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Title: Should we use CT or MRI for detection and characterization of benign adrenal lesions?

Abstract

Objectives: Computed tomography (CT) and magnetic resonance imaging (MRI) are the main imaging modalities used for analysis of adrenal lesions. We compared the ability of CT and MRI to detect and characterize benign adrenal lesions.

Material and methods: Unenhanced abdominal CT and MRI were performed in 16 patients (age range 39-77), and reviewed by a radiologist with 6 years of experience in abdominal imaging. The presence, number, size, and structure of each mass were analyzed and compared between the two modalities.

Results: There were 18 adrenal masses in 11 patients, four patients had adrenal hyperplasia (AH), whereas one patient had left-sided AH and right-sided adenoma. Ten masses were ≥ 2 cm in diameter, and were perfectly depicted using CT and all MRI techniques. There were nine masses with diameter < 2 cm detected by CT, three of them were missed using MRI. AH was detected in five patients using CT, but its mild form was missed in one patient using MRI. Four masses with attenuation values of > 10 Hounsfield units could not have been characterized using unenhanced CT, but three of them were characterized using MRI.

Conclusion: CT has higher sensitivity for detection of small adrenal tumours and adrenal hyperplasia than MRI. MRI is an important tool in characterization of adrenal masses that could not be characterized using unenhanced CT.

Keywords: adrenal gland, computed tomography, magnetic resonance imaging

Introduction

Computed tomography (CT) and magnetic resonance imaging (MRI) are the main imaging modalities used for detection and characterization of adrenal lesions. Detection of small adrenal neoplasms is essential in patients with endocrine hypertension because most adrenal adenomas in patients with primary aldosteronism are smaller than 2 cm in diameter.¹

Moreover, over 20% of hypersecreting tumours are less than 1 cm in diameter. On the other hand, characterization of adrenal pathology is very important, especially in patients with a known malignancy, because incidental adrenal nodules are present in approximately 5% of abdominal CT exams.^{2,3}

Despite of frequent use of CT and MRI in clinical practice, there are limited data in the literature showing which technique is more sensitive in detection of benign adrenal lesions, and which one should be preferred for their characterization. Moreover, most of the papers on this topic are concentrated on characterization of adenomas only,^{4,5} or were published before the era of contemporary multidetector CT and high magnetic field strength MRI scanners.^{6,7}

According to American College of Radiology (ACR) Appropriateness Criteria, CT and MRI are rated equally appropriate for the initial evaluation and follow-up of incidentally discovered adrenal masses >1 cm, but there are no data for determining the accuracy of imaging for masses measuring less than 1 cm.⁸ The decision to obtain CT or MRI is usually left to clinician preference and depends also on institutional experience.⁹ According to our experience, contrast-enhanced adrenal CT is a complex procedure that requires a radiologist available during the scanning, in order to immediately detect the mass, measure its attenuation, and decide whether contrast administration is needed. Therefore, our clinical experience with adrenal imaging in patients with endocrine hypertension is to start the evaluation using non-enhanced CT irrespective of patient's age and renal function. Non-enhanced is then followed by adrenal MRI if the lesion cannot be completely characterized

using non-enhanced CT. We also use MRI for further characterization of adrenal incidentalomas that are most frequently detected during CT examinations. In this study we compared the ability of these two modalities to detect and characterize benign adrenal lesions with special emphasis on small adrenal tumours (<2 cm).

Material/Patients

There were 16 patients (7 males and 9 females, age range 39-77) retrospectively included into the study. In all patients MRI examination of the adrenal glands was performed during one-year period before the beginning of the study, and all patients had previous CT scan of adrenal glands available for comparison. Although arterial hypertension (blood pressure >140/80 mmHg) was present in 13 patients, suspicious secondary hypertension was indication for adrenal imaging in 9 patients only, whereas in all other hypertensive and non-hypertensive patients adrenal pathology was incidentally discovered during radiological workup of other diseases (Table 1). One hypertensive patient had biochemically proven primary aldosteronism, and the other previously underwent unilateral adrenalectomy because of pheochromocytoma. In one patient with previous colorectal and endometrial malignancy and incidentally discovered multiple adrenal masses, subclinical Cushing's syndrome was detected after overnight dexamethasone suppression test. Hospital's institutional review board approved the study, and informed consent was obtained from all patients.

