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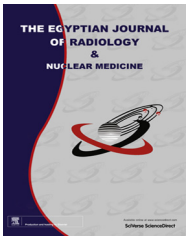

ORIGINAL ARTICLE

Diagnostic value of combined versus individual MRI parameters in distinguishing adenomatous from non-adenomatous adrenal lesions in cancer patients

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KEYWORDS

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Abstract *Purpose:* Our aim was to evaluate the diagnostic value of MRI using different parameters in differentiation of adenomas versus non-adenomas adrenal lesions.
Materials and methods: Forty-five patients with 48 adrenal masses (28 lipid rich adenomas, 3 lipid poor adenomas, 15 metastases and 2 lymphoma) were retrospectively evaluated with MRI. The mean diameter of adrenal mass, T2WI signal, signal drop on chemical shift imaging (CSI) and enhancement pattern were assessed separately and in various combinations. Accuracies, sensitivities, specificities, PPV, NPV and *P* values by Chi-square test were calculated for individual and combined parameters.
Results: Signal drop on CSI and enhancement pattern were the most statistically significant diagnostic discriminators of adenomatous and non-adenomatous lesions with accuracies, specificities and sensitivities of 93.8%, 90.3%, 100% and 91.7%, 93.5%, 88.2%, respectively (*P*-value <0.0001). The best performance of a combination of parameters was obtained after exclusion of the size, with an accuracy of 89.6% (*P*-value <0.0001).
Conclusion: The most specific predictors for adrenal mass characterization were CSI signal drop and Gd-DTPA enhancement characteristics. Combining the MR parameters did not prove superior

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to those two individual parameters, however it yielded a valuable diagnostic protocol for distinguishing the adrenal masses, considering that size criterion should not be used as an individual discriminator.

1. Introduction

With the increasing use of cross-sectional imaging to investigate a whole host of abdominal diseases, adrenal gland abnormalities are being detected all the time (1). Adrenal lesions are most commonly encountered incidentally at examinations performed for other purposes (2). The adrenal gland is a relatively frequent site for metastatic disease (3). The most common malignant lesions that metastasize to the adrenal gland include malignant melanoma, breast, lung, kidney, esophagus, pancreas, liver, stomach, and colon cancers (4–6). In patients with a primary neoplasm, in whom an adrenal metastasis is an important consideration, most adrenal masses are benign, commonly non-hyper functioning adenomas (7). So accurate characterization of these masses and proper discrimination between adenomatous and non-adenomatous lesions are essential because the nature of the mass may have a profound effect on patient's care and would obviate both percutaneous biopsy and repeated interval follow-up imaging (8).

Imaging of the adrenal gland to diagnose a mass is typically accomplished using computed tomography (CT) or magnetic resonance imaging (MRI) (4). CT is often considered the cornerstone of adrenal imaging, being performed before and after intravenous (iv) injection of contrast material (9). CT measures attenuation to differentiate between benign and malignant lesions, but the use of attenuation is not always possible depending upon the characteristic of the lesions (10,11).

MRI of the adrenal glands can help in characterizing lesions not properly assessed with CT. This should include T1 and T2WI, plus chemical shift (CS) imaging which consist of in phase (IP) and out of phase (OP) imaging. T1-fat-supression imaging before and after iv gadolinium administration is optional. Multi-planar MRI allows precise localization and separation of adrenal masses from the surrounding structures (9,12).

CS MRI, being based on the principle of different resonance frequency rates of protons in fat and water, has played a role in confident differentiation of adrenal adenomas from metastases (8). By intermittently imaging the adrenal gland with variable T1 gradient-recalled echo (GRE) sequences, it is possible to summate fat and water signal during in phase sequences but null out the signal on out of phase sequences for those voxels with equal quantities of fat and water (9,13–15).

Although MRI with conventional sequences may be useful in characterizing adrenal lesions, a serious limitation is the 20–30% of indeterminate lesions seen (16).

The aim of this work was to evaluate whether or not the use of combined MRI parameters including the size, T2 signal, CSI signal drop and the post-contrast enhancement pattern would be more effective than the use of individual parameters in distinguishing benign from malignant adrenal masses in cancer patients.

2. Patients and methods

2.1. Patients

The institutional review board allowed retrospective review of patient data sets. Among all consecutive MR abdomen studies performed in our department from January 2012 to September 2013, we retrospectively selected patients with the following criteria (1): patients with a known primary extra-adrenal malignancy and adrenal masses (2). MR imaging including T1, T2, CSI in phase/out of phase sequences as well as post contrast sequences.

We excluded patients with inadequate follow up or pathologic proof of diagnosis. Also patients with adrenal cysts (diagnosed on MRI by water signal intensity, lack of enhancement or signal drop, thin imperceptible walls) and pheochromocytoma (diagnosed on the basis of their clinical and hormonal findings) were excluded as well.

Forty-five patients with 48 adrenal masses (2 patients with lung cancer and 1 patient with lymphoma had bilateral lesions) fulfilled these criteria and constituted our study group. They include 18 females and 27 males). They range in age between 29 and 75 years (mean 52.67 ± 10.64).

They all had tumors of variable sites of origin, the primary sites of tumors were lung cancer ($n = 15$), renal cell carcinoma ($n = 4$), colonic cancer ($n = 8$), bladder cancer ($n = 4$), breast cancer ($n = 4$), prostatic cancer ($n = 3$), gastric cancer ($n = 3$), uterine cancer ($n = 2$), Kaposi sarcoma ($n = 1$), and lymphoma ($n = 1$). Demographic data of the patients are presented in Table 1. The adrenal lesions were either discovered incidentally at abdominal MR imaging done for metastatic work-up purposes or were known to be there by previous US or CT imaging and required further assessment for accurate characterization.

2.2. Imaging protocol

MR imaging was performed with a 1.5 Tesla unit (Gyroscan Intera, Philips Medical System, Netherland) with a phased-array body coil in the supine position. All MRI examinations included (a) Axial SE T1WI (TR/TE 425/15 ms, matrix 204 × 256) (b) Axial and Coronal FSE T2 W (TR/TE 1800/100 ms, matrix 204 × 256). The slice thickness of T1 and T2 sequences was 4 mm with an intersection gap of 0.4 mm. Respiratory gating was used for SE imaging with flow compensation.

After localization imaging, CSI was performed at the level of the adrenal mass using a T1WI Gradient Recalled Echo (GRE) sequence with breath-holding (TR: 68–160 and TE 4.9 ms for IP images and 6.3 ms for OP images). The flip angle = 30°, the matrix size = 128 × 256 and FOV varied from 320 to 375 cm.

Table 1 Demographic data of the patients.

