Diffusion-Weighted MR Imaging in the Differential Diagnosis of Adrenal Adenomas and Nonadenomatous Adrenal Masses

Adenom ile Adenom-Dışı Sürrenal Bez Lezyonlarının Ayırıcı Tanısında Difüzyon Ağırlıklı MRG Tetkikinin Yeri

Barış BAKIR, MD,[a]
Artür SALMASLIOĞLU, MD,[a]
Koray GÜVEN, MD,[a]
Arzu POYANLI, MD,[a]
Teoman Cem KADIOĞLU, MD[b]

Departments of
[a]Radiology, [b]Urology,
İstanbul University,
İstanbul Faculty of Medicine, İstanbul

Geliş Tarihi/*Received:* 04.08.2008
Kabul Tarihi/*Accepted:* 18.11.2008

Yazışma Adresi/*Correspondence:*
Barış BAKIR, MD
İstanbul University,
İstanbul Faculty of Medicine,
Department of Radiology,
İstanbul,
TÜRKİYE/TURKEY
drbarisbakir@yahoo.com

ABSTRACT Objective: The aim of our study was to demonstrate the feasibility of body diffusion-weighted magnetic resonance (DW MR) imaging in the differential diagnosis of adrenal adenomas and non-adenomatous adrenal masses. **Material and Methods:** Thirty-seven adrenal masses in 32 consecutive patients (18 women, 14 men) were included in this prospective study. Of all the masses, 21 were adenomas and 16 were non-adenomatous adrenal masses. DW MR images were obtained by a body coil using a multisection single-shot echo planar sequence on the axial plane without breath holding (water excitation with b value of 50, 400 and 800 s/mm^2). Signal intensities of the adenomas and non-adenomatous masses were measured for each b factor of 400 and 800 s/mm^2 using a region of interest (ROI). In addition, the signal intensities for apparent diffusion coefficient (ADC) calculation were measured. Mann Whitney U Test was used to compare signal intensities for each b factor (400 and 800 s/mm^2) and for ADC values between the adenomas and non-adenomatous masses. **Results:** No significant difference was noted ($p > 0.05$) for ADC values between the two groups. Similarly, signal intensities with b factors of 400 and 800 s/mm^2 did not demonstrate a significant difference ($p > 0.05$) between the groups. **Conclusion:** DW MR imaging is not an effective method in the differential diagnosis of adenomatous and non-adenomatous lesions in adrenal glands.

Key Words: Adrenal gland neoplasms, diffusion magnetic resonance imaging

ÖZET Amaç: Bu çalışmadaki amacımız, adenom ve adenom dışı sürrenal lezyonlarının ayrıcı tanısında difüzyon ağırlıklı manyetik rezonans görüntüleme (DA-MRG) tetkikinin tanı değerini araştırmaktır. **Gereç ve Yöntemler:** Otuz iki (18 kadın, 14 erkek) hastada 37 sürrenal bez lezyonu bu prospektif çalışmaya dahil edildi. Bu lezyonların 21'i adenom, 16'sı adenom dışı lezyon idi. DA-MRG tetkiki beden sargısı kullanarak "multisection single-shot echo planar sekans" ile (b değerleri 50, 400 ve 800 s/mm^2) gerçekleştirildi. Adenom ve adenom dışı lezyonların sinyal yoğunluğu değerleri b 400 ve 800 değerlerinde ve "apparent diffusion coefficient (ADC)" haritalamasında alan ölçümü yapılarak hesaplandı. Sinyal yoğunluğu ve ADC değerleri arasındaki farkı hesaplamak için Mann-Whitney U testi kullanıldı. **Bulgular:** ADC değerleri karşılaştırıldığında, her iki grup arasında istatistiksel açıdan anlamlı fark saptanmadı ($p > 0.05$). Ayrıca her iki grup arasında b faktörü 400 ve 800 s/mm^2'deki sinyal yoğunlukları açısından da anlamlı bir fark bulunmadı ($p > 0.05$). **Sonuç:** Çalışmamız, DA-MRG tetkikinin adenom ve adenom dışı sürrenal lezyonların ayırıcı tanısında etkin bir radyolojik yöntem olmadığını göstermiştir.