Methods/Imaging Protocols

CT scanning was performed on a 40-detector row CT scanner (SOMATOM Sensation 40, Siemens Medical Solutions, Erlangen, Germany) without contrast administration, with collimation of 1.2 mm and breath-hold technique. 2-mm-thick slices were used for image analysis. The attenuation coefficient was measured within the lesions using circular region of

interest (ROI) as large as possible to include major part of the lesion and exclude surrounding structures. The mass was considered to be adrenocortical adenoma if it had attenuation values of -30 to +10 Hounsfield units (HU), whereas the mass was described to be myelolipoma if it had attenuation values of fat tissue (i.e. -150 to -31 HU).

MRI examination was performed on a 1.5T scanner (MAGNETOM Avanto, Siemens Medical Solutions, Erlangen, Germany) using multichannel phased-array body coil. The scanning protocol included breath-hold nonenhanced axial gradient-recalled echo (GRE) T1 chemical-shift imaging (TR 160 ms, TE 4.9/2.4 ms, slice thickness 4 mm, slice gap 20%, matrix 256), coronal GRE T1 chemical-shift imaging (TR 160 ms, TE 4.9/2.4 ms, slice thickness 3 mm, slice gap 10%, matrix 256), and axial three-dimensional (3D) volumetric interpolated breath-hold examination (VIBE) fat-saturated T1-weighted sequence (TR 4.9 ms, TE 2.4 ms, slice thickness 3 mm, matrix 320). Furthermore respiratory triggered axial T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) images (TR 1350 ms, TE 91 ms, slice thickness 4 mm, slice gap 20%, matrix 256), and coronal T2 weighted HASTE images (TR 1350 ms, TE 91 ms, slice thickness 3 mm, slice gap 10%, matrix 256) were acquired. Circular ROI used to measure signal intensity (SI) within the lesion on chemical-shift MRI was as large as possible to cover the majority of the mass and not to include retroperitoneal fat tissue. Signal intensity index (SII) was calculated for all masses (SIIP SI on in-phase images, SIOP SI on out-of-phase images):

$$SII = \frac{SIIP - SIOP}{SIIP}$$

The mass was characterized as adrenocortical adenoma if SII had value of >16.5%. The mass was classified as myelolipoma if it had high-signal of in-phase T1-weighted images with suppression of the signal on 3D VIBE T1-weighted fat-saturated images.

Data Analysis

All CT and MRI exams were retrospectively reviewed by the same radiologist with 6 years of experience in abdominal imaging, who was blind on the clinical and hormonal data, as well on the results of the other imaging modality. The time interval between CT and MRI scanning ranged from 2 weeks to 57 months depending on the presence of extraadrenal malignancy and morphology of the adrenal mass. In all patients the morphology of adrenal glands has not been changed during this time interval. In all patients the presence, number, size, and structure of the mass were analyzed and compared between the two modalities. The final diagnosis was established based on CT and MRI findings, because none of the patients underwent adrenalectomy with pathohistological analysis of the adrenal glands. The patient with primary aldosteronism was treated conservatively with eplerenone because of high operative risk and good control of blood pressure and plasma potassium levels on conservative therapy. The patient with morphologically evident pheochromocytoma of the right adrenal gland has not undergone surgery because of previous left-sided adrenalectomy, and normal total urinary metanephrines. The patient with subclinical Cushing's syndrome wasn't treated surgically because adrenocortical adenomas were present bilaterally.

Results

There were 18 adrenal masses detected in 11 patients (10 adrenocortical adenomas, 5 myelolipomas, 1 pheochromocytoma, 1 cyst, and 1 mass that remained uncharacterized), four patients had adrenal hyperplasia (3 unilateral and 1 bilateral), whereas one patient had left-sided adrenal hyperplasia and adrenocortical adenoma of the right adrenal gland.

Ten masses were ≥ 2 cm in diameter (8 adrenocortical adenomas, a pheochromocytoma and a cyst), and were perfectly depicted using CT and all MRI techniques. There were 9 masses with diameter < 2 cm (3 adrenocortical adenomas, 5 myelolipomas and one uncharacterized

mass), three of them were smaller than 1 cm in diameter (one adenoma, two myelolipomas). All masses with diameter <2 cm were detected using CT. Three masses with diameter <2 cm were missed using MRI: one right-sided adrenocortical adenoma, and 2 left-sided myelolipomas. This right-sided adrenocortical adenoma was located in proximity to the right hepatic lobe and inferior caval vein, and was overlooked because of poorer spatial resolution of MRI compared to CT. One myelolipoma with diameter <1 cm was missed due to insufficient spatial resolution of MRI and looked as incisure within the adrenal gland parenchyma (Fig. 1), whereas the other was located extraadrenally and could not be differentiated from the retroperitoneal adipose tissue using MRI.