Age		
-Range	29–75	
-Mean	52.67	
	Number	Percentage (%)
Sex		
-Females	18	40
-Males	27	60
Side		
-Right	24	50
-Left	18	37.8
-Bilateral	3	12.5
Primary tumor		
-Lung	15	31.25
-Breast	4	8.3
-Prostate	3	6.25
-Colon	8	16.67
-Uterine	2	4.17
-Kaposi sarcoma	1	2.08
-Lymphoma	1	2.08
-Renal	4	8.3
-Gastric	3	6.25
-Bladder	4	8.3

Axial T1WI was then repeated after iv administration of 0.1 mmol/kg of Gadopentetate dimeglumine-DTPA (Magnevist; Schering, Berlin, Germany), using a dynamic technique with preset scan times and image acquisition in the arterial (30 s), portal (60 s) and late equilibrium phases (180–300 s).

2.3. Image analysis

The images were transferred to an independent workstation (Philips MR extended workspace, software version 2009) and were independently reviewed and qualitatively analyzed by two experienced radiologists having knowledge of clinical but no histologic information at that time.

Size was recorded with the MRI distance cursor to measure the largest diameter in the axial plane on the unenhanced series. Masses <4 cm were presumed to be benign while masses >4 cm were presumed to be malignant (12).

MR signal intensity of adrenal lesions on T2WI was described as either iso/hypointense (adenomatous lesion) or hyperintense/heterogeneous (non adenomatous lesion) relative to the liver parenchyma (16).

Qualitative assessment of the CS images was done with a definite signal loss on out of phase images relative to in phase images considered significant for adenomatous lesions. Absence of signal drop was considered significant for non-adenomatous lesions (16).

Homogeneous enhancement of a mass on the dynamic scan was considered to be an indication of benignity while heterogeneous enhancement was considered an indicator of malignancy (12).

The final analysis made use of all the imaging data from the protocol. For analysis of combined parameters the following scoring system was used:

- Size $<$ 4 cm: 0 / $>$ 4 cm: 1
- T2 signal iso-hypointense: 0 / hyper-heterogeneous: 1
- CSI signal drop: 0 / no signal drop: 1
- Contrast enhancement homogeneous: 0 / heterogeneous: 1

Whenever at least one parameter corresponded to a non-adenomatous lesion, the combination of parameters and hence their score was considered in favor of an adrenal non-adenomatous lesion rather than an adenomatous one. At follow-up imaging, 6 months of stability was considered an indicator of benignity. On the other hand increased size of the lesion or development of a new adrenal lesion/s was considered to be indicative of malignancy.

Our reference standards included pathologic proof of diagnosis in 17 lesions including histopathology after adrenalectomy and biopsy, clinical and imaging follow up (at least 6 months) in 31 lesions.

2.4. Statistical analysis

Statistical analysis was performed with SPSS (Statistical Package for the Social Sciences) V21. Results of the qualitative analysis of MR images were classified as true positive, true negative, false positive and false negative for the diagnosis of adenoma. These results were entered into an excel worksheet. Sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV), accuracies, were calculated for individual MR parameters then for the combined parameters used for the differentiation of adenomatous and non-adenomatous adrenal masses. The P values by Chi-square test were determined: >0.05 = non-significant, <0.05 = significant and <0.01 = highly significant.

3. Results

The final diagnosis of the 48 adrenal lesions included 31 (64.6%) adenomatous benign lesions (28 lipid rich (58.4%), 3 lipid poor adenomas (6.2%) and 17 (35.4%) non adenomatous malignant lesions (2 lymphoma and 15 metastases).

Characteristic individual MR imaging features of the adrenal masses including the size, the T2 signal intensity, the signal drop on CSI and the post-contrast pattern of enhancement used for the differentiation of adenomatous and non-adenomatous malignant adrenal masses are presented in Table 2. The sensitivity, specificity, PPV, NPV, and accuracy as well as *P*-values of the individual and combined CT parameters are presented in Table 3.

3.1. Size

All 31 adenomatous lesions ranged in sizes from 1 to 11 cm in maximum transverse diameter (mean 4.39 ± 3.01), whereas non-adenomatous lesions ranged in sizes from 2 to 10 cm in maximum transverse diameter (mean 5.86 ± 2.55).

Twenty-nine adenomas were <4 cm in maximum transverse diameter (94%), among which 27 were lipid rich (Fig. 1), while 2 only were lipid poor (Fig. 2).

Two adenomas were >4 cm in maximum transverse diameter (6%), including 1 lipid rich and 1 lipid poor. The lipid rich adenoma showed isointense T2 signal, signal drop on CSI together with homogeneous enhancement and it was stable on follow-up. The lipid poor adenoma showed hyperintense T2 signal, no signal drop on CSI and heterogeneous

Table 2 Individual and combined MRI parameters for differentiation of adenomatous and non-adenomatous lesions in cancer patients.

MRI parameter	Type of lesion			
	Adenoma		Non-Adenoma	
	Number	%	Number	%
Size				
< 4 cm	29	94	5	29.4
> 4 cm	2	6	12	70.6
T2 signal				
Iso, hypo	28	93.3	2	16.7
Hyper, heterogeneous	3	6.7	15	83.3
In phase/out phase				
Signal drop	28	90.3	0	0
No drop	3	9.7	17	100
Contrast enhancement				
Homogenous	29	93.5	2	11.8
Heterogeneous	2	6.5	15	88.2

enhancement. Diagnosis was confirmed by histopathology after adrenalectomy (Fig. 3).

Twelve non-adenomatous lesions (70.6%) were > 4 cm in maximum transverse diameter while 5 lesions (29.4%) were < 4 cm in maximum diameter (Fig. 4). Three out of these 5 lesions presented with typical malignant features namely hyperintense/heterogeneous T2 signal, no signal drop on CSI and heterogeneous enhancement. Whereas 2 lesions presented overlapping features with benignity including hypointense T2 signal and homogeneous contrast, yet with no signal drop on CSI. All these 5 lesions were proved to be malignant by histopathology.

The size criterion was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 41/48 masses (85.4%). This was the lowest accuracy among evaluated parameters. The size criterion showed the highest sensitivity (93.5%), lowest specificity (70.6%), and lowest Chi square value (21.9) but was statistically significant.

3.2. T2 signal intensity

Among 31 adenomatous lesions, 28 (93.3%) showed iso/hypointense T2 signal intensity while 3 lesions (6.7%) showed hyper/heterogeneous signal. The lipid rich adenomas presented with iso/hypointense T2 signal, except for 2 lesions, which presented with hyperintense signal and a mixture of hypo and hyperintense signals (Fig. 5). The first lesion had other criteria favoring the diagnosis of adenoma such as size < 4 cm, signal drop on CSI and homogeneous enhancement, and it was stable on follow-up. The other one was also < 4 cm, with signal drop on CSI, yet it showed heterogeneous enhancement, it was stable on follow up images.

Two out of 3 lipid poor adenomas showed isointense T2 signal while the third one showed hyperintense signal. This lesion with hyperintense T2 signal also had features suggesting non-adenomatous etiology such as size > 4 cm, no signal drop on CSI and heterogeneous pattern of enhancement. Its final diagnosis was established via histopathology.