Anahtar Kelimeler: Sürrenal bez lezyonları; difüzyon ağırlıklı manyetik rezonans görüntüleme

Turkiye Klinikleri J Med Sci 2009;29(5):1191-7

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Adrenal masses are relatively common; they are incidentally found in about 1-5% of patients undergoing routine computed tomography (CT) study of the abdomen and in 2-10% in autopsy series.[1,2] An ad-

renal mass detected in a patient with a known malignancy requires further assessment, as in oncological practice where the adrenal gland is the fourth most common site for metastatic spread.[3] Even in patients with a known extraadrenal malignancy, most adrenal masses are adenomas.[2] Imaging plays a critical role not only in the detection, but also in characterization and classification of the adrenal masses as benign or malignant. CT and MRI are well-established methods used to differentiate adenomas from nonadenomatous adrenal lesions.[4-6] As most adenomas are rich on lipids, they demonstrate low attenuation on unenhanced CT and signal loss on out-of-phase chemical shift MRI.[7] However, 15–20% of adenomas, namely atypical adenomas, which do not contain sufficient amount of lipids, cannot be characterized by unenhanced CT or chemical-shift MRI.[3] However, the literature suggests that delayed contrast-enhanced imaging with CT or MRI may be helpful in this regard, with most adenomas demonstrating a more rapid wash-out of contrast material than metastases.[4,8,9] However, various threshold attenuation values have been reported to distinguish adrenal adenomas from nonadenomas with unenhanced and delayed contrast material–enhanced CT imaging.[10,11] CT and MRI with conventional sequences may be useful in characterizing adrenal lesions, but in some cases like lipid-poor adenomas, these techniques provide limited diagnostic information. The development of a more precise imaging technique would reduce the need for invasive diagnostic procedures, such as percutaneous fine-needle biopsy and surgical resection and would avoid the expense of prolonged imaging follow-up. This is the main reason for researchers to develop new CT and MRI protocols, which would yield results that are more accurate. MR-spectroscopy has also been used in the differential diagnosis of adrenal lesions.[12] However, to our knowledge, no study has ever determined the value of DW MR imaging on adrenal masses.

We aimed in our study to demonstrate the feasibility of body DW MR in the differential diagnosis of adrenal adenomas and nonadenomatous adrenal masses.

MATERIAL AND METHODS

SUBJECTS

Between May 2006 and June 2008, 37 adrenal masses detected in 32 consecutive patients (18 women, 14 men) either incidentally or in cases with a suspected adrenal lesion on ultrasonography (US), CT, and MRI of the abdomen were included in this prospective study. Because of the limited resolution of the diffusion weighted MRI, lesions smaller than 1 cm in diameter were not included. Of the masses, 21 (in 18 patients) were adenomas and 16 (in 14 patients) were non-adenomatous adrenal masses.

The mean patient age was 59 years (range= 31-78 years) in the adenoma group and 55 years (range= 42–72 years) in the non-adenomatous group. The non-adenomatous masses consisted of 10 metastases, 4 pheochromocytomas, 1 adrenocortical carcinoma, and 1 adrenal lymphoma (diffuse large cell lymphoma). Primary malignancies in the 8 patients with adrenal metastases (10 masses) were as follows: 5 (6 masses) patients had lung cancer, 2 (3 masses) patients had breast cancer, and 1 (1 mass) patient had adenocarcinoma of the rectum. Five patients had bilateral masses (bilateral adenomas in three patients, bilateral metastases in two patients). Eighteen of the adenomas were non-functional and three were hyperfunctional (one producing cortisol and two producing aldosterone). The mean diameters, with standard deviations, and diameter ranges (in parentheses) were 22 mm ± 0.9 (15-34 mm) for adenomas and 34 mm ± 1.4 (28-54 mm) for non-adenomatous lesions.

