CT and MR Imaging of the Adrenal Glands in Cortisol-secreting Tumors*

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Abstract. Cushing’s syndrome (CS), first described by the neurosurgeon Harvey Cushing in the 1930s, is the result of chronic glucocorticoid excess. In patients with adrenocorticotropic hormone (ACTH)-dependent CS, bilateral hyperplasia of the adrenal cortex occurs, while in those with ACTH-independent primary CS, either adrenocortical tumors or primary adrenal hyperplasia can be observed. Cortisol-secreting adrenocortical tumors are more frequently adenomas, while adrenal carcinoma accounts for only 5% of cases. Unfortunately, no reliable endocrinological tests are available and no specific tumor markers exist to differentiate between benign and malignant adrenal tumors, so computed tomography (CT) and magnetic resonance (MR) imaging studies are currently required to localize and define adrenal lesions. Additional information to conventional imaging can be obtained using ¹⁸F-fluoro-2-deoxyglucose (FDG)-positron emission tomography (PET)/CT, while percutaneous image-guided fine-needle aspiration cytology (FNAC) in some cases has shown a high accuracy in detecting malignancy and in confirming adrenal metastases. New PET tracers with selective affinity for the adrenal tissue are still under evaluation. Multidetector CT scan, with the combination of unenhanced and dynamic scans, represents the single most accurate modality for the detection and the characterization of adrenal adenomas. In these lesions, chemical-shift MR imaging produces a typical loss of signal intensity on out-of-phase breath-hold gradient-echo images in lipid-rich adenomas. For these lesions there is no difference between CT and MR imaging, while MR chemical shift imaging is very helpful in identifying the additional small group of adenomas where intracellular lipid content is minimal.

Cushing’s syndrome (CS), first described by the neurosurgeon Harvey Cushing in the 1930s, is the result of chronic glucocorticoid (i.e. cortisol) excess (1). Once iatrogenic causes and pseudo-Cushing’s states, such as chronic alcoholism, depression, or polycystic ovary syndrome, have been excluded and the diagnosis of primary hypercortisolism is confirmed, the second step should be to differentiate between adrenocorticotropic hormone (ACTH)-dependent and ACTH-independent CS. In patients with ACTH-dependent CS, bilateral hyperplasia of the adrenal cortex occurs, while in those with ACTH-independent ‘spontaneous’ CS, either adrenocortical tumors or primary adrenal hyperplasia can be observed (Figure 1). Cortisol-secreting adrenocortical tumors are more frequently adenomas, while adrenal carcinoma accounts for only 5% of cases of CS (2). Unfortunately, no reliable endocrinological tests are available and no specific tumor markers exist to differentiate between benign and malignant adrenal masses, so computed tomography (CT) and magnetic resonance (MR) imaging studies are currently required to localize and define adrenal lesions, although these techniques sometimes fail to characterize some small adrenal masses (3, 4). Additional information to conventional imaging can be obtained using ¹⁸F-fluoro-2-deoxyglucose (FDG)-positron-emission tomography (PET)/CT, where tumor/liver maximum standardized uptake values ratio can be helpful in cases of doubtful visual uptake (5). In some cases, percutaneous image-guided fine-needle aspiration cytology (FNAC), as well as ¹³¹I-6- β-iodomethyl-norcholesterol scintigraphy, have shown high accuracy and were useful to confirm adrenal metastases or rare primary adrenal hyperplasia, in combination with CT and MR imaging (2, 6, 7).

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Computed Tomography Scanning

In clinical practice, the adrenal glands can be well demonstrated with both single and multidetector CT scanners, using slice thickness 2.5-3 mm with 1.5-3 mm interval, before and after 100-150 ml of iodinated contrast administration. Usually, a portal venous phase (60-90 s) is preferred (8). Multidetector scanners offer higher performance, with collimation even smaller than 1 mm, allowing better multiplanar reconstructions (in coronal and sagittal planes), useful for depicting all anatomic relationships of the adrenal mass (9). On CT scan, normal adrenal glands appear symmetric and homogeneous, with a density approximately equal to that of the kidney (10). Adrenal adenomas usually appear relatively small (1-5 cm), round or ovoid, homogeneous, with smooth borders and lower than water density (<10 Hounsfield units [HU] without contrast), due to abundant intracellular lipid content (9-13). Two thirds of adenomas contain significant intracellular lipid and show the typical unenhanced CT attenuation <10 HU, while 25-30% of them are lipid-poor, with unenhanced CT attenuation >10 HU (10, 14, 15). Large adenomas may appear inhomogeneous, containing cystic degeneration, calcifications, hemorrhage and necrosis (15). On contrast-enhanced CT, performed 60 s and 15 min after intravenous contrast medium administration, adenomas show both a rapid enhancement and a rapid wash-out loss of contrast, while non-adenomas typically show a slower contrast washout phase (Figure 2). When the 15-min delay protocol is used, an absolute contrast washout of >60% and a relative contrast washout of >40% have 86-88% sensitivity and 92-98% specificity for the diagnosis of adenomas, respectively (9, 10, 12, 14). With the combination of unenhanced and dynamic scans, CT represents the single most accurate modality for detection and characterization of adrenal adenomas (9, 10).