Four masses with attenuation values of >10 HU could not be characterized using unenhanced CT (two masses in patients with known malignancy, one in a patient with previously resected pheochromocytoma, and one in a patient with incidentally discovered adrenal mass during health check-up ultrasonography). Three of these masses were characterized using MRI as an adrenal cyst (Fig. 2), pheochromocytoma (Fig. 3), and adrenocortical adenoma (Fig. 4). In a patient with a mass described as pheochromocytoma, there was no biochemical evidence of pheochromocytoma and the patient has not undergone surgery. One mass with diameter <2 cm in a patient with previous colorectal and endometrial cancer couldn't be characterized using any of the techniques (Fig. 5), but remained unchanged during 14 months and was therefore considered to be benign. One mass with attenuation values of -30 HU was incorrectly characterized as adrenocortical adenoma using non-enhanced CT, whereas on MRI it was evident that it was myelolipoma, composed mostly of adipose tissue that lost its signal after fat suppression (Fig. 6).

Adrenal hyperplasia was detected in five patients, and it was bilateral in one patient only.

Two patients had more extensive form of hyperplasia with crural thickness of >1 cm. In these two patients and in two patients with unilateral mild form of adrenal hyperplasia, it was

detected using both CT and MRI. Adrenal hyperplasia was easily detected using CT, whereas in all patients out-of-phase GRE technique was the best MRI sequence to depict adrenal hyperplasia because hypertrophic adrenal gland was surrounded by india ink artifact (Fig. 7). In one patient with contralateral adrenocortical adenoma, the mild form of unilateral adrenal hyperplasia was detected using CT, but was missed using MRI due to lower spatial resolution.

Discussion

Depiction of discrete adrenal changes is of utmost importance in patients with endocrine hypertension because it is frequently caused by hormone hypersecretion within small adrenal tumours. Using imaging techniques it may be difficult to accurately identify and measure the adrenal glands and distinguish them from normal adjacent structures.¹⁰ According to the results of our study, CT has better sensitivity for detection of small adrenal tumours than MRI that missed 3 out of 9 small tumours detected using CT. The main explanation for the greater sensitivity of CT is the better spatial resolution, smaller slice thickness and paucity of respiratory artifacts on CT compared to MRI. CT is fast and readily available technique with lower cost than MRI, and can detect adrenal masses >5 mm in diameter.¹¹ Therefore, we believe that CT should be preferred method for detection of adrenal pathology in patients with clinical and laboratory findings of an adrenal endocrinopathy, because it is frequently caused by a lesion <2 cm in size. In such patients MRI could be used for follow-up, especially in younger patients, in order to prevent unnecessary use of ionizing radiation, and to characterize the tumour if the characterization was not possible using CT.

In our study, only one out of 19 tumours could not have been characterized using MRI, compared to 4 out of 19 tumours that were not characterized using unenhanced CT.

Furthermore, one mass was incorrectly characterized based measurement of attenuation values on unenhanced CT. Characterization of adrenal masses is especially important in

patients with a known malignancy, because adrenal gland is the frequent site of metastatic disease that presents up to 36 percent of incidentally discovered adrenal tumours in patients with known malignancy.¹² Adrenal metastases should be morphologically differentiated from non-functioning adrenal adenomas that are incidentally discovered in up to 5% of abdominal CT examinations in adult patients without malignancy,^{2,3} and even more often in patients with a known malignancy.¹³ In patients with a primary extraadrenal neoplasm and no other evidence of distant metastatic disease, characterization of the lesion using noninvasive imaging can reduce the necessity for percutaneous adrenal mass biopsy in most patients.¹⁴ Characterization of lipid-rich adenomas is straightforward using both unenhanced CT and MRI, and represented with attenuation values of ≤ 10 HU on CT, and obvious signal drop on opposed-phase MRI.¹³ Unfortunately, about 29% of adenomas have attenuation values higher than 10 HU and remain indeterminate on unenhanced CT scan.¹⁵ They could be distinguished from other pathology on contrast-enhanced CT with quantification of contrast material washout, but the radiologist should be available during examination in order to decide whether additional contrast-enhanced scanning is needed. For washout calculation, the scanning protocol requires at least dual-phase acquisition (i.e. venous and delayed phase), which is usually not performed in patients with malignancies and other extraadrenal pathology. That could lead to insufficient characterization of the mass on CT, even after contrast administration. Furthermore, intravenous contrast administration should be avoided in patients with renal insufficiency and allergy to contrast media, which makes the washout calculation impossible. For quantification of relative washout dual-phase acquisition is sufficient, while for calculation of absolute washout, unenhanced, venous and delayed phase should be scanned, leading to high radiation dose. Moreover, the assessment of enhancement washout of adrenal masses is valid only for lesions with relatively homogeneous attenuation after contrast administration.¹⁴ To avoid unnecessary use of ionizing radiation, especially in

younger patients, adrenal MRI could be of great help in characterization of adrenal masses.

