The Egyptian Journal of Hospital Medicine (October 2017) Vol.69 (2), Page 1998-2007

Role of Diffusion MRI in Evaluation of Renal Masses

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ABSTRACT
Background: renal masses are being exposed more frequently in the last decades due to advances in cross sectional imaging such as CT and MR. Accurate characterization of renal masses is essential to ensure appropriate case management, to assist in staging and prognosis and to differentiate surgical lesions from nonsurgical lesions. However, in some cases there is an overlapping between the ADC values of benign and malignant masses. Thus, the use of ADC values alone may lead to inaccurate assessment of renal masses.
Aim of the Study: to assess the roles of DWI in combination with quantitative ADC measurements the differentiation between benign and malignant renal masses. **Conclusion:** The combination of conventional MRI and ADC value in the diagnosis of renal masses can increase the diagnostic accuracy and considered of most value in cases where IV contrast agents are contraindicating.
Keywords: MRI, DWI, carcinoma, renal masses, kidney cancer.

INTRODUCTION

Renal cell carcinoma (RCC, also acknowledged as Hypernephroma, renal adenocarcinoma and Grawitz tumor) is a kidney cancer that initiates in the lining of the proximal convoluted tubes, which is a part of the small tubes present in the kidney that carry waste particles from blood to urine. RCC is the furthermost common type of kidney cancer in adults, accountable for nearly 90-95% of the cases[1]. Epidemiological evidence supported the fact that renal cancer is estimated to be the 13th most common cancer in the world, with about 270,000 new cases identified in an annual basis with approximately 116,000 people dying from the disease [2]. In general, the common symptoms of renal cancer are: flank and back pain, fatigue, anaemia, haematuria, weight loss, and so forth.

Nevertheless, there is consensus that MRI diffusion-weighted imaging technique plays a more important role in the differential diagnosis of benign and malignant renal tumors [3]. Diffusion-weighted imaging (DWI) evaluates random movement of water molecular diffusion process in vivo, which can provide information on the spatial structure and biophysical characteristics of tissue such as cellular structure, cellular density, microstructure, and microcirculation [4]. In general, most neoplasm show restricted diffusion owing to the dense cellular packing of solid tumors and increased cell membranes per unit volume, leading to the restriction of water molecular movement and corresponding high signal intensity on DWI . The degree of water molecules diffusion can be evaluated quantitatively by the apparent diffusion coefficient (ADC) value [5]. As a quantitative parameter calculated from the DWI images, the ADC value can reflect the pathological changes of tissues and is very useful in the clinical diagnosis of central nervous system disease, various abdominal lesions, and especially renal disease [6].

The ADC value is inversely proportional to cellular density because increased cellular density limits water diffusion in the interstitial space. In the past few decades, a large body of evidence has suggested that DWI with quantitative ADC measurements can act as predictor in differentiating malignant renal lesions from normal kidney and benign renal lesions [7].

The aim of the present study is to evaluate the recent role of Diffusion MRI in the evaluation of renal masses.

Aim of the present study was to assess the roles of DWI in combination with quantitative ADC measurements the differentiation between benign and malignant renal masses.

The study was approved by the Ethics Board of Ain Shams University.

PATHOLOGY OF RENAL MASSES

Cancer of the kidney amounts to 2% of the total human cancer burden, with approximately 190,000 new cases diagnosed each year. They occur in all world regions, with a preference for developed countries. Etiological factors include environmental carcinogens (tobacco smoking) and lifestyle factors, in particular obesity [8].

The recently introduced 2004 World Health Organization (WHO) classification of the adult renal epithelial neoplasms is meant to replace the previous 1998 WHO classification. The 2004 WHO classification is based on pathology and genetic abnormalities. The description of categories has been

Received: 3 / 8 /2017
Accepted: 12 /8 /2017
DOI : 10.12816/0041047

expanded to improve their recognition and new diagnostic categories are included [9].

I-NEOPLASTIC RENAL MASSES

WHO CLASSIFICATION OF RENAL TUMORS (2004)[9]

1-Familial renal cancer.

2-Renal cell tumors:

A-Malignant:

- Clear cell renal cell carcinoma
- Papillary renal cell carcinoma
- Xp11 translocation carcinomas
- Carcinoma of the collecting ducts of Bellini
- Mucinous tubular and spindle cell carcinoma
- Multi-locular clear cell carcinoma
- Chromophobe cell carcinoma.
- Renal medullary carcinoma
- Carcinoma associated with neuroblastoma
- Renal cell carcinoma unclassified

B-Benign:

- Papillary adenoma
- Oncocytoma

3-Metanephric tumors

- Metanephric adenoma
- Metanephric adenofibroma
- Metanephric stromal tumors

4-Mesenchymal tumors

Occurring Mainly in Children

- Clear cell sarcoma
- Rhabdoid tumor
- Congenital mesoblastic nephroma
- Ossifying renal tumor of infants