Unfortunately, no differentiation can be made between cortisol-secreting adenomas and incidentally discovered nonfunctioning adrenal masses on the basis of imaging features alone (9, 11, 15). Imaging findings more suspicious of adrenal carcinomas are large lesion size (>4 cm), irregular or unclear margins, heterogeneous appearance and attenuation higher than 10 HU on unenhanced CT (9, 10, 14). On contrast-enhanced CT, adrenal carcinomas enhance avidly, with relative and absolute percentage washout of <40% and <60%, respectively, and exceptionally, they remain stable for more than 3-4 months (10, 14).

Magnetic Resonance Imaging

The appropriate MR imaging study protocol of adrenal glands should include (9): T1-weighted (T1w) gradient-recalled echo (GRE) sequences in- and out-of-phase, slice thickness of 3-5 mm; T2-weighted (T2w) turbo spin-echo (TSE) sequences with fat suppression, slice thickness of 3-5 mm and T2w half-Fourier acquisition single-shot turbo-spin-echo (HASTE) sequences, slice thickness of 5 mm. The use of breath-hold sequences mostly eliminates most motion artifacts (16). Intravenous gadolinium (Gd) administration allows the characterization of the vascular pattern of adrenal masses, like contrast-enhanced CT. Axial images are standard, while coronal and sagittal images may help in delineating large adrenal masses (9). On MR, normal adrenal glands show low to intermediate T1- and T2-signal intensity, equal to or slightly lower than that of the normal liver (11, 14). Adrenal adenomas usually appear homogeneous on all sequences, mostly isointense to T2w TSE sequences and slightly hypointense to T1w TSE sequences compared with the liver, and show moderate and relatively uniform enhancement on early Gd-enhanced images (17). Small areas of abnormal signal intensity within an adenoma may be due to cystic change, hemorrhage or necrotic foci (9, 14). Chemical-shift images (CSI), based on the physical property of fat protons that precess at a lower frequency than water protons, produces loss of signal intensity on out-of-phase breath-hold gradient-echo images in lipid-rich lesions, typical of adenomas (8) (Figure 3). The abundant intracellular lipid content characteristic of benign adrenal masses is responsible for the typical dropout of 40% at CSI (11, 17).

CSI is very helpful in identifying the additional small group of adenomas in which intracellular lipid content is minimal, whereas for lipid-rich adenomas, there is no particular difference between CT and MR imaging, since CT should be considered virtually 100% accurate for their detection (9, 10, 13, 14). Adrenal carcinomas are usually larger than adenomas, heterogeneous on both CT scan and MR imaging, due to areas of necrosis, hemorrhage and calcifications (10, 11). On MR, they appear large, heterogeneous, invasive and bright enhancing, with intermediate signal intensity at T2w TSE sequence, with nonhomogeneous vascularization pattern, and without decrease of signal intensity at opposed-phase imaging compared with in-phase imaging (9).

In conclusion, for all patients with CS, both CT and MR imaging are usually performed, especially when a differentiation between benign and malignant adrenal masses is required. In selected cases, when requested for surgical planning, image-guided FNAC may represent a safe and sensitive procedure. On 18F-FDG-PET and PET/CT, malignant lesions usually show a high uptake, while the uptake is in the range of hepatic activity for benign lesions (18). New PET tracers with selective affinity for the adrenal tissue, such as 11C-metomidate (MTO) and 18F-etomidate (FETO), are still under evaluation (19, 20).
Figure 1. Computed tomography (CT) images of the adrenal glands in Cushing’s syndrome. (a) Increased adrenal gland thickness on both sides in a case of adrenal hyperplasia on axial contrast-enhanced CT, with some preservation of gland shape. (b) Bilateral nodular hyperplasia on axial contrast-enhanced CT scan. (c) A case of adrenal carcinoma on portal venous phase CT coronal image, depicting a large left adrenal mass with heterogeneous contrast enhancement, containing hypodense necrotic areas.

Figure 2. Cushing’s syndrome due to a cortical adenoma: note the regular contours of a homogeneous, hypodense adenoma in the left adrenal gland on axial CT. Lesion attenuation was measured by placing a single region of interest (ROI) over the adrenal mass: unenhanced CT showed a density measurement of 2 HU (a), contrast-enhanced CT in venous (b) and delayed (c) phases showed significant enhancement and rapid washout, with absolute washout 70%, indicating a lipid-rich adenoma.

Figure 3. Left adrenal cortisol-secreting adenoma. (a) Unenhanced CT scan shows a smooth, ovoid, well-defined low-attenuation mass, with an HU measurement of -4 HU. Axial in-phase (b) and out-of-phase (c) gradient-echo T1w MR images (chemical-shift imaging) show the mass with the classic signal dropout, a finding that confirms the presence of intracellular lipid, characteristic of benign adenoma.
References