Fifteen (83.3%) out of 17 non-adenomatous malignant lesions showed hyper/heterogeneous T2 signal, whereas 2 lesions (16.7%) showed hypointense T2 signal. These 2 lesions had overlapping benign features such as a diameter < 4 cm and a homogeneous enhancement (Fig. 6). However both showed no signal drop on CSI. They were concluded definitely malignant by histopathological assessment.

T2 signal intensity was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 43/48 masses (89.6%). Its accuracy was greater than the size parameter; the Chi square value (28.9) was also higher and statistically significant.

3.3. CSI signal drop on out of phase compared to in phase images

Twenty eight (90.3%) out of 31 adenomatous lesions, showed significant signal drop on CSI, whereas 3 (9.7%) showed no signal drop. Those 3 lesions were diagnosed as lipid-poor adenomas; diagnosis was confirmed by histopathology in 2 of these lesions, while the remaining one showed stability on follow-up imaging.

All 17 non-adenomatous lesion (metastases and lymphoma) showed no signal drop on CSI (100%).

CSI signal drop was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 45/48 masses (93.8%). This was the highest accuracy between evaluated individual as well as combined parameters. It also showed the highest specificity (100%), a PPV of 100%, as well as the highest Chi square value (36.9) and was statistically significant.

3.4. Post-contrast enhancement pattern

Twenty nine (93.5%) out of 31 adenomatous lesions showed a homogeneous pattern of enhancement while 2 lesions (11.8%) showed heterogeneous enhancement, 1 lipid rich and 1 lipid poor. Both were stable on follow-up imaging and confirmed to be adenoma by histopathology.

Table 3 Statistical assessment of the MRI parameters used in differentiation of benign and malignant adrenal masses.

MRI parameters	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Chi square	*P* value
Size	85.4	93.5	70.6	85.3	85.7	21.9	< 0.0001
T2 signal intensity	89.6	90.3	88.2	93.3	83.3	28.9	< 0.0001
Signal drop	93.8	90.3	100	100	85	36.9	< 0.0001
Enhancement	91.7	93.5	88.2	93.5	88.2	32.1	< 0.0001
All parameters	87.5	80.6	100	100	73.9	28.6	< 0.0001
All excluding signal drop	85.4	83.9	88.2	92.9	75	23.5	< 0.0001
All excluding the size	89.6	83.9	100	100	77.3	31.1	< 0.0001

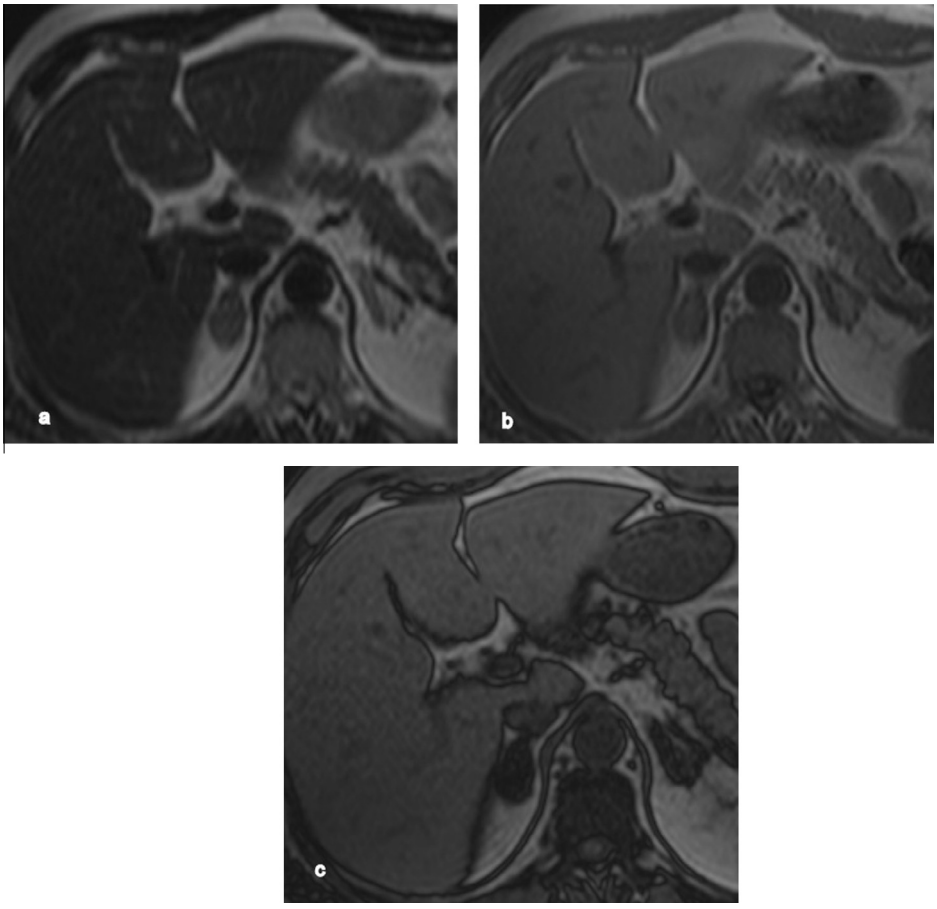

Fig. 1 Lipid rich adenoma: 45-year-old female patient with history of uterine carcinoma and right adrenal lesion 2 cm in diameter. (a) Axial T2WI image shows homogenous isointense signal of the adrenal lesion. (b) Axial T1 IP and (c) OP MR images show uniform significant drop of signal. Follow-up CT done a year later showed stability of the lesion.

Fifteen (88.2%) out of 17 lesions diagnosed as non-adenomatous malignant lesions presented a heterogeneous pattern of enhancement (Fig. 7), whereas 2 lesions (11.8%) enhanced homogeneously. Despite presenting with a size <4 cm and hypointense T2 signal, these 2 lesions showed no signal drop on CSI and were confirmed malignant by histopathology.

The post-contrast enhancement pattern was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 44/48 masses (91.7%). It also had the highest sensitivity along with the size parameter (93.5%) and was statistically significant.

3.5. Combined MRI patterns

The combined MR parameters succeeded in diagnosing 42 (87.5%) of the total 48 cases (89.2% of the lipid rich adenomas, 0% of lipid poor adenomas and 100% of malignant masses). Six out of 48 masses (12.5%) were misdiagnosed: 3 lipid poor and 3 lipid rich adenomas equivalent to 6 of 31 benign adenomatous masses and 0 case of the 17 malignant non-adenomatous masses. Combined parameters showed a 100% specificity, a Chi square value of 28.6 and was statistically significant.

When we excluded CSI from our statistical evaluation of combined parameters, we obtained the lowest accuracy (similar to that of the size), with Chi square value dropped to 23.5 (compared to 28.6 for combined parameters), yet it was still statistically significant.