Occurring Mainly in Adults

- Angiomyolipoma
- Epithelioid angiomyolipoma
- Haemangioma
- Lymphangioma
- Haemangiopericytoma
- Angiosarcoma
- Leiomyoma
- Leiomyosarcoma
- Rhabdomyosarcoma
- Schwannoma
- Osteosarcoma
- Juxtaglomerular cell tumor
- Renomedullary interstitial cell tumor
- Malignant fibrous histiocytoma
- Solitary fibrous tumor

5-Mixed mesenchymal and epithelial tumors

- Cystic nephroma
- Synovial sarcoma
- Mixed epithelial and stromal tumor

6-Nephroblastic tumors

- Nephrogenic rests
- Nephroblastoma
- Cystic partially differentiated nephroblastoma

7-Neuroendocrine tumors

- Carcinoid
- Neuroendocrine carcinoma
- Neuroblastoma
- Phaeochromocytoma
- Primitive neuroectodermal tumor(Ewing's sarcoma)

8-Haematopoietic and lymphoid tumors

- Lymphoma
- Leukaemia
- Plasmacytoma

9-Germ cell tumors

- Teratoma
- Choriocarcinoma

10-Metastatic tumors

II. INFLAMMATORY RENAL MASSES[10]

A-Acute renal abscess B-Chronic renal abscess

C. Peri-nephric abscess or hematoma D. Xanthogranulomatous pyelonephritis

E. Acute focal pyelonephritis F. Renal tuberculosis

III. OTHER CAUSES OF RENAL MASSES (PSEUDOMASSES)

A. Focal hydronephrosis: Hydronephrosis confined to one part of the kidney can simulate a mass. This commonly occurs in patients with an obstructed upper segment of a duplex kidney. Obstruction to an in fundibulum may be caused by a variety of conditions, such as tuberculosis and tumor [10].

B. Renal Sinus Lipomatosis: Sinus lipomatosis is an overabundance of renal sinus fat, which may produce stretching of the infundibulum and compression of the renal pelvis, simulating a parapelvic cyst or other hilar renal mass [10].

Technique of DWI

DWI is a recent MRI technique used to show molecular diffusion, which is the Brownian motion of the spins in biological tissues, but it cannot be explained only by this motion. Other additional factors have been considered, such as perfusion in the capillary network. Therefore, the diffusion phenomenon is measured by the ADC rather than by the diffusion coefficient[11].

The kidney is well suited for diffusion studies because of its high blood flow and its fluid transport function. According to some authors; these factors can explain the higher renal ADC values as compared with other organs [11].

DW-MRI provides unique insight into tissue cellularity, tissue organization, integrity of cells and membranes, as well as the tortousity of the extracellular space, which can be helpful for detecting malignant diseases, and for distinguishing tumor tissues from non-tumor tissues[12].

The ADC has been related to the state of tissue during the growth of tumors or progression of cancer. With proliferating cells, there is an increase in cellular density and a decrease in the amount of intracellular space or extracellular space available, leading to a reduction in the ADC[12].

Restriction to the molecular diffusion of water in neoplastic tissues can be related both to the greater cellular density in the tissues, generated by the high index of neoplastic replication with a consequent reduction in the width of intercellular spaces, and to the ultra structural alteration of the kidney tissue[13].

An image of low b-value (0s/mm^2) has higher SNR, less distortion, but less diffusion weighting. Conversely, high b-factor (400–800 s/mm^2) images have more diffusion weighting but suffer from low signal-to-noise ratio and severe image distortion. DWI using b values of 0, 400 and 800 s/mm^2 was included in the routine MRI examination to differentiate benign and malignant kidney masses. Some investigators have recommended a b value >400 s/mm^2 because it can reduce ‘‘T2 shine-through’’ and intra-voxel perfusion effects [5].

INTERPRETATION AND ASSESSMENT OF DWI

DW MR has a promising role in the characterization of renal masses. Highly cellular neoplasms, such as solid renal cell carcinomas (RCCs), typically maintain bright signal intensity compared to normal renal parenchyma on high b-value images. Conversely, renal masses with low cellularity such as benign cysts typically have less restricted water diffusion and lose signal on high b-value images[4]. Nonetheless, RCC can have a varied appearance on DW MRI owing to differing degrees of cellularity and elements of cystic change, necrosis, orhemorrhage. In complex renal masses, solid enhancing tumor components demonstrate lower ADC values than necrotic or cystic regions [14]. Areas of restricted diffusion in a mixed solid and cystic renal mass may help differentiate an RCC with cystic or necrotic areas from a benign complicated cyst that might otherwise appear similar on conventional MRI obtained without contrast [14].

In a study conducted by **Zhang *et al.*** [15], 29 cases proved to have RCC, one case of cystic RCC, whereas the 28 cases were solid. The mean ADC value of RCC (1.43 ± 0.19), which was significantly lower than that of normal renal parenchyma and benign renal lesions **(p value 0.001)**.

