

Role of MR Apparent Diffusion Coefficient in Characterization of Cystic Renal Masses Using 3T MRI

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Abstract

Now it is more than 30 years since we are using the Bosniak classification for cystic renal masses, which represents the scale for cancer probability using imaging features. First, we used ultrasound, then CT then MRI for characterization.

Many studies were conducted try to characterize the lesions using the ADC values trying to reach solid values for characterization and subgrouping which we can use especially for indeterminate lesions and for benign lesions which are radiologically characterized as Bosniak III and IV and underwent unnecessary nephrectomies.

Objectives: Retrospective evaluation the efficiency of DWI and ADC values in characterization of benign, indeterminate, and malignant renal masses using 3T MRI.

Results: We found the ADC values of the benign cysts are significantly higher than malignant cysts (3.03 versus 2.35 10 mm/s), Median, P=0.0001 with sensitivity and specificity 84% and 92%, however still no definite cut off values for indeterminate lesions.

Conclusion: MRI ADC values can be used for differentiation of benign and malignant lesions with high sensitivity and specificity however still no definite cut off values for radiologically indeterminate cystic renal masses.

Keywords: Cystic renal masses; Retrospective evaluation; Benign; Malignant lesions

Introduction

Cystic renal masses are commonly encountered in clinical practice. Improved resolution of imaging modalities has in part led to the improved ability to detect these abnormalities. Yet the Bosniak criteria have stood the test of time as radiologists and urologists still primarily rely on these [1,2].

The conventional CT and MRI sequences cannot easily differentiate benign from malignant lesions in many cases. Studies have shown that 16%-33% of nephrectomies are performed on benign lesions [3].

There is also a strong need for alternatives to gadolinium-enhanced sequences in patients at risk for nephrogenic systemic fibrosis (NSF) [4].

Percutaneous biopsy of renal tumors has been widely demonstrated to be an accurate method of diagnosing preoperative pathologic subtypes in many patients.

However, the risk of procedural complications and the potential for sampling error have hindered universal acceptance of percutaneous biopsy [5-9].

The basic physical principle of diffusion-weighted imaging is based on the random movements of molecules (Brownian motion) in a spatial plane.

This is affected by differences in the nucleocytoplasmic ratio and factors that change water diffusion in the interstitial space such as increased cell density and viscosity [9].

DWI has become more familiar and has gained a definitive role in the characterization of abdominal