Depiction of calcifications within the tumour is not possible using MRI, but calcifications are not typical for benign adrenal masses and visualization of calcification doesn't help much in adrenal mass characterization in adults.

We showed that MRI has very good soft-tissue resolution that allowed correct characterization of an adrenal cyst. Lipid-rich adrenal adenomas and cysts have similar attenuation to water, and a cyst can be misinterpreted as an adenoma on non-enhanced CT. To differentiate adrenal cysts from adenomas using CT, contrast material should be administered in order to show its lack of enhancement.¹⁶ In our patient the cyst could not have been characterized using non-enhanced CT because of dense intracystic content with attenuation values of 20 HU. On MRI this mass had homogeneous low T1 and high T2 signal, characteristic of a cyst, contained a thin rim, and did not lose signal on chemical-shift imaging (Fig. 2).

In the other patient with previously resected huge pheochromocytoma of the left adrenal gland, we found the heterogeneous right adrenal mass with high signal intensity on T2-weighted MRI examination (Fig. 3), that has been described as a typical characteristic of pheochromocytoma.^{17,18} The mass of the right adrenal gland had diameter of 2,2 cm, and was unchanged compared to preoperative imaging. The diagnosis of pheochromocytoma was not confirmed biochemically probably because of the size of the tumour, and the patient has not been operated. However, the diagnosis of pheochromocytoma could not have been excluded since 7% of pheochromocytoma patients have normal 24-hour urinary fractionated catecholamines, and 7% have normal total urinary metanephrines.¹⁹

Furthermore, using chemical-shift GRE imaging, we managed to depict intracellular lipids within a mass with density of 31 HU on unenhanced CT scan, confirming that it was adrenocortical adenoma (Fig. 4). The loss of SI on out-of-phase images was visually obvious,

and SII was calculated to be 67%. MRI can identify a small group of lipid-poor adenomas with the density of >10 HU on unenhanced CT, but with sufficient lipid content to be detected using chemical-shift GRE imaging [11]. The sensitivity of chemical-shift MRI for adenoma is 89% for masses with attenuation coefficient of 10-30 HU, and 75% for adenomas with attenuation of 20-30 HU.²⁰ Quantitative approach with calculation of SII allows their correct characterization, obviating the need for contrast administration. Therefore, chemical-shift MRI should be the second-line imaging tool for characterization of hyperattenuating adrenal masses.

MRI was also helpful in correct characterization of a myelolipoma. The presence of gross fat on CT with density of less than 30 HU is diagnostic of myelolipoma.¹⁸ One mass in our study had density of -30 HU and on CT it was described as a lipid-rich adenoma (Fig. 6). In this patient the mass had high signal on T1 weighted images, with obvious fat-suppression on 3D VIBE MRI technique, confirming that the lesion consisted of macroscopic fat tissue and that the mass was myelolipoma.

Adrenal hyperplasia can also be the cause of hormone hypersecretion leading to secondary hypertension. The normal adrenal body measures less than 10-12 mm, and the adrenal limbs normally measure less than 5-6 mm.¹⁸ In hyperplasia the adrenals are usually enlarged bilaterally, and maintain an adreniform shape with smooth surface, less often they are nodularly enlarged. In our study, its mild form was missed in one out of five patients on MRI, due to lower spatial resolution compared to CT. This further confirms our hypothesis that CT should be the first imaging modality for detection of adrenal pathology in patients with endocrine hypertension. If MRI is used for follow-up, out-of-phase chemical shift imaging allows better depiction of adrenal hyperplasia than in-phase and T2 weighted images, because the enlarged adrenal gland is surrounded by india ink artifact.