Nevertheless, the range of ADC values was wide and showed some overlap with the normal parenchyma, it was agreed and has been observed in previous studies by **Sandrasegaran *et al.*** [16] **and Taouli *et al.*** [167]**,** Normal renal parenchyma ranges from 1.621 to 2.721 x 10^{-3} mm^2/s and there were only 4 cases of RCC with their ADC measured 1.699, 1.719, 1.878 and 1.901 x 10^{-3} mm^2/s (all of their ADC values are higher than the lowest normal parenchymal ADC value).

Manentiet al. [17] reported a statistically significant difference among the ADCs of the carcinomas and normal parenchyma; however, their analysis did not reveal a statistically significant difference in the mean ADC of the individual histological variants of the renal carcinoma.ADC values were found to be different for necrotic/cystic and hemorrhagic areas of RCC, as compared to the solid portions. In this study the ADC value of the necrotic/cystic areas of the tumor was higher than

that of solid areas and they were not always lower than that of normal renal parenchyma. That is why necrotic/cystic and hemorrhagic areas must be avoided for ROI placement as these may hamper useful interpretation of ADC values.

Moreover, the free diffusion and high ADC value of the cystic changes and necrosis in cases of RCC were helpful to confirm the diagnosis of tumor against inflammatory lesion. This was an agreement with **Goyal *et al***.[18], who had demonstrated that the ADC values of cystic portions of RCC were significantly higher than those of (cystic portions of) inflammatory lesions. While the former were higher than normal renal parenchyma (indicating free diffusion), the latter were markedly lower (indicating restricted diffusion).

This finding is important because it implies that in a predominantly cystic indeterminate renal lesion, presence of restricted diffusion in the fluid component favors inflammatory etiology, while the presence of relatively free diffusion (with restricted diffusion in the solid components) indicates malignancy[18].

The mean ADC of RCC is significantly lower than high ADC of renal cysts (Bosniak I, II and III) with p values 0, 001 and 0.003 respectively. This was an agreement with the previous reports by **Zhang*et al*.** [14], **Sandrasegaran*et al.*** [15] **andInci *et al.*** [7].Though, **Yoshikawa*et al.*** [5]and **Squillaci *et al.*** [19]reported no significant difference between the ADCs of RCCs and the ADCs of complex cysts.

Urothelial carcinomas also exhibit restricted diffusion due to high cellularity; they stand out as areas of bright signal intensity against a background of suppressed signal within the collecting system and adjacent normal renal parenchyma on high b-value images while demonstrating low signal on the corresponding ADC map [20].**Yoshida *et al.*** [21] havefound that the accuracy and sensitivity for detecting upper urinary tract carcinoma at MRI can be significantly improved by adding DW imaging to standard anatomic and fluid-sensitive sequences; in fact, the diagnostic abilities of DW MRI alone in comparison to dynamic contrast-enhanced MRI were not markedly different.

There was one case of **TCC** in our study with its ADC value was 1.154 x 10^{-3} mm^2/s that was lower than mean ADC of normal renal parenchyma (2.016 ± 0.15), and RCC (1.43 ± 0.19 x 10^{-3} mm^2/s). This was in agreement with **Yoshida*et al.*** [21]who reported lower ADC values in TCC (1.29±0.15x10^{-3} mm^2/s) when compared with renal parenchyma (2.19 x 10^{-3} mm^2/s). Angiomyolipoma (AML) is a common benign renal neoplasm that occurs in 0.3–3% of the population [7].AML is composed of variable amounts of fat, muscle tissue, and abnormal blood vessels. These tissues prevent the molecules of water from spreading freely, and causing a low ADC value in these tumors. They considered that the decreased ADC of AMLs may be explained by restricted diffusion caused by the muscle and fat components[7].Only two cases were diagnosed as angiomyolipoma in our study, they recognized on conventional MRI with typical fat components. Their ADC values were 1.597 and 1.028 x 10^{-3} mm^2/s with the mean ADC was 1.312 x 10^{-3} mm^2/s which was lower than the mean ADC of RCC 1.43 ± 0.19 with no statistical significance due to limited number of AML cases.

Our findings were in concordance with those of the study by **Zhang*et al*.**[14], the reported one case of AML with ADC value of 1.23 x 10^{-3} mm^2/s that was lower than the mean ADC value of RCC cases in the same study (2.03±0.10 x 10^{-3} mm^2/s). This was an agreement with the previous studies of **Sandrasegaran *et al.*** [15]**, Taouli *et al.*** [16] and **Yoshikawa *et al.*** [5] who found significantly lower ADC of the AMLs were lower than that of RCCs. This might be related to higher lipid contents of the angiomyolipomas they have studied; However **Kilickesmez *et al.*** [13]recorded a mean values ADCs of AMLs (1.40± 0.21) higher than that of RCCs (1.06±0.39).They stated that the ADC value of AML is related to its fat content with gradually decreasing the ADCs of AML with inverse correlation of its fatty content.