The diagnosis of the masses was confirmed by biopsy (1 adrenal lymphoma, 2 lipid-poor adenomas), surgery (3 hyperfunctional adenomas, 4 pheochromocytomas, 1 adrenocortical carcinoma) and clinical and radiological follow-up (18 adenomas, 10 metastatic diseases). For the follow-up, all patients underwent a baseline US examination. Lesions detectable by US were monitored with US, but for lesions invisible by US, MRI was used in order to avoid the X-ray exposure from CT (US every 3 months, MRI every 6 months). Sixteen lesions with a suggestive radiological diagnosis of adenoma sho-

wed no change in size during the radiological follow-up (12-24 months, mean= 15.3 months); besides, no clinical or imaging evidence of an extraadrenal primary neoplasm was present; thus they were considered adenomas. As the remaining 10 lesions (all with known extra-adrenal primary neoplasms and other evidence of widespread metastatic disease) displayed an increase in size (>3 mm/6 month) during the radiological follow-up for 9-24 months (mean 12.2 months), they were considered metastatic masses. For these cases without histopathological confirmation, a diagnostic consensus was reached between the Departments of Radiology, Surgery and/or Endocrinology and Medical Oncology. Informed consent was obtained from all patients.

MR PROTOCOL

All scans were performed on the same 1.5 T imaging system (Magnetom Symphony, Siemens Medical Solutions, Germany). The system provides a maximum gradient strength of 30 mT/m with a peak slew rate of 100 mT/m/msec. DW MR images were obtained by a four-element phased-array multicoil for the body, using a multisection single-shot echo planar sequence on the axial plane without breath holding. The following parameters were used for DW sequence; parallel imaging reduction factor of two; TR/TE= 4400/85 ms; section thickness, 6 mm; intersection gap, 1 mm; matrix size, 128 x 128; field of view, 400 x 400 mm; partial Fourier factor, 6/8; bandwidth, 1370 Hz per pixel; seven excitations, water excitation with b value of 50, 400 and 800 s/mm^2. Fat saturation was used to avoid chemical shift artifacts. The whole sequence consisted of 30 sections. The study was performed during normal respiration. In addition, the routine abdominal imaging protocol was applied, which included axial and coronal breath-hold T2-weighted HASTE sequences, axial and coronal in-phase and opposed-phase images and breath-hold T1-weighted fat-suppressed spoiled gradient-echo shared prepulse sequences acquired before contrast administration and during the arterial phase (15-20 seconds) and venous and delayed phases (60 and 180 seconds) after contrast administration.

IMAGE ANALYSIS

Diffusion sequence was acquired at the first MRI session in all patients and measurements were performed based on this sequence.

Quantitative measurements were made using a dedicated workstation (Leonardo, Siemens Medical Solutions). Signal intensities of the adenomas and non adenomas were measured for each b factor of 400 and 800 s/mm^2, using a similarly sized ROI. However, as T2 shine through effect, which can alter measurement results, is stronger on lower b values, no signal intensity measurement was performed on b factor of 50.[13] The ROI was placed centrally and the size of the ROI was kept as large as possible, covering at least two thirds of the lesions. In addition, all the ADC maps were created automatically on a workstation with standard software (Leonardo, Siemens Medical Solutions); the mean ADC values were determined on images with b factors of 50 and 800 s/mm^2. The signal intensities for ADC calculation were measured by using a similar size ROI. Calculated ADC values were expressed in square millimeters per second ($\times 10^{-3}$ mm^2/s).

Mann Whitney U Test was used to compare signal intensities for each b factor (400 and 800 s/mm^2) and ADC values between the adenomas and non-adenomas.

RESULTS

The results of the quantitative analysis of the ADC values were presented in Table 1. ADC values demonstrated no significant difference ($p > 0.05$) between the two groups. Signal intensities with b factors of 400 and 800 s/mm^2, demonstrated no significant difference either ($p > 0.05$). The mean signal intensities for adenomas with a b factor of 400 and 800 were 52 ± 17.9 and 31 ± 12.2, respectively. The mean signal intensities for non-adenomas with a b factor of 400 and 800 were 62 ± 18.7 and 34 ± 14.3, respectively.

DISCUSSION

DW imaging is based on the restriction of random translational molecular motion (brownian motion) of water, determined by the diffusion coefficient. For two decades, it has been used mainly for the

TABLE 1: ADC values of adenomas compared to ADC values of non-adenomatous adrenal masses. Mann-Whitney U Test demonstrated no significant difference (p> 0.05).