The accuracies of combined MR parameters before and after exclusion of the size parameter were 87.5% and 89.6%, respectively. After size exclusion the Chi square value was high 31.1 and statistically significant.

The size had the lowest accuracy and Chi square statistical diagnostic values, while the CSI signal drop had the highest ones obtained among the studied MR parameters. The enhancement pattern was then closely following the CSI signal drop pattern as regarding its high accuracy and Chi square values. Both individually were better at diagnosis than various combinations of the MR parameters. The accuracy and Chi Square values of various individual and combined MR parameters are illustrated in Diagrams 1 and 2.

4. Discussion

The adrenal gland is a common site for metastasis in patients with cancer with the rate of metastasis being between 25% to 75% depending on the type and size of the primary tumor (5). Characterizing adrenal masses is important because the nature of the mass may have a profound effect on patient's care (9).

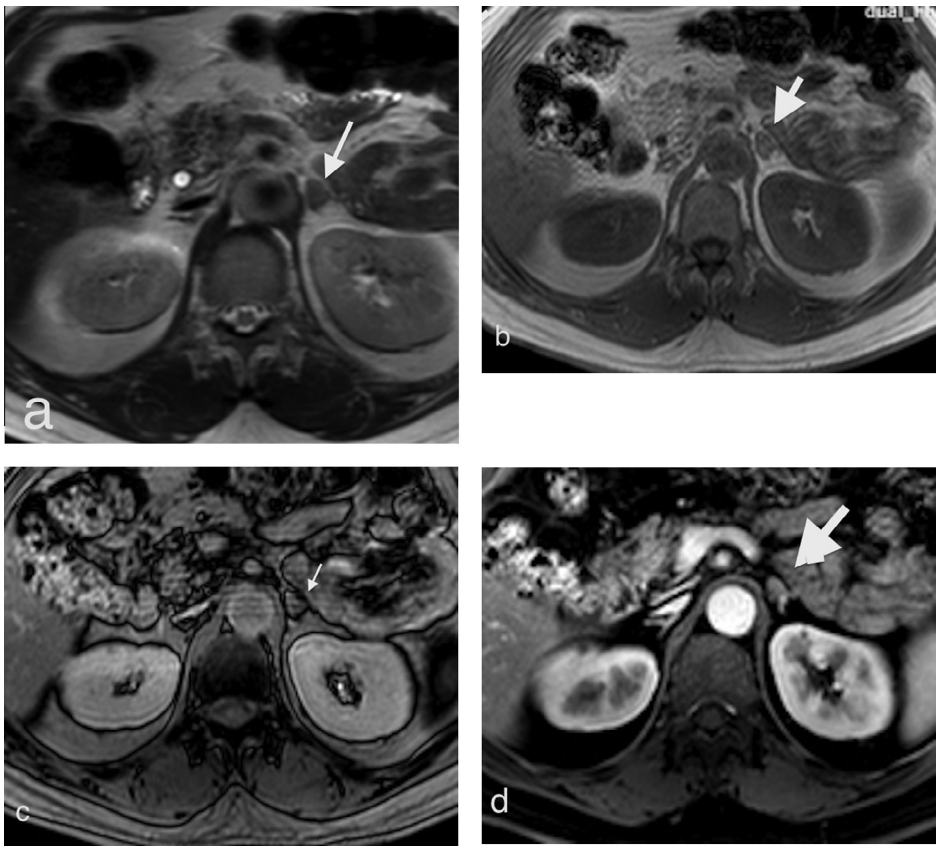

Fig. 2 Lipid poor adenoma: 55-year-old male patient with history of right hemicolectomy for colonic cancer 18 months ago and left adrenal lesion 1.2 cm in diameter. (a) Axial T2WI shows isointense signal of the adrenal lesion (b) Axial T1WI IP and (c) OP MR images show no significant signal drop of the lesion. (d) Axial post contrast T1WI with fat suppression shows homogenous enhancement of the lesion. The lesion was stable during 18 months follow up period.

The probability of a specific type of adrenal mass varies with the clinical picture. For example, in patients with cancer, up to 75% of adrenal incidentalomas are metastatic lesions but in patients with no history of cancer two-thirds are benign (17). However even in patients with a primary neoplasm, in whom an adrenal metastasis is an important consideration, a lot of adrenal masses are also benign (7). The majority of benign lesions are adenomas, of which 80% are benign non-functioning adenomas (3,18). This goes in accordance with our current study conducted on 45 patients with extra-adrenal cancer, where 31/48 adrenal masses were diagnosed as benign adenomatous lesions (64.58%), while 17 lesions (35.42%) were diagnosed as malignant non-adenomatous lesions.

The most common malignant lesions that metastasize to the adrenal gland include malignant melanomas, kidney, liver, gastrointestinal, breast, colon, lung, and bronchial carcinomas (4,5). In our study, the most common primary cancer that metastasized to the adrenal gland was lung cancer (31.25%) followed by colon then prostatic cancer.

MRI with its inherent tissue characterization ability can be utilized for the assessment of adrenal masses, with several MRI parameters proposed in this assessment (19).

In this retrospective study we used MRI to evaluate characteristics of adrenal lesions in patients with extra-adrenal primary tumor. We used the following individual parameters: Size, T2 signal intensity, signal drop on CSI and post contrast enhancement pattern. Then we evaluated the discriminatory power of combined parameters.

In this study, when using a size cut-off value of 4 cm, 41/48 masses were properly diagnosed ($P < 0.0001$), with the mean axial diameter of adenomatous lesions being 4.39 ± 3.01, whereas that of non-adenomatous lesions was 5.86 ± 2.55. This was in concordance with the findings of Miller et al. who reported that, the sizes of malignant adrenal lesions were greater than those of the remaining lesions ($P < 0.05$) (20). Also Sandrasegaran et al. reported the median size of malignant lesions was 4.86 cm (interquartile range, 2.77–8.52 cm), which was greater than that of benign lesions (1.98 cm, 1.58–2.58 cm, $P < 0.05$) (21).

Our results showed that size was the least accurate (85.4%) of all parameters in differentiation of adrenal adenomatous from non-adenomatous lesions. It also showed the lowest specificity (70.6%) and lowest Chi square value (21.9). This is comparable to previous studies where considerable overlap in size has been demonstrated between adenomas and non-adenomas, especially metastases (10).

The size criterion showed 98% sensitivity and 53% specificity in a previous study by Kamiyama et al. (22). Similarly, it yielded the lowest sensitivity (58.8%), specificity (72.7%) and accuracy (66.6%) in a study done by Mohamed et al. (23).