In addition, **Inci *et al.*** [7]**,** recorded a mean ADC value of 1.19±0.36 for 16 cases of AML, with no significant difference from RCCs (1.12±0.23). The detection of intra-tumoral fat allows the radiologist to reliably and accurately identify AML**.** They also observed decreasing ADC values of angiomyolipomas with inverse correlation of the fatty content. We have studied 4 cases of lymphoma, they had the lowest ADC values, ranging between 0.58 to 1.21x10^{-3} mm^2/sec and mean value was 0.85±0.27. This was an agreement with the findings of ***Guo and his colleagues***[22]*who* reported a mean ADC value of lymphoma cases of0.64 to 0.76 x 10^{-3} mm^2/s**.** *This* can be explained with densely packed cells at histologic analysis. All lymphoma lesions were easily seen with high signal on DWI. The advantage of DWI was obvious detection of multiple lesions against a suppressed background signal. The most common renal mass is the benign cyst[7]. The differentiation of benign cystic lesions of the kidney

from those that require surgical management is a common and often difficult problem. In general, there is no difficulty in differentiating a simple cyst from a malignant cystic neoplasm; however, accurate classification of complex cystic masses is helpful in determining their proper management.

In 1986, Bosniak [23] described a categorization system that was designed to help radiologists determine which cystic lesions require surgical treatment and which do not **[23]**. In their study, there were 31 benign cystic renal lesions, with 23 cases of (Bosniak type I) cysts, 5 cases of Bosniak type II cyst and 3 cases of Bosniak III cyst. All of these cysts showed hemorrhagic components with high T1 signal intensity.

There was only one case of cystic RCC which appeared as multi-locular cystic lesion with thick septae and heterogeneous contents of high T1 signal likely hemorrhagic and, it was misdiagnosed as benign Bosniak III, based on combined conventional MRI and DW findings[23].

The mean ADC of cystic renal masses (2.79□0.73) were significantly higher than ADCs for solid renal masses (1.33□0.26) **(p value 0.001**).** ***Kilickesmez et al.***[13], **Taouli *et al.*** [16] and **Inci *et al.*** [7] also reported similar findings. The highest ADC value of all lesions was that of simple renal cyst (Bosniak I). There was significant difference between the ADC value of simple renal cysts (Bosniak I), their mean ADC value (3.164 x 10^{-3} mm^2/s± 0.34) and ADC value of complicated cysts (Bosniak II and III), their mean ADC=1.82 x 10^{-3} mm ^{2}/s± 0.59 In addition it was significantly higher than RCC (**p value 0.001****).

Kilickesmez et al. [13] explained the highest ADC value of simple renal cysts due to their fluid content, with non-restricted motion of water molecules.

The findings of our study are in concordance with the previous reports by ***Zhang et al., 2008*** , **Taouli *et al.*** [16], ***Sandrasegaran et al.***[15], and **Inci *et al.*** [7]. In this study the mean ADC values of complicated cysts (Bosniak II and III) was 1.82 x 10^{-3} mm^2/s □□0.59 significantly higher than mean ADC of RCC 1.43□□0.19 x 10^{-3} mm^2/s **(p value 0.003).** ***Sandrasegaran et al.*** [15] have concluded that complicated benign cysts with increased blood or protein content show reduced diffusion compared with simple cysts. The presence of large molecules or cellular debris within a complex cyst may impede diffusion. Renal hemorrhagic cysts can sometimes demonstrate very low signal on the ADC map, a finding that may relate to the ‘‘T2 blackout’’ effects of an intrinsically T2 hypo intense lesion and/or restricted diffusion in blood products [20] have demonstrated that the presence of fluid–fluid or hematocrit levels observed in some hemorrhagic cysts and the absence of solid enhancing components can help in the diagnosis of hemorrhagic cyst, however the small lesion size and motion artifact may limit accurate evaluation. Renal infection and some associated complications also demonstrate restricted diffusion and should not be mistaken for malignancy. Pyelonephritis results in patchy non-mass like areas of restricted diffusion in portions of the renal parenchyma, a finding that may relate to inflammatory cell infiltration and possible ischemic effects of infection [24]. In a study carried out by **Bittencourt *et al.*** [24], one case was diagnosed as multifocal pyelonephri.