	Adenomas ADC[a] Values (n= 21)	Nonadenomatous Adrenal Masses ADC[a] Values (n= 16)	Mann-Whitney U Test z	p
Mean	1.096	1.034		
Standard devriation	0.128	0.179	1.412	0.158*
Median	1.090	1.035		
Minimum	0.82	0.82		
Maximum	1.27	1.43		

* p> 0.05

[a]x 10-3 mm^2/s.

ADC: Apparent diffusion coefficient

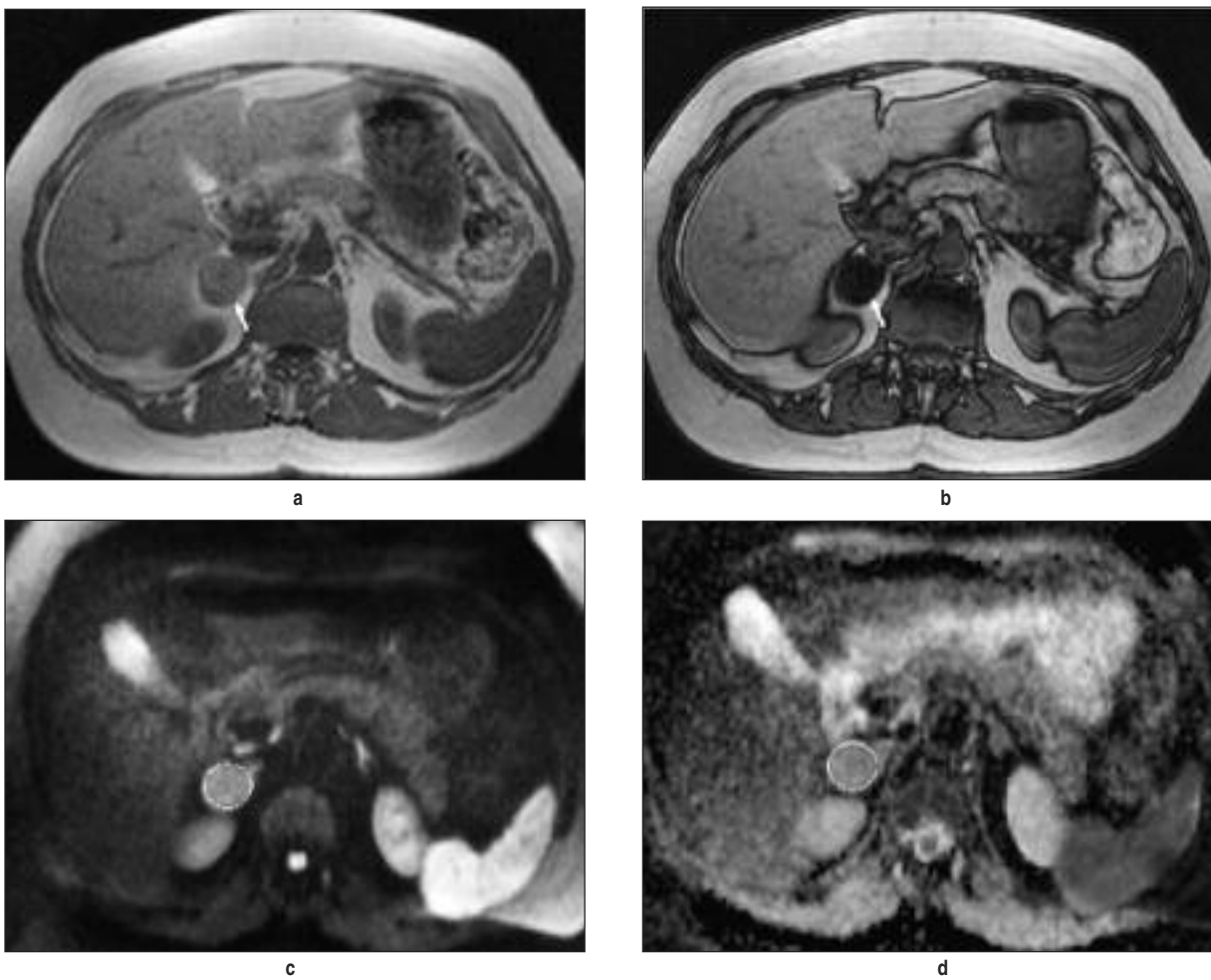

FIGURE 1: A 59-year-old man with right-sided adrenal adenoma. A- In-phase MRI shows right adrenal mass that is slightly hyperintense compared to the spleen (arrow). B-Opposed-phase MRI shows decrease in signal intensity in adrenal gland compared to the spleen (arrow). C- The ROI placed over the lesion on diffusion weighted (b= 400) axial MRI, D- The ROI placed over the lesion on ADC map image.