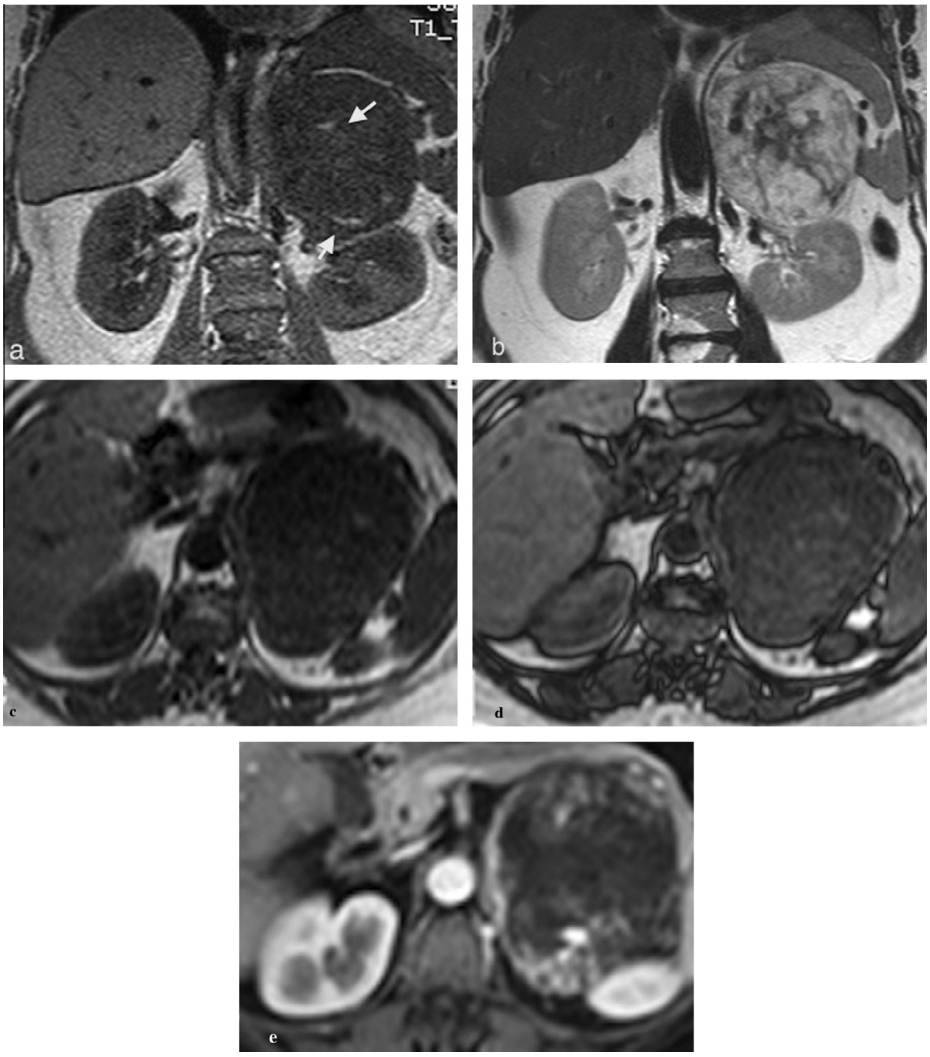

Fig. 3 Atypical hemorrhagic lipid poor adenoma: 61-year-old female patient recently diagnosed with breast cancer and large left adrenal mass 11 cm in diameter. (a) Coronal T1 image shows predominantly hypointense T1 signal with intralesional hemorrhagic changes of high T1 signal (b) Coronal T2 WI images show high T2 signal with areas of low signal (c) Axial T1 WI IP and (d) OP MR images show no signal drop. (e) Post contrast axial T1WI shows heterogeneous enhancement of the lesion. Adrenalectomy was done and pathology revealed atypical hemorrhagic lipid poor adenoma.

Frilling et al. previously reported that the incidence of metastatic adrenal lesions increases to 71% if the adrenal mass is larger than 4 cm and demonstrates an increase in size on follow-up imaging within 1 year (24).

In this study, most adenomatous lesions were hypo/isointense on T2WI compared to the liver whereas most non-adenomatous lesions were hyperintense or heterogeneous on T2WI. This was supported with the previous findings of Inan and his colleagues, who reported that 64.58% of adenomas display iso-intense T2 signal, whereas 68.75% of metastases were clearly hyperintense on T2WI (25).

In this study T2 signal intensity was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 43/48 masses (89.6%). Its accuracy was higher than that of the size parameter as well as its specificity (88.2%) and Chi square value (28.9, $P < 0.0001$) but yielded a lower sensitivity (90.3%). PPV and NPV were 93.3% and 83.3%, respectively. This was in agreement with a previous study conducted by Maurea et al. who had analyzed T2 signal of 41 adrenal masses, with reported diagnostic accuracy, sensitivity, specificity, PPV and NPV of 80%, 72%, 100%, 100% and 60%, respectively (16).

The use of MRI can be problematic since the malignant and benign lesion signal intensity overlap (4). Adrenal cortical adenomas have homogeneous signal intensity and enhancement patterns, however T1WI and T2WI signal intensity characteristics of benign adrenal adenomas are not specific and overlap significantly with non-adenomas, especially metastases (26). On the other hand adrenal metastases vary in size and appearance on MRI, and they are often heterogeneous and are usually hyperintense compared to the normal liver on T2WI (27,28), also they may have a low T2 signal (12).

The CS MR sequence has often been described as the mainstay MR examination for imaging of the adrenal gland. This