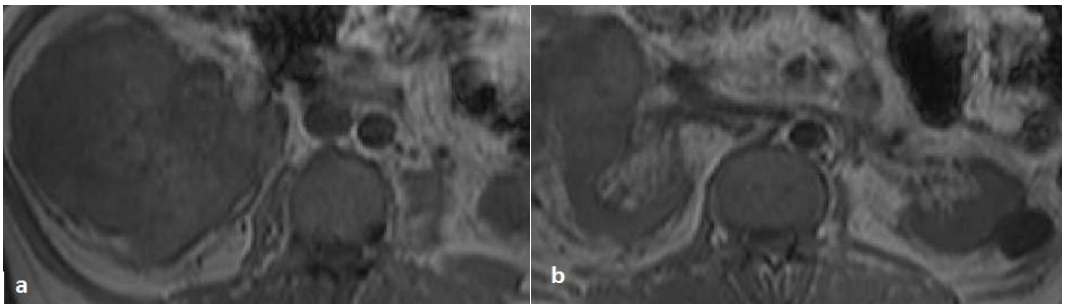
CLINICAL CASES

CASE 1

Clinical data

- Seventy years old male patient complaining of loss of weight and attacks of hematuria. MRI was requested for assessment of right renal solid mass lesion detected by CT to rule out renal vein thrombosis.