Although lesions with diameter <1 cm are usually considered to be too small to be characterized,²¹ we managed to characterize all three tumours that were smaller than 1 cm. Two masses with diameter <1 cm were myelolipomas, that could easily be differentiated from the adrenal gland due to very different density and signal intensity. The third mass was small lipid-rich adenoma of the right adrenal gland in a patient with abundant retroperitoneal fat tissue. However, although small adrenal tumours can easily be misinterpreted due to partial volume effects,²¹ in some instances they can be detected and characterized using imaging techniques. With technical improvement of the scanners, it can be expected that we would be able to detect and characterize more masses with diameter <1 cm, even in slim patients. The main limitation of our investigation is the low number of patients and lesions included in the study. The lesions were of different size and aetiology, and were not confirmed histologically. Therefore, we believe that these very indicative results of our investigation should be confirmed in a larger group of patients.

Conclusion

We believe that in clinical practice unenhanced CT should be the first-line modality for adrenal imaging in patients with endocrine hypertension, since it is readily available, rapidly performed, and has good sensitivity for detecting adrenal lesions. For lesions that remain indeterminate on unenhanced CT, the lesion should be characterized using MRI.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Table 1 Demographic, clinical and radiological data of patients included in the study.

Patient No	Age (years)	Gender	Arterial hypertension	Indication for imaging	Hormone analysis	Interval between CT and MRI (months)	Final diagnosis	CT findings	MRI findings
1	77	M	no	urolithiasis	normal	11	adenoma (≥ 2 cm)	lipid-rich adenoma	lipid-rich adenoma
2	51	F	yes	arterial hypertension	normal	6	adenoma (≥ 2 cm)	lipid-rich adenoma	lipid-rich adenoma
3	54	F	yes	abdominal pain	normal	6	adenoma (≥ 2 cm)	lipid-rich adenoma	lipid-rich adenoma
4	69	M	yes	arterial hypertension	primary hyperaldosteronism	36	right-sided adenoma (≥ 2 cm), left-sided adrenal hyperplasia (< 1 cm)	lipid-rich adenoma, adrenal hyperplasia	lipid-rich adenoma
5	65	F	yes	arterial hypertension	normal	18	bilateral adrenal adenomas (one < 2 cm and one ≥ 2 cm)	bilateral lipid-rich adenomas	bilateral lipid-rich adenomas
6	61	M	no	staging of urinary bladder cancer	normal	0.5	unilateral adrenal hyperplasia (> 1 cm)	adrenal hyperplasia	adrenal hyperplasia
7	52	F	yes	arterial hypertension	normal	16	unilateral adrenal hyperplasia (< 1 cm)	adrenal hyperplasia	adrenal hyperplasia
8	39	F	yes	previously operated pheochromocytoma	normal	12	pheochromocytoma (≥ 2 cm)	uncharacterized mass (attenuation 20 HU) with calcification	heterogeneous mass with high signal on T2wI
9	54	F	yes	arterial hypertension	normal	8	adenoma (≥ 2 cm)	lipid-rich adenoma	lipid-rich adenoma
10	57	M	yes	arterial hypertension	normal	27	bilateral adrenal hyperplasia (> 1 cm)	bilateral adrenal hyperplasia	bilateral adrenal hyperplasia
11	44	M	no	ultrasonographically detected mass (health checkup)	normal	5	adenoma (< 2 cm)	uncharacterized mass (attenuation 31 HU)	lipid-rich adenoma

12	57	F	yes	arterial hypertension	normal	30	unilateral adrenal hyperplasia (<1 cm)	adrenal hyperplasia	adrenal hyperplasia
13	67	M	yes	arterial hypertension	normal	57	adrenal myelolipoma (<2 cm)	lipid-rich adenoma	adrenal myelolipoma
14	66	M	yes	liver lesion	normal	27	4 adrenal myelolipomas (<2 cm)	4 adrenal myelolipomas	2 adrenal myelolipomas
15	58	F	yes	colorectal and endometrial cancer follow-up	subclinical Cushing's syndrome	14	3 adenomas (one <2 cm and two ≥2 cm), one uncharacterized mass (<2 cm)	3 lipid-rich adenomas, one uncharacterized mass (attenuation 27 HU)	2 lipid-rich adenomas, one uncharacterized mass
16	65	F	yes	renal-cell carcinoma follow-up	adrenal cyst	5	adrenal cyst (≥2 cm)	uncharacterized mass (attenuation 20 HU)	adrenal cyst

Figure Captions

Fig. 1 66-year-old men with diffuse liver lesion. Small myelolipoma (arrow) of left adrenal gland on CT (a), that looked as an incisure within the adrenal gland parenchyma on MRI (b, axial gradient-echo fat-saturated T1-weighted image)