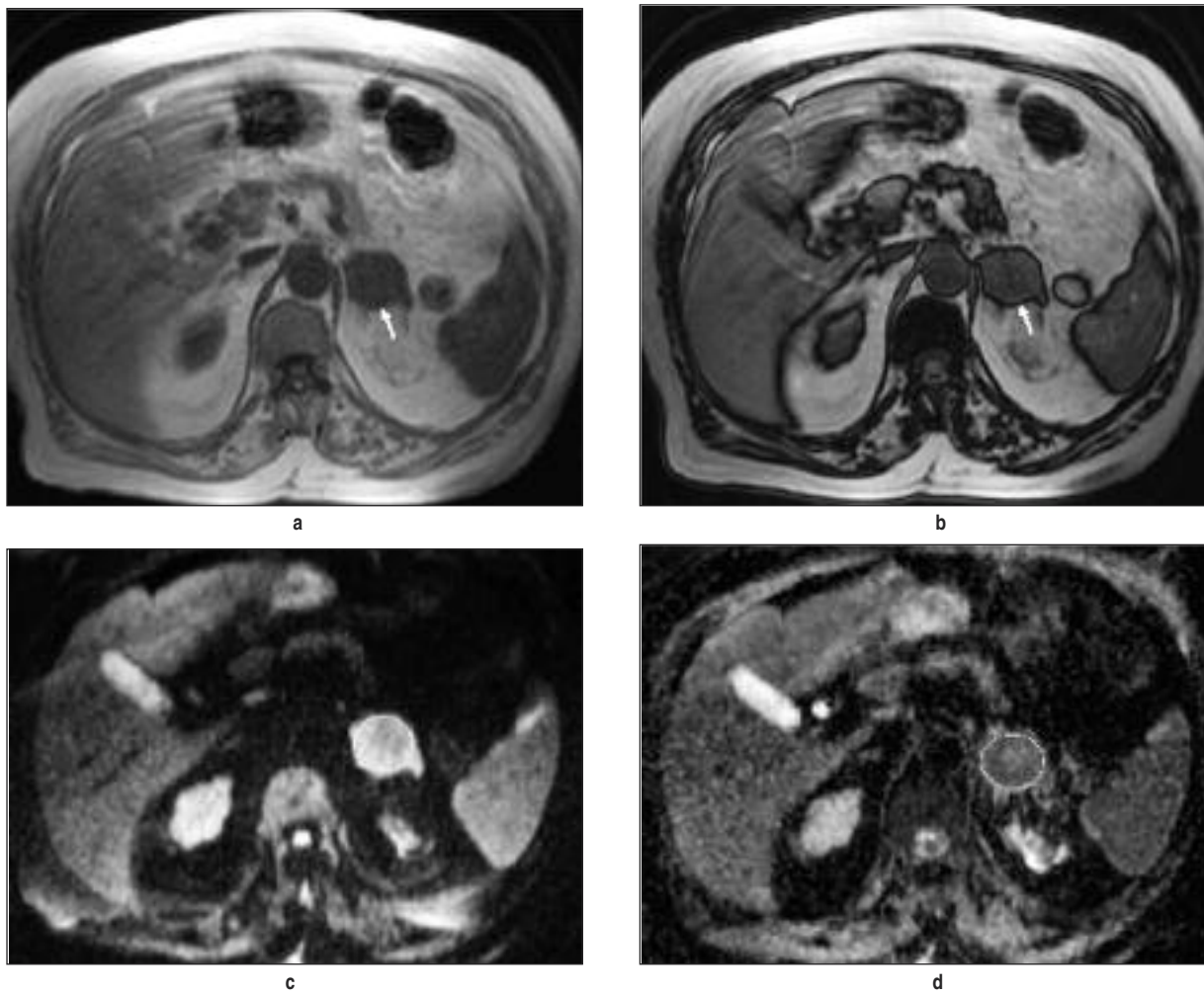

FIGURE 2: A 46-year-old woman with left adrenal non-adenomatous mass. A- In-phase MRI shows right adrenal mass that is slightly hyperintense compared to the spleen (arrow). B-Opposed-phase MRI shows no change in signal intensity in adrenal gland compared to the spleen (arrow). C- The ROI placed over the lesion on diffusion weighted (b= 400) axial MR image. D- The ROI placed over the lesion on ADC map image. Biopsy proved the mass was adrenal lymphoma (diffuse large cell lymphoma).