MR Findings



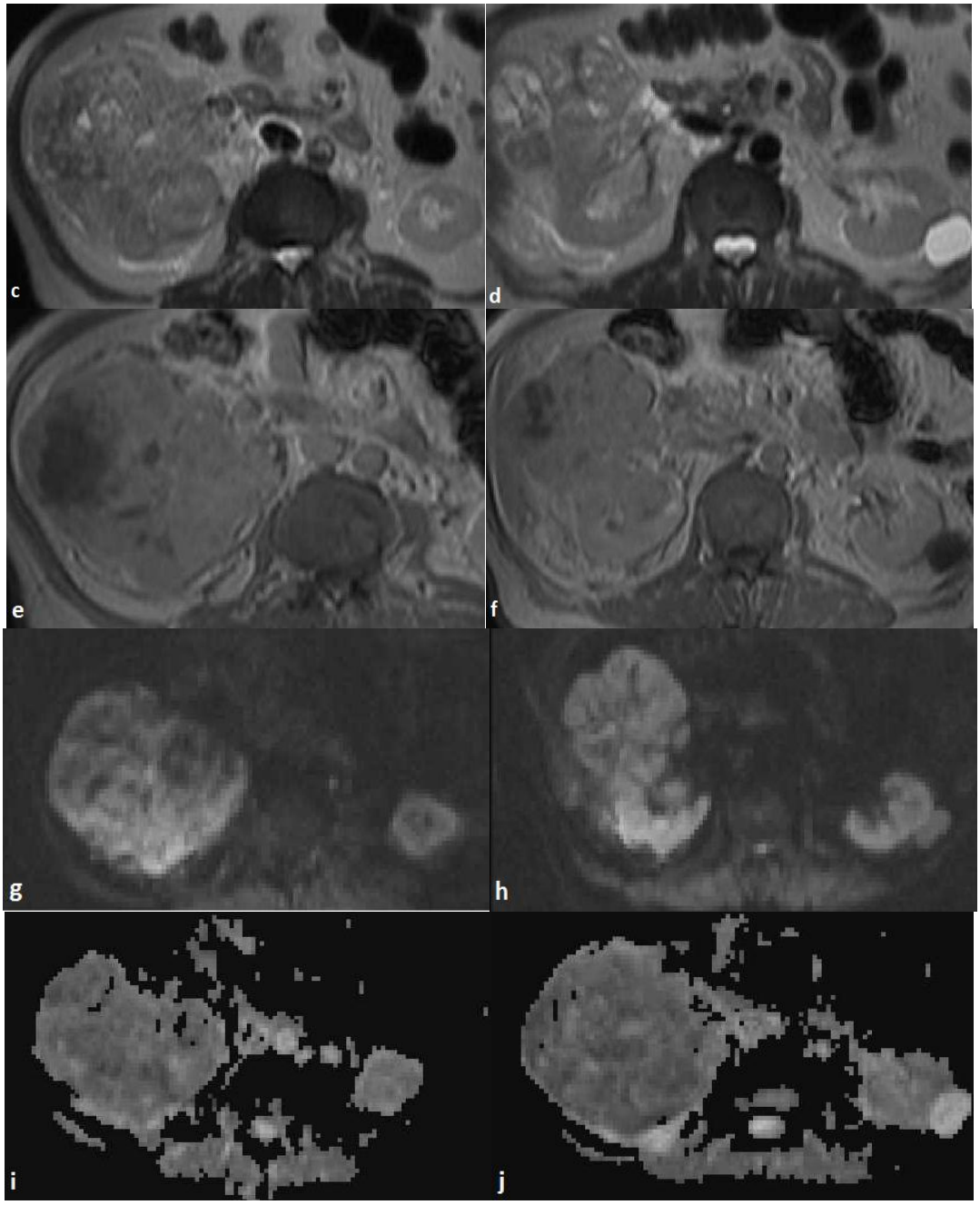


Figure 1: (a-b): Axial T1 WIs and (c-d) Axial T2 WIs showed 7 cm right renal upper pole large solid mass lesion of iso intense T1 and high T2 signal with intra lesional areas of breakdown of low T1 and high T2 signal. A small left upper pole renal cystic lesion is also seen. (e-f) Post contrast axial T1 WIs showed heterogenous enhancement of the lesion with central non enhancing areas of break down. The surrounding fat planes are clear with no extra renal extension or regional lymph nodes. No renal vein or IVC invasion. The left upper pole cyst did not enhance. (g-h) DWI with b value of 800 and (i-j) ADC map showed restricted diffusion of the solid portion of the lesion, the ADC was **1.503×10^{-3} mm^2/sec** with increased diffusion of the central necrotic area of cystic degeneration, the ADC was **2.094×10^{-3} mm^2/sec.** Facilitated diffusion of the left cystic lesion, the ADC was **3.153×10^{-3} mm^2/sec.**

DIAGNOSIS

MRI diagnosis

- *Right renal malignant neoplastic lesion, (RCC stage T1b).*
- *The left renal cystic lesion was categorized as Bosniak type I.*

Final diagnosis

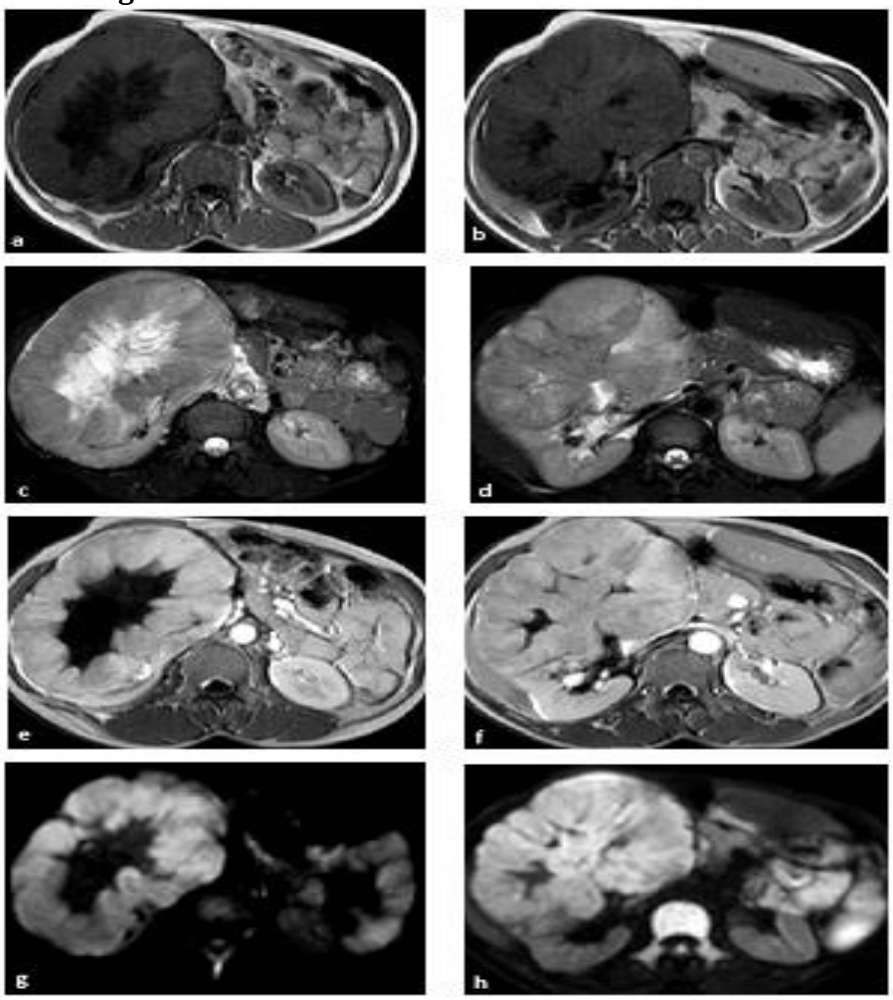
- *The patient underwent right nephrectomy, and pathology revealed renal cell carcinoma (clear cell type) (Stage T1b- Renal vein free).*
- *The left upper pole simple cyst had a stable appearance on follow up MRI done 6 months later.*

CASE 2

Clinical data

- Thirty years old female patient with right loin pain and swelling.
- MRI was requested for further evaluation of right renal solid mass suspected to be oncocytoma on CT scan.