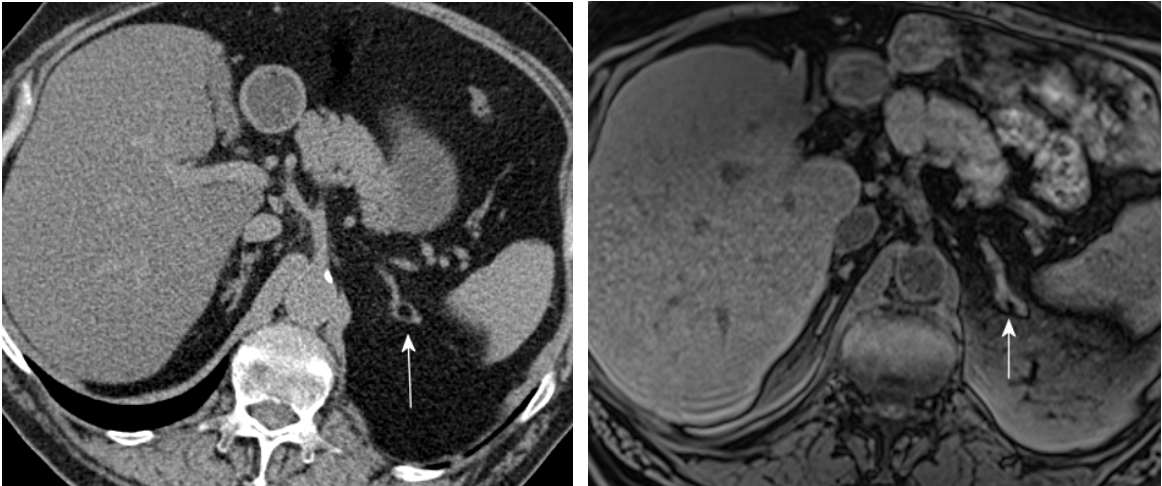


Fig. 2 65-year-old female referred for follow-up of renal cancer. A mass (arrow) of the right adrenal gland with attenuation value of 20 Hounsfield units could not have been characterized using unenhanced CT (a). It was characterized using T2-weighted MRI as an adrenal cyst (b)



Fig. 3 39-year-old woman with residual arterial hypertension after left-sided adrenalectomy due to pheochromocytoma. The right adrenal mass (arrow) had attenuation value of 20 HU on non-enhanced CT with a punctiform calcification (a), whereas it had typical high-signal intensity of pheochromocytoma on T2-weighted MRI (b)

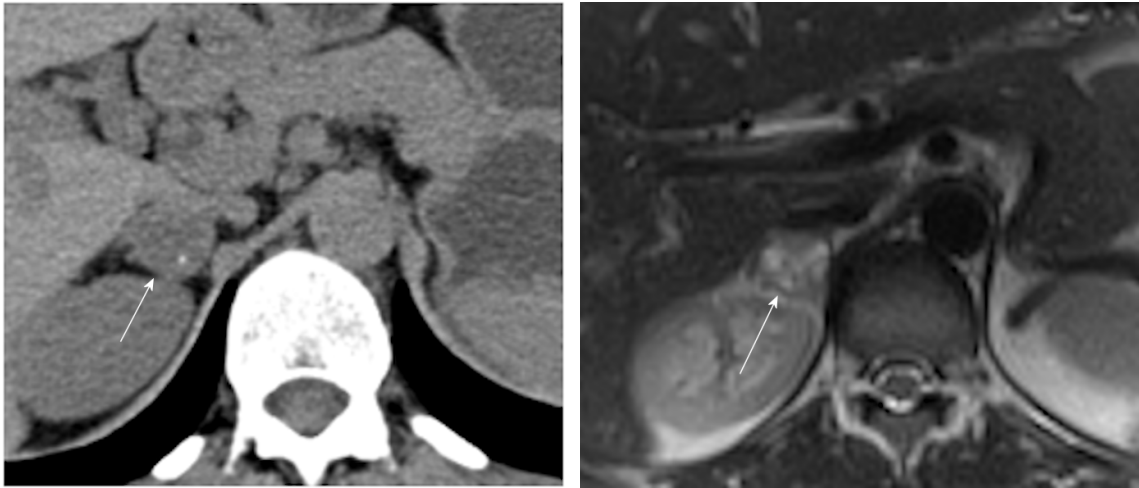


Fig. 4 44-year-old male with left-adrenal mass detected on check-up ultrasonography. Small left-sided adrenal adenoma (arrow) with attenuation of 31 Hounsfield units could not be characterized on non-enhanced CT (a), whereas it had obvious signal drop on out-of-phase MRI (b) compared to in-phase MRI (c) with signal-intensity-index of 67%