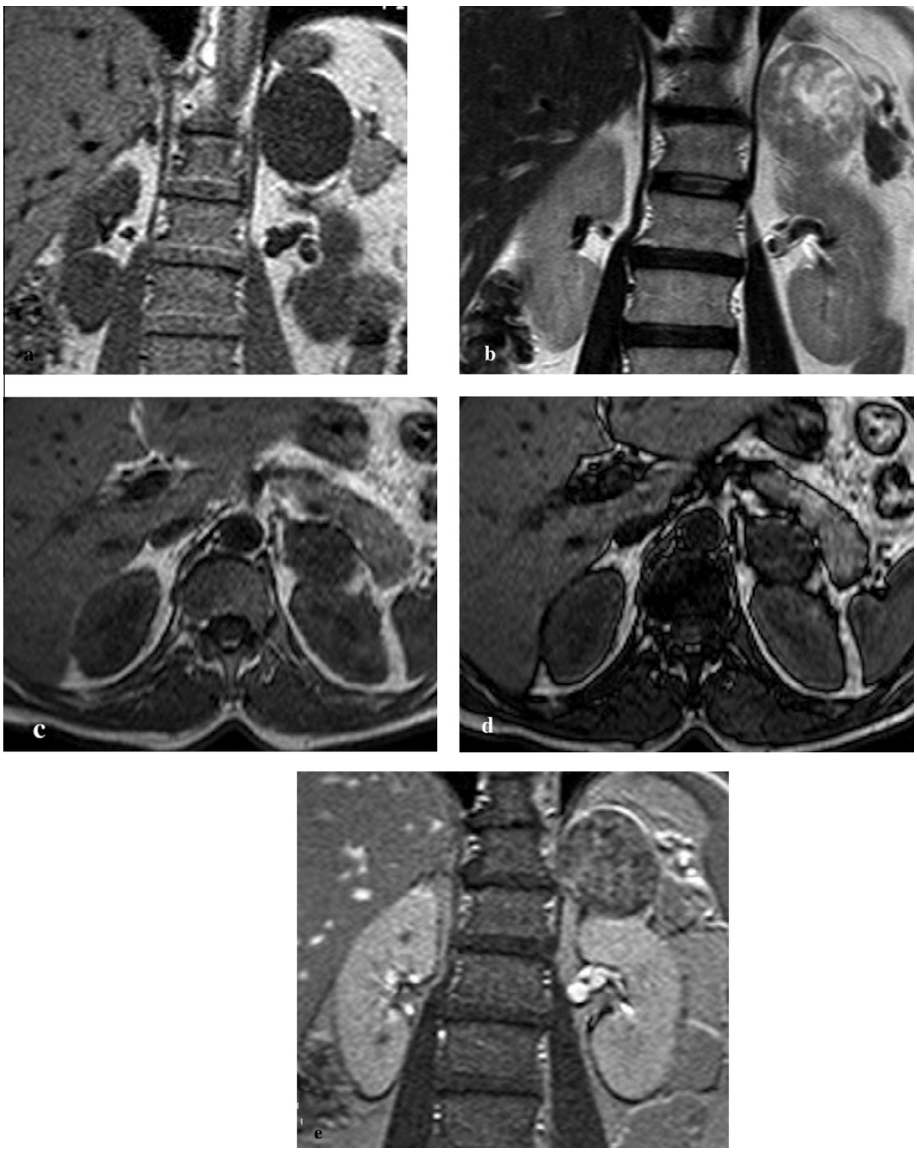

Fig. 4 Adrenal metastatic deposit: 48-year-old male patient with recently diagnosed nasopharyngeal carcinoma and large, rounded left adrenal lesion 6 cm in diameter. (a) Coronal T1 WI image shows hypointense signal of the adrenal lesion (b) coronal T2WI shows isointense signal with areas of high signal. (c) Axial IP and (d) OP MR images show no signal drop. (e) Post contrast axial T1WI image shows heterogeneous enhancement of the lesion. Biopsy revealed metastatic disease.

sequence takes advantage of the reduced signal on OP images due to the high cytoplasmic lipid concentration in adenomas (29–31). Visual analysis of signal intensity loss on OP images is widely performed in everyday radiological practice, but in some cases adrenal lesions demonstrate heterogeneous signal intensity suppression which is difficult to interpret (32). Atypical signal characteristics of adrenal masses on CSI may reflect variable amounts and types of lipid cells (combination of lipid-rich and lipid-poor cells) within adenomas or come from intratumor lipid in malignant lesions (e.g. adrenal cortical carcinoma or metastases from renal cell carcinoma, hepatocellular carcinoma, or liposarcoma) (32–34).

Previous studies reported that CS MRI can characterize some lesions as lipid rich that were identified as lipid poor adenomas on unenhanced CT. This was explained by the potential advantages of MRI over unenhanced CT in showing the presence of microscopic fat (20,35).

In our study, CSI signal drop was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 45/48 masses (93.8%). This was the highest accuracy between evaluated individual as well as combined parameters. Its sensitivity was 93%. It also showed the highest specificity (100%), as well as the highest Chi square value (36.9) and was statistically significant. Its PPV was 100% and NPV was 85%.

Similarly in a study conducted by Maurea et al. on 41 adrenal masses, CSI significantly improved characterization of adrenal masses compared with conventional T2WI. The Diagnostic accuracy, sensitivity, specificity, PPV and NPV were 93%, 90% ($P < 0.05$ versus T2 analysis) 100%, 100% and 80% ($P < 0.05$ versus T2 analysis), respectively (16).

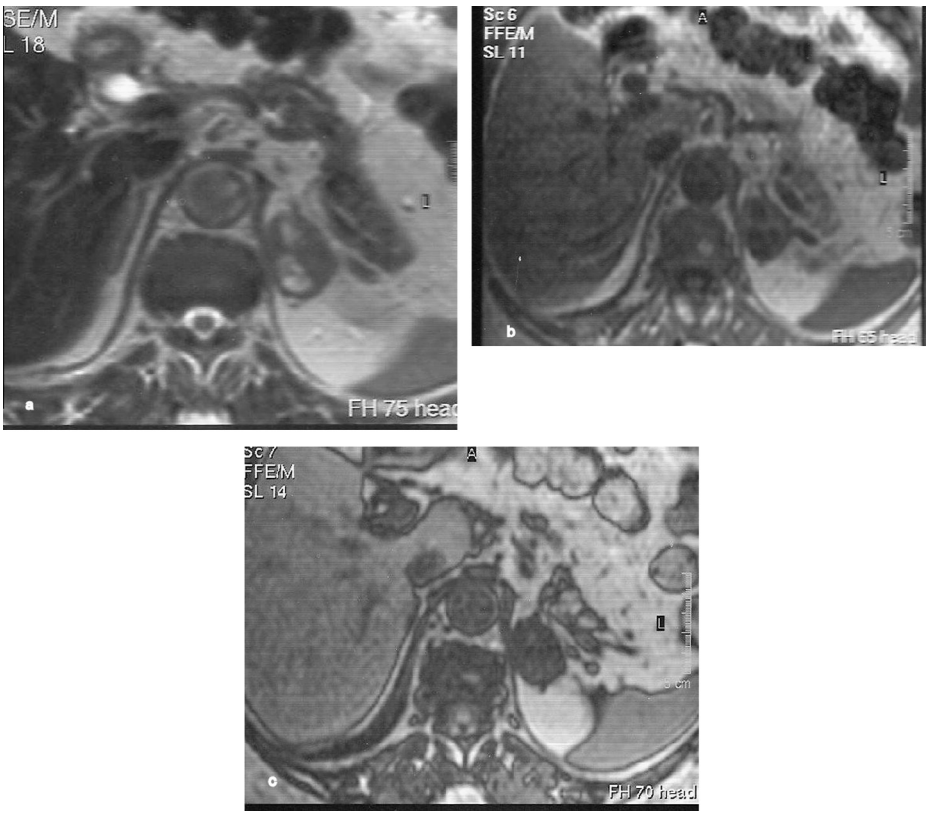

Fig. 5 Lipid-rich adenoma: 69-year-old male patient with history of Bronchogenic Carcinoma and left adrenal mass 3.8 cm in diameter. (a) Axial T2 WI image shows predominantly low signal with intralesional areas of cystic degeneration of high signal intensity. (b) Axial T1 WI IP and (c) OP MR images show a significant drop of signal of the lesion. The lesion was diagnosed as adenoma based on CS MRI findings. It showed stability on follow-up US done 6 months later.