MR Findings



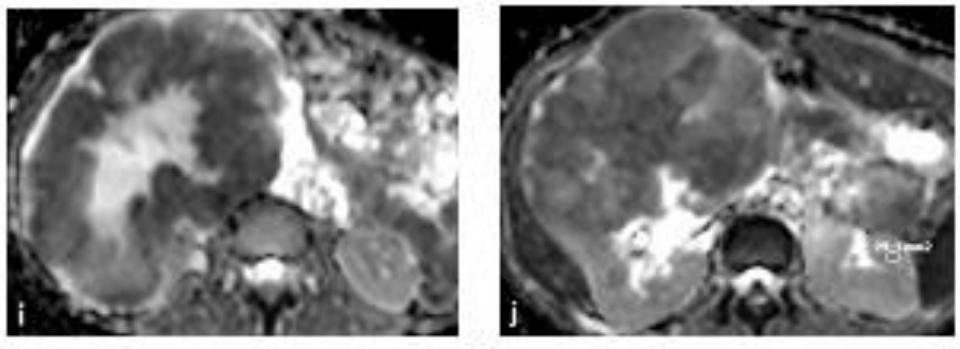


Figure 2: (a-b) Axial T1 and (c-d) axial T2 WIs showed a large 17 cm exophytic right renal mass, most of the lesion displays iso-intense on T1 and high signal on T2WI with central area of low T1 and bright T2 signal. (e-f) Post contrast axial T1 WIs showed heterogenous enhancement of the lesion with non enhancing central area. The surrounding fat planes are clear with no regional lymph nodes. No renal vein or IVC invasion. (g-h) DWI with b value of 800 and (i-j) ADC map showed restricted diffusion of the peripheral solid part and facilitated diffusion of the central area. The ADC values of the peripheral solid part and central area were ***1.273* x 10^{-3} mm^2/sec** and***2.853* x 10^{-3} mm^2/sec** respectively. The bright T2 signal intensity and facilitated diffusion of the central changes were suggestive of central necrosis not scar tissue.

DIAGNOSIS

MRI diagnosis

- ***Malignant neoplastic lesion, RCC (stage T2b)***

Final diagnosis

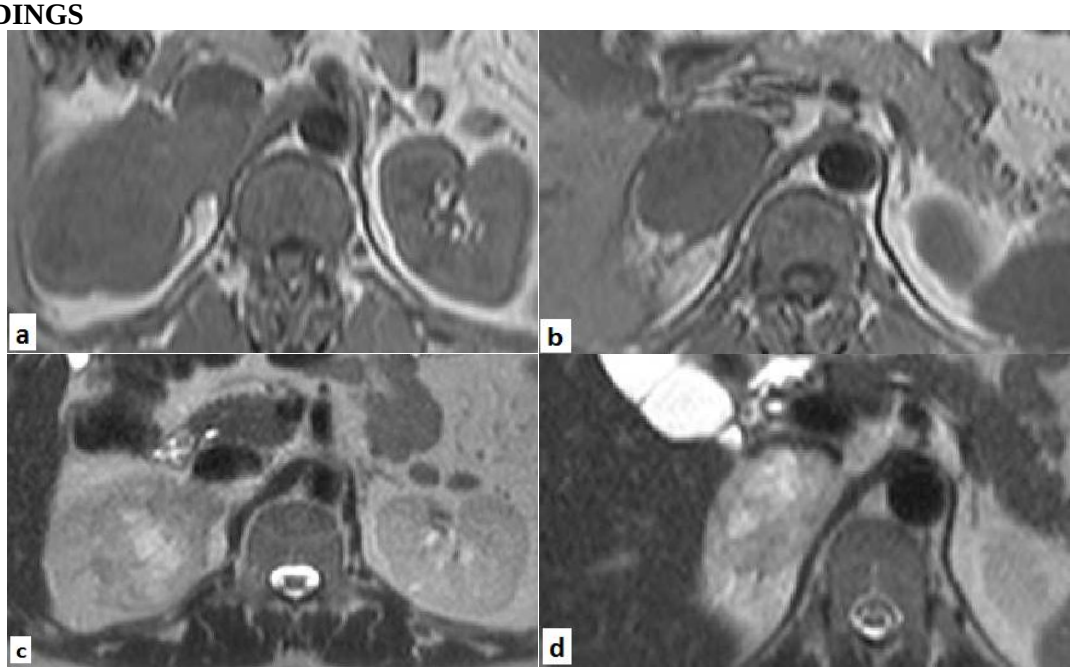
- ***Radical nephrectomy was done and pathology revealed RCC-Chromophobe type. (Stage T2b- renal vein free)***

CASE 3

Clinical data

- Fifty-two years old male patient coming with right lower limb edema with history of recurrent attacks of hematuria.
- MRI was requested for further assessment and staging of right renal solid mass lesion detected by Ultrasound to rule out renal vein thrombosis.