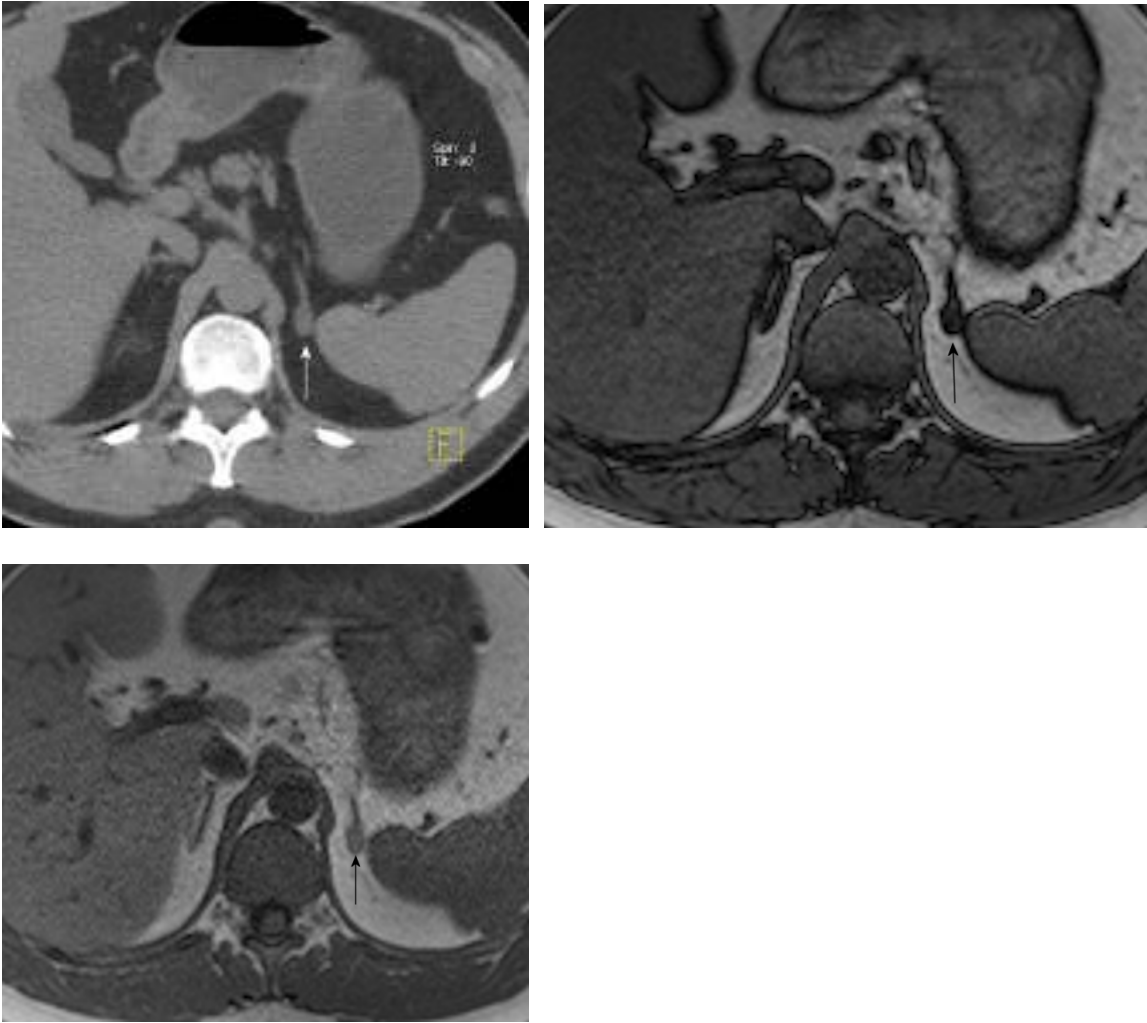


Fig. 5 58-year-old female referred for follow-up of colorectal and endometrial cancer. The left-sided adrenal mass (arrow) remained uncharacterized after CT (a) and MRI (b, out-of-phase chemical-shift MRI). It remained unchanged after 14 months and was therefore considered to be benign. Typical lipid-rich adenoma of the right adrenal gland (asterisk)