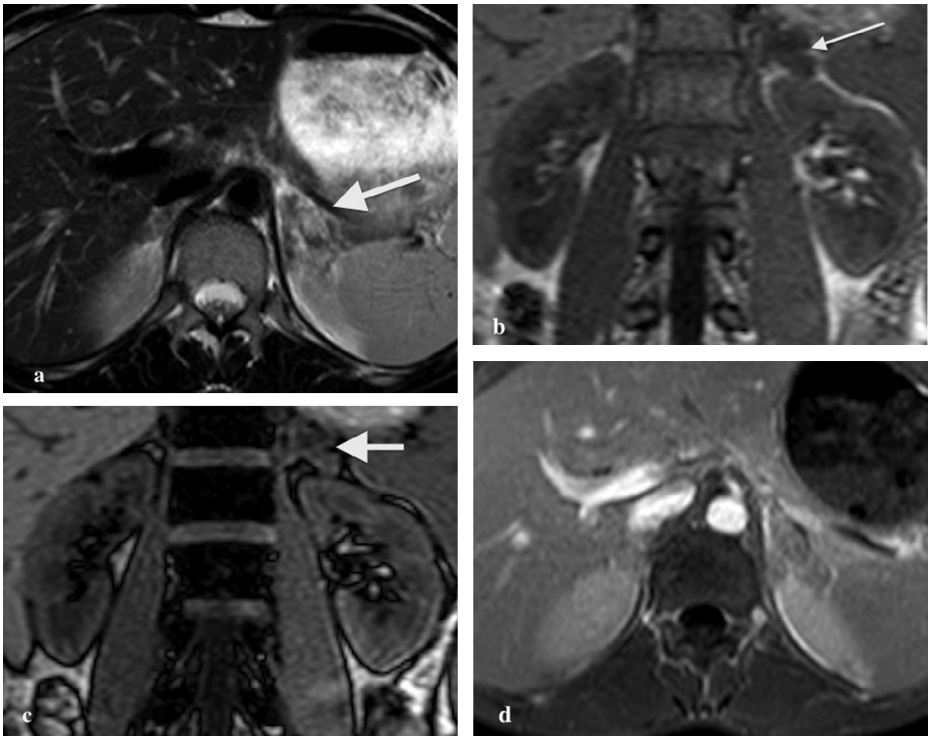

Fig. 6 Adrenal metastatic deposit: 30-year-old male patient recently diagnosed with Kaposi sarcoma and small left adrenal nodule 2 cm in diameter. (a) Axial T2WI shows high signal of the adrenal lesion. (b) Axial T1WI in-phase and (c) OP MR images show no signal drop. (d) Post contrast axial T1WI image shows faint homogenous enhancement of the lesion. Adrenalectomy was done and pathology revealed metastatic disease.

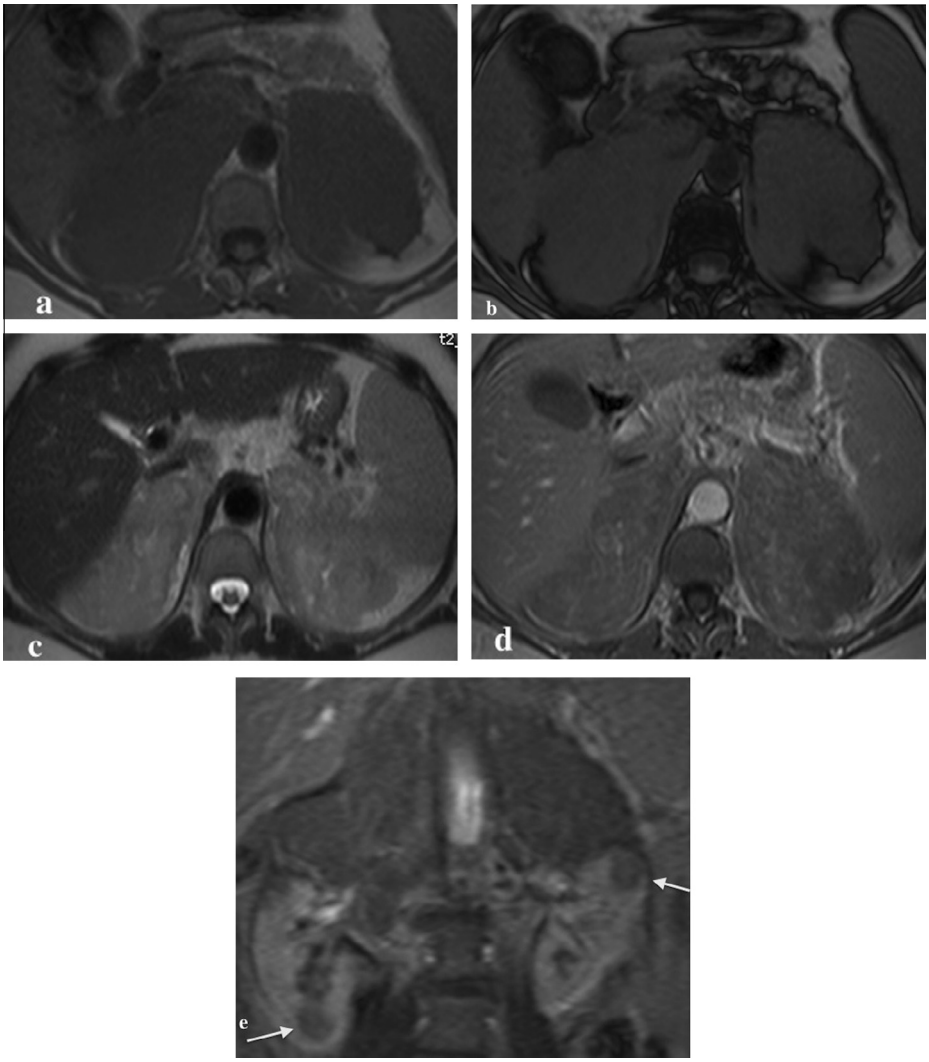

Fig. 7 Bilateral adrenal lymphoma: 55-year-old female patient recently diagnosed with lymphoma and bilateral large adrenal masses 10 cm in diameter each. (a) Axial T1 WI IP and (b) OP images show hypo-intense signal of the lesions with no significant signal drop. (c) Axial T2WI show faint heterogeneous high signal intensity of the lesions. (d–e) Contrast-enhanced (d) axial and (e) coronal T1WI images show faint heterogeneous enhancement of the lesions. Note bilateral small renal lesions (arrowed).

Our findings were in agreement with those of a study conducted on 182 patients with adrenal masses assessed qualitatively by the CSI sequence (36). Sensitivity, specificity and accuracy values in this study were 89%, 99% and 94%, respectively indicating high predictive values for the CS sequence in the characterization of adrenal adenomas versus non-adenomas.