MR FINDINGS



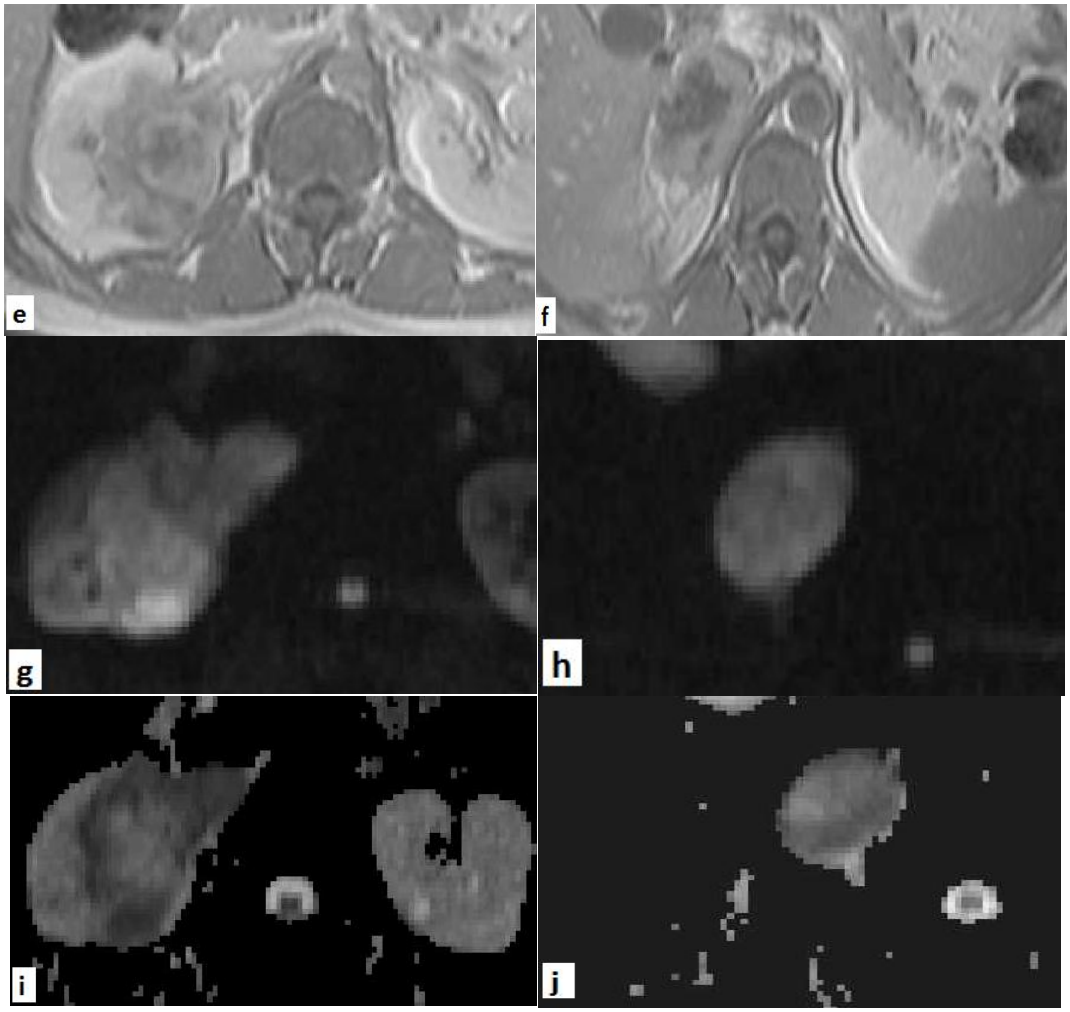


Figure 3: **(a-b)** Axial T1 and (c-d) T2 WIs showed large right renal solid mass lesion. The mass displayed iso-intense signal on T1WI and slightly high signal on T2WI with central area of cystic degeneration of low T1 and bright T2 signal. (e-f) Post contrast axial T1 WI showed heterogenous enhancement of the lesion with non enhancing central area of cystic degeneration. The right renal vein and IVC were distended with enhancing tumor thrombus (g-h) DWI at b value = 800 and (i-j) ADC map showed restricted diffusion of the solid portion of the lesion, the ADC was **1.245×10^{-3} mm^2/sec,** and facilitated diffusion of the central necrotic changes, the ADC was **2.134×10^{-3} mm^2/sec.**

DIAGNOSIS

MRI diagnosis

- *Malignant neoplastic lesion, with renal vein and IVC malignant thrombosis (RCC stage T3b).*

Final diagnosis

- *The patient underwent radical right nephrectomy and pathology revealed Renal Cell Carcinoma (clear cell type). (Stage T3b- renal vein infiltrated)*

CONCLUSION AND RECOMMENDATION

The combination of conventional MRI and ADC value in the diagnosis of renal masses can increase the diagnostic accuracy and considered of most value in cases where IV contrast agents are contraindicated. We recommend that DWI with low and high b value (b 0-800) and quantitative ADC measurements to be added to the routine Renal MR imaging protocol for better differentiation between benign and malignant renal masses. Further research is still needed to validate the potential diagnostic role of this imaging

technique in assessment of renal masses in clinical practice.

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