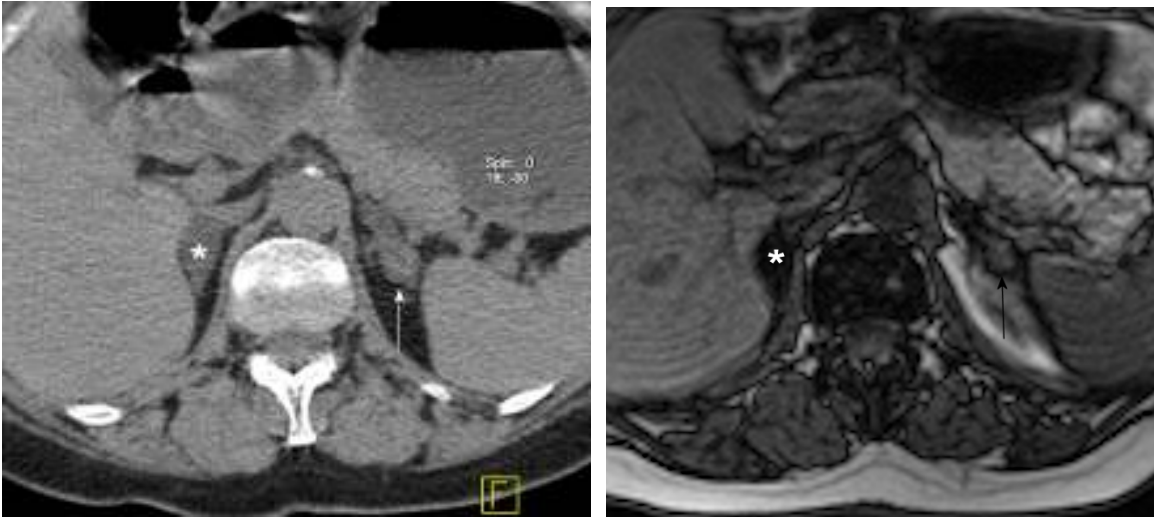


Fig. 6 67-year-old men with arterial hypertension and myelolipoma of the left adrenal-gland (arrow). On non-enhanced CT (a) the mass had attenuation coefficient of -30 Hounsfield units, and was therefore interpreted as adenoma. On MRI signal loss on gradient-echo fat-saturated T1-weighted image was obvious (b)

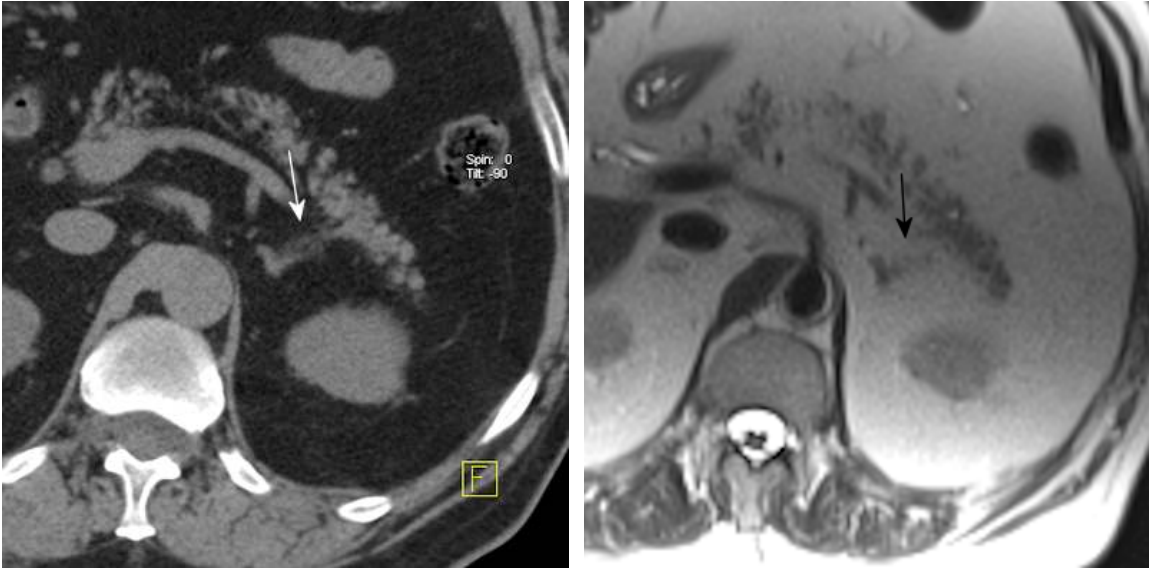


Fig. 7 61-year-old male referred for follow-up urinary bladder cancer. Adrenal hyperplasia (arrow) was easily detected using CT (a), and out-of-phase gradient-echo MRI sequence where hypertrophic adrenal gland was surrounded by india ink artifact (b)