In our study, CSI was not a powerful diagnostic tool for evaluation of lipid-poor adenomas. The 3 lipid-poor adenomas showed no signal drop on CSI. This is in agreement with previous studies that have reported that the role of MR for characterizing lipid-poor adrenal masses is limited (37–39). In a previous study by Inan et al. there were significant signal loss in 38/48 adenomas (79.16%), moderate signal loss in 6/48 adenomas (12.5%), no remarkable signal loss in the remaining 4 (lipid-poor) (8.33%) adenomas. None of the malignant masses showed signal loss. Quantitative analysis of CSI sequences revealed a sensitivity of 93.5%, a specificity of 100% and a PPV of 100% for the Signal Intensity Index. Apart from the 4 lipid-poor adenomas which did not show signal loss, all adenomas and malignant masses could be differentiated by CSI (25).

Metastases from hepatocellular carcinomas, renal cellcarcinomas, liposarcomas and, rarely, adrenocorticalcarcinomas can contain fat, thus resulting in false-negative images (27). In our study, no lesions with a final diagnosis of metastases showed signal loss in OP imaging.

The post-contrast enhancement pattern was accurate in the differentiation of adenomatous and non-adenomatous adrenal lesions in 44/48 masses (91.7%). It also had the highest sensitivity along with the size parameter (93.5%) and closely followed the CSI signal drop parameter as regarding its diagnostic discriminatory power with accuracy, specificity, PPV, NPV and Chi square values of 91.7%, 88.2%, 93.5%, 88.2% and 32.1% ($P < 0.0001$) respectively.

This was supported by the previous findings of Maurea et al. who had proved that the T1 sequence after Gadolinium

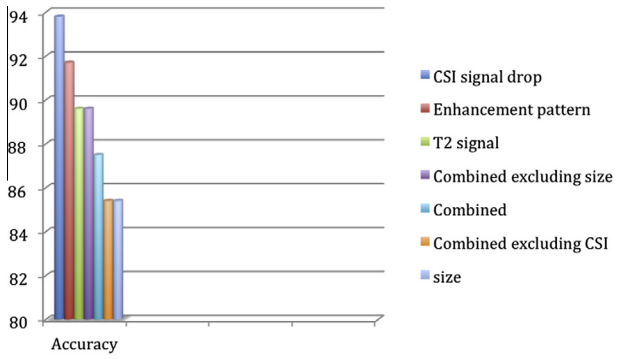

Diagram 1 shows the accuracy of various individual and combined MR parameters.

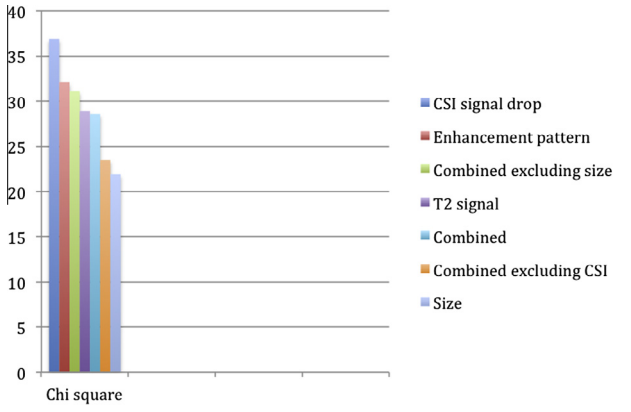

Diagram 2 shows the Chi square value for various individuals and combined MR parameters.

administration significantly improved characterization of adrenal masses compared with conventional T2WI. The Diagnostic accuracy, sensitivity, specificity, PPV and NPV were 93%, 90% ($P < 0.05$ versus T2 analysis) 100%, 100% and 80% ($P < 0.05$ versus T2 analysis) respectively, similar to the values obtained with the CSI sequence (16).

Slapa and his colleagues previously assessed the potential role of spin-echo, CSI and gadolinium-enhanced MRI in the differentiation of adrenal masses, they concluded that CSI ratio and Gd-DTPA were the most specific indicators of adrenal mass characterization. The CSI ratio based on OP and IP images, reflected lipid content in the lesion, while Gd-DTPA dynamic studies ratios reflected contrast agent inflow and washout in the lesion (34).

Inan et al. concluded that on visual evaluation of dynamic MR images, contrast enhancement patterns were homogeneous in 75% of the adenomas, whereas all of the malignant masses showed heterogeneous enhancement (25).

The combination of various MR parameters has previously been suggested for increasing the diagnostic discrimination between adenomas and non-adenomas (34). In our study we evaluated the diagnostic value of all parameters together, then we excluded the CS parameter and the size.

All combined MR parameters succeeded in diagnosing 42 (87.5%) of the total 48 cases (89.2% of the lipid rich adenomas, 0% of lipid poor adenomas and 100% of malignant masses). Six out of 48 masses (12.5%) were misdiagnosed: 3 lipid poor and 3 lipid rich adenomas equivalent to 6/31 benign adenomatous masses and 0 case of the 17 malignant masses. Therefore the accuracy of combined parameters was not the highest in our study. Actually it was only higher than the accuracy of the size and the accuracy of the combined parameters excluding CSI. Combined parameters showed a 100% specificity, a Chi square value of 28.6 and was statistically significant.

When we excluded CSI from our statistical evaluation of combined parameters, we obtained the lowest accuracy (similar to that of the size). Chi square value dropped to 23.5 (compared to 28.6 for combined parameters).

The accuracies of combined MR parameters before and after exclusion of the size parameter were 87.5% and 89.6%, respectively. After size exclusion the Chi square value was high 31.1 and statistically significant. The combination with higher statistical diagnostic values was a combination of MR parameters after size exclusion. This was in agreement with the previous findings of Slapa et al. who proved that the best performance of a combination of mean tumor diameter with single MRI signal intensity parameter was achieved in combination with CSI ratio and in combination with T2 (liver) index for all adrenal masses (34).

This study has few limitations. First, our study was retrospective in nature and had a potential for sampling bias with a relatively small number of adrenal malignancies compared with the large number of benign lesions. A prospective study with a larger population is required to confirm our results. The second potential limitation was the lack of histopathologic data from all patients with lipid rich adrenal adenomas; however, the use of 6-month follow-up has been confirmed to diagnose adenomas in multiple studies (20,37,40,41).

Finally, the absence of quantitative assessment of signal-intensity variations on out of phase images was compared with in phase images through calculation of the signal intensity index of an adenoma and non-adenoma lesion. However in general practice, the qualitative assessment of the adrenal adenomas and the presence of signal loss of the mass on opposed-phase images to define an adrenal adenoma is often used (30,35,37).

5. Conclusion

The most specific indicators and predictors of adrenal mass character proved to be the CSI signal drop on out of phase images, reflecting lipid content in the lesion and Gd-DTPA enhancement characteristics. Combining the MR parameters did not prove superior to those two individual parameters, however it yielded a valuable diagnostic protocol for distinguishing the nature of adrenal masses, considering that size criterion should not be used as an individual discriminator.

Conflict of interest

The authors declare no conflict of interests.

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