evaluation of intracranial diseases. The use of DWI in the abdomen is hindered by certain limitations such as physiologic motion artifacts caused by respiration and cardiac motion, the short relaxation times of the abdominal organs and long acquisition times. In the 1990s, a series of technologic advances made it possible to translate DWI measurements to extracranial sites, including the abdomen.[13]

Today DWI can be used for tumor detection, tumor characterization, distinguishing tumors from nontumoral lesions and monitoring treatment response. Tumors are frequently more cellular than the tissue from which they originate and thus appear to be of relatively high signal intensity (restricted diffusion) at DWI.[13] There are reports in the literature about the contribution of DWI to tumor detection.[13,14] Tumors differ in their cellularity and this difference may reflect their histological composition and biologic aggressiveness.[13] The utility of DWI for tumor characterization was first demonstrated in brain tumors.[13] Today it is used for the differential diagnosis of benign and malignant masses of the liver and the breast, in differentiating solid or cystic renal masses and soft tissue tumors, and demonstrating cystic lesions in pancreatic and ovarian cancers.[15-22] DWI can also be used to differentiate tumoral tissues from non-tumoral tissues.

DWI has shown potential for differentiating tumor from other etiologies in prostate cancer and for distinguishing a malignant cause of vertebral collapse in spine from a nonmalignant one.[23-26]

To our knowledge, there are no studies on DWI in adrenal lesions. In our study, we investigated the contribution of DWI in differentiating adenomas and non-adenomatous lesions. However, our results indicated that DWI was not useful for this purpose. There were no significant differences in ADC values and signal intensities between the two groups ($p > 0.05$). This finding may be attributed to the structural architecture of these two groups. In biologic tissue, the DW imaging signal is derived from the motion of water molecules in the extracellular space, the intracellular space, and the intravascular space.[27] The degree of restriction to water diffusion is inversely correlated to the tissue cellularity and the integrity of cell membranes.[28-31] The motion of water molecules is more restricted in tissues with a high cellular density associated with numerous intact cell membranes. The lipophilic cell membranes act as barriers to motion of water molecules in both the extracellular and intracellular spaces.[13] By contrast, in areas of low cellularity or where the cellular membrane has been breached, the motion of water molecules is less restricted. A less cellular environment provides a larger extracellular space for diffusion of water molecules, and these molecules may also freely transgress defective cell membranes to move from the extracellular into the intracellular compartment.[13] The lack of difference in the brownian motion of water molecules between two groups could be attributed to a contribution of these factors, which is due to the structural architecture of those lesions.

There are several limitations to our study. First, our study population and the number of lesions were small. Second, the echo-planar sequence used with a higher b value had a lower signal to noise ratio (SNR) resulting in greater image distortion. In addition, the echo-planar sequence causes anatomic distortion due to susceptibility effects. Third, although it is common to use a 6-month follow-up to determine benignity, slow-growing malignancies may develop and may appear as stable masses at subsequent examinations. In our study, we followed-up non-adenomatous lesions for at least 9 months and on average 12.2 months. In this period, every lesion with a diagnosis of metastasis demonstrated an increase in size. However, some adenomas also show growth occasionally. In a study by Barzon and colleagues, adrenal adenomas demonstrated an 8% cumulative risk of enlargement after 1 year.[32] None of the enlarged adrenal adenomas developed malignancy. In our study, we followed-up adenomas for at least 12 months and on average 15.3 months and there was no increase in size of any lesion during this period.

We concluded that DW MR imaging was not an effective method in the differential diagnosis of adenomatous and non-adenomatous lesions in adrenal glands.

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