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Review

Contemporary imaging of incidentally discovered adrenal masses

Daniel J. Wale[a,b,*], Ka Kit Wong[a], Benjamin L. Viglianti[a,b], Domenico Rubello[c], Milton D. Gross[a,b]

[a] Department of Radiology, University of Michigan Hospital, Ann Arbor, MI 48109, USA
[b] Department of Nuclear Medicine, Department of Veterans Affairs Health System, Ann Arbor, MI 48105, USA
[c] Radiology, Medical Physics, Santa Maria della Misericordia Hospital, 45100 Rovigo, Italy

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ABSTRACT

Adrenal lesions are routinely encountered incidentally in clinical practice. Although most of these lesions are benign, malignancy needs to be excluded. Therefore, the initial clinical workup is to exclude aggressive characteristics suggesting malignancy and to identify characteristics predictive of the most common benign lesion, an adrenal adenoma. Predicting a benign adenoma using a variety of imaging modalities has been widely studied using unenhanced computed tomography (CT), contrast enhanced CT, and magnetic resonance (MR) imaging. This review article describes the currently used imaging protocols and clinical interpretation criteria of common adrenal lesions. An adenoma can be predicted if a homogenous soft tissue adrenal mass demonstrates low attenuation (upper threshold value of 10 Hounsfield Units) on unenhanced CT, demonstrates an absolute enhancement washout of $\geq$ 60% and/or relative enhancement washout of $\geq$ 40% on adrenal washout contrast enhanced CT, or demonstrates signal loss in opposed-phased MR imaging. If an adrenal adenoma cannot be predicted based upon these criteria, the lesion should be evaluated for other imaging characteristics that suggest a specific pathology, such as an adrenal cyst or myelolipoma. Although nonspecific and with limitations, 18F-fluorodeoxyglucose (FDG) PET/CT has a potential role for differentiating benign from malignant lesions based upon the amount of radiopharmaceutical uptake with malignant lesions generally having greater uptake. If clinical and/or hormonal screening suggests a pheochromocytoma, consideration can be given to 18F-dihydroxyphenylalanine (DOPA) or 123I-metaiodobenzylguanidine (MIBG) in addition to CT and MR. Finally, this review proposes a diagnostic work-up strategy for routine use in clinical practice.

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Contents

* Corresponding author at: VA Medical Center, Department of Nuclear Medicine D748, 2215 Fuller Road, Ann Arbor, MI 48105, USA.
E-mail address: dwale@med.umich.edu (D.J. Wale).

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1. Introduction

Adrenal lesions are routinely encountered incidentally in clinical radiologic and nuclear medicine practice and are commonly referred to as adrenal incidentalomas. In one study evaluating chest CT performed for lung cancer screening, the prevalence of adrenal incidentalomas was 4.4% [1]. As these lesions can arise from a wide variety of processes, their clinical evaluation must be multifactorial, including biochemical and imaging studies tailored to each patient, with particular emphasis on identification of hormonally active adrenal lesions and exclusion of malignancy [2].

Benign adrenal lesions can be found in 3–10% of the general population, and of these, the most frequent lesion in more than 80% of cases is a non-functioning, benign adrenal adenoma. By contrast, adrenal metastases are by far the most common malignant lesion [3,4]. Additional primary adrenal lesions encountered include macronodular hyperplasia, adrenocortical carcinoma, myelolipoma, pheochromocytoma, cyst, and hemorrhage [4].

A variety of imaging modalities exist to aid the clinician in the workup of patients with adrenal incidentalomas. The most common include computed tomography (CT), magnetic resonance (MR) imaging, and 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT. A variety of other radiopharmaceuticals are also available in the evaluation of adrenal masses including 18F-dihydroxyphenylalanine (DOPA) and 123I-metaiodobenzylguanidine (MIBG) for assessment of the sympathetic-medullary system, and 11C- and newer 123I-labeled metomidate (MTO) that is used for adrenal cortical imaging, although not all are in routine use [5].

This article will review imaging protocols and findings of CT, MR, and 18F-FDG PET/CT in the evaluation of adrenal incidentalomas highlighting key studies in the literature. These protocols are important for the referring physician to be familiar with as they differ from many standard non-adrenal mass CT and MR protocols and therefore must be communicated to the imaging facility by the referring physician to ensure the proper imaging test is performed to ensure diagnostic efficacy. Additionally, a review of patient work-up strategies will be presented.

For this review, a literature search was performed in September 2016 using Medline (OVID) and PubMed. Search terms included *adrenal incidentaloma*, *adrenal adenoma*, *adrenal cortical carcinoma*, *adrenal myelolipoma*, *adrenal metastases, pheochromocytoma*, *CT*, *MR*, *18F- DOPA,* and *18F- FDG PET/CT* and combinations thereof. The authors (D.J.W., B.L.V., and K.K.W.) reviewed and identified the key publications that are the most clinically applicable and reflect the current state of contemporary adrenal imaging.

2. Imaging findings

2.1. CT

2.1.1. Adenomas

Unenhanced CT has value in differentiating benign adrenal adenomas from other lesions, most commonly metastases, with high specificity. This strategy of confirming benign adrenal adenomas with high positive predictive value and diagnostic confidence is helpful as adrenal adenomas are the most common etiology of adrenal incidentalomas. Additionally, unenhanced CT is technically simple and less complex and time consuming than contrast enhanced washout protocols that require multiple images at set time-points and administration of intravenous iodinated contrast.

The presence of intracellular lipids in adrenal adenomas results in a relatively low homogenous attenuation on CT that can be measured in Hounsfield units (HU) [6]. Boland, et al. evaluated characterizing adrenal lesions as adenomas based upon HU in 495 adrenal lesions from 10 different research studies. Using an upper threshold value of 2 HU resulted in 47% sensitivity and 100% specificity in characterizing adrenal adenomas. Increasing the upper threshold value to 10 HU increased the sensitivity to 71% with a minimal decrease in specificity to 98%. At a threshold of 20 HU, sensitivity increased to 88% with a corresponding decrease in specificity to 84% [7]. The current consensus uses an upper threshold value of 10 HU in routine clinical practice for characterizing an adrenal incidentalomas as a benign “lipid rich” adenoma [3,8–10].

Similar to unenhanced CT, benign adrenal adenomas have unique imaging characteristics on contrast enhanced CT. Compared to other lesions, adrenal adenomas classically demonstrate more rapid washout of iodinated contrast than other adrenal masses [11]. Two equations are routinely used to quantify adrenal washout, the absolute enhancement washout (AEW) and the relative enhancement washout (REW). AEW calculations require an unenhanced CT (UCT), initial contrast enhanced CT (ICT), and a 15-min contrast enhanced delayed CT (DCT). The AEW can then be calculated: $AEW = 100 \times [(ICT–DCT)/(ICT–UCT)]$ [11,12]. REW calculations require only ICT and DCT. The REW can be calculated: $REW = 100 \times [(ICT–DCT)/ICT]$ [11,12]. Benign adenomas typically demonstrate AEW $\geq$ 60% and REW of $\geq$40% [13].

Utilizing both unenhanced and enhanced CT creates a powerful diagnostic tool to distinguish primary adrenal lesions from metastases to the adrenal. An initial unenhanced CT is performed and reviewed by a radiologist. If the adenoma is lipid-rich and confirmed by demonstrating HU of 10 or less, the study is ended and the lesion is characterized as an adenoma. Otherwise, the patient is administered IV contrast and initial and 15 min delayed images are obtained. If there is homogenous enhancement, AEW and REW calculations are obtained in order to determine the presence of a lipid-poor adenoma. If the AEW is $\geq$60% and/or the REW $\geq$40%, the lesion is characterized as an adenoma. Otherwise, the lesion is characterized as a non-adenoma and the diagnosis is considered indeterminate.

Caoili, et al. characterized 166 adrenal lesions using a combined unenhanced and enhanced protocol using AEW measurements. They accurately predicted 160 of 166 adrenal lesions. In their study, three adenomas demonstrated AEW of $<$60%. Additionally, three non-adenomas demonstrated an AEW of >60% (one pheochromocytoma, one adrenal cortical carcinoma, and one metastasis from renal cell carcinoma) [14].

2.1.2. Non-adenomas

A myelolipoma is a benign adrenal mass that classically appears as a lesion with mixed density including areas of macroscopic fat [15]. The presence of fat density in the mass on CT is a very useful feature to characterize a lesion as a myelolipoma (Fig. 1). However, there are rare reports of other lesions also demonstrating fat density on CT including adrenal cortical carcinoma [16] and pheochromocytoma [17]. Additionally, a malignant lesion can occur in an adrenal that has a pre-existing benign lesion such as a myelolipoma. These are commonly referred to as “collision” tumors [18].

Adrenal cortical carcinoma usually presents as a large mass, often 6 cm or greater [19]. These masses usually demonstrate aggressive imaging characteristics such as necrosis, heterogeneous enhancement and/or attenuation, and can present with metastases to the liver and abdominal lymph nodes [20]. Calcifications within the lesion, direct invasion of other organs, and vascular invasion are also commonly seen [18]. Timely diagnosis of adrenal cortical carcinoma is crucial due to the poor prognosis and lack of effective therapies, with complete surgical resection being the only chance for cure.

Pheochromocytomas have a wide-range of appearances on CT, making them difficult to predict by CT imaging alone (Fig. 2).