidentalomas [AI]) are a common finding during imaging and are present in up to 5% of the computed tomography (CT) scans performed on the general population. The best way to manage these lesions is still under discussion.
Objective: To evaluate recent literature and available guidelines regarding the work-up of AIs.
Evidence acquisition: We used a medical search engine to identify studies published in the past 5 yr regarding AIs. We also evaluated current guidelines and the most relevant papers published before 2010.
Evidence synthesis: Unenhanced and contrast-enhanced CT, with laboratory tests to exclude functional lesions, are the most sensitive and specific methods currently available for the characterisation of adrenal masses. Magnetic resonance imaging, positron emission tomography–CT and fine-needle aspiration biopsy can be used as adjunct diagnostic tools in indeterminate lesions but are rarely indicated. In a relatively high number of indeterminate nodules, follow-up or surgery is suggested, although most of these lesions turn out to be benign.
Conclusions: Various imaging modalities, with CT being most important, are available to diagnose malignant and functional lesions in AIs. An improved identification of benign lesions is warranted to reduce the number of unnecessary surgeries and follow-up examinations in patients with benign lesions.
Patient summary: We performed a review of the literature on and guidelines for the management of incidental adrenal masses. It is possible to detect the presence of lesions that require surgery in the majority of cases. Follow-up is required for lesions that are not treated surgically.

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1. Introduction

An incidental adrenal mass (or adrenal incidentaloma [AI]) is defined as an adrenal lesion >1 cm identified in an imaging examination performed as a result of a clinical question neither related to nor suspicious for adrenal disease in patients who have no clinical suggestion of adrenal disease [1]. By this definition, adrenal masses in patients with a known malignancy and those showing clinical signs or symptoms hinting at an underlying adrenal disorder discovered before or after imaging are not called AIs [2]. AIs are discovered during thoracic or abdominal cross-sectional imaging in 0.8–5.0% of examinations [3–5]. Their incidence tends to increase with age, increasing

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the prevalence of AIs up to 10% in computed tomography (CT) scans performed in the elderly population [4,6].

The majority of AIs, even if present in cancer patients, are nonfunctional, benign lesions that account for 82.5% of cases. These nonfunctional benign lesions comprise adenomas (61%), myelolipomas (10%), adrenal cysts (6%), and ganglioneuromas (5.5%) [3,6,7]. The remaining adrenal pathologies of AI include cortisol-secreting adenomas (5.3%), pheochromocytomas (5.1%), adrenocortical carcinomas (4.7%), metastatic lesions (2.5%), and aldosteronomas (1%) [3,6,7].

When an AI lesion is detected, a clinical examination checking for subtle signs and symptoms of adrenal dysfunction and a laboratory work-up to exclude functional lesions are mandatory. Functional lesions, such as cortisol-secreting lesions or pheochromocytomas, are associated with higher morbidity and mortality [8,9]. Currently, in spite of several limitations, CT is considered the most useful imaging technique in the differential diagnosis of adrenal masses; magnetic resonance imaging (MRI) and positron emission tomography (PET)/CT appear to have an ancillary role for indeterminate lesions. The majority of the evidence on AIs stems from retrospective studies only; as a consequence, indications given in the currently available guidelines vary [2,10,11].

2. Evidence acquisition

We performed a qualitative literature search of studies published in English using the terms *incidental adrenal mass* and *adrenal incidentaloma*. We searched Medline for the period January 2010 to September 2015, considering both original research and review papers. We examined only peer-reviewed articles. We considered further literature, including works published before 2010, by screening the references of the identified articles.

3. Evidence synthesis

When an AI is discovered, the main task is to exclude functional or malignant disease. Functional adrenal lesions are commonly related to a subclinical Cushing syndrome, symptoms associated with pheochromocytoma or hyperaldosteronism. Primary malignant adrenal tumours and metastases should be ruled out, particularly in patients who have a known or suspected primary tumour. Imaging studies and a laboratory work-up are necessary to exclude these entities [12].

3.1. Role of computed tomography

CT is currently the imaging modality of choice according to all guidelines for the work-up of adrenal masses. A literature overview demonstrates that size is a risk factor both for functional and malignant adrenal lesions, with a general cut-off for increased risk at 4 cm [13]. With this cut-off, the sensitivity of CT is about 93%, but the specificity is fairly low (42%) because of the relative rarity of malignant adrenal lesions [14]. Precontrast CT is usually sufficient to accurately diagnose a lipid-rich benign adenoma irrespective of its size [15]. In the case of non–lipid-containing lesions or incidental masses in the absence of a precontrast scan, delayed enhanced scans are diagnostically helpful because they identify an absolute or relative wash-out of the contrast medium that is typical for benign lesions. Further evaluation of nonfunctional lesions using PET or fine-needle aspiration (FNA) is recommended only in selected cases.

According to a meta-analysis of 10 studies that included 495 adrenal lesions (223 malignant), the recommended threshold for CT density measurements to identify benign lipid-rich adenomas correctly is $\leq$10 Hounsfield units (HU). At this threshold, pooled sensitivity and specificity were 71% and 98%, respectively. HU $\leq$2 were reported as always benign. Although specific for diagnosis of benign lesions, these results imply that, given the low prevalence of malignancy [13,16], a large number of benign adenomas are nonlipid-containing (lipid-poor) adenomas, and further tests are necessary to exclude malignancy in these lesions. Bae and co-workers [17] suggested a histogram analysis of unenhanced CT density values to identify lipid-containing adenomas not evident in simple density analysis. An improved characterisation of lipid-poor adenomas as benign in up to 52% of cases using this method has been described [18]. Both lipid-rich and lipid-poor benign adenomas show a faster wash-out of contrast medium than other adrenal masses. This feature can be exploited diagnostically, leading to high performance indices. Wash-out is measured as either *absolute* (calculated as [portal venous HU – delayed phase HU] / [portal venous HU – precontrast HU]) or *relative* (calculated as [portal venous HU – delayed phase HU] / portal venous HU) wash-out. Although absolute wash-out may be more exact when taking into account precontrast lesion density [19], the diagnostic performance of both methods seems to be largely equivalent [15]. The relative method is also applicable if no precontrast scan is performed, as done in the majority of abdominal CT examinations. Short CT protocols are needed in clinical practice. Although abbreviated, 10-min–delay CT protocols seem to provide high specificity [20], more recent results indicate that sensitivity is not as high as prior research had indicated [21]. According to initial research, a 5-min delay may be sufficient to determine a diagnostic degree of wash-out compared to a 10-min delay, allowing clinicians to further tailor CT protocols to address the needs of clinical practice [19]. Of note, there is no consistent definition of absolute and relative wash-out.

The reproducibility of CT measurements in terms of inter- and intrareader agreement is underinvestigated in the literature. Although the agreement appears generally to be good, various factors related to patients' characteristics, acquisition parameters, and observer characteristics could influence the quantitative evaluation of adrenal masses [22]. Consequently, great caution has been advised when using specific attenuation threshold values for diagnosis of adrenal lesions [22].

Besides these quantitative approaches, qualitative criteria such as irregular borders; thickened enhancing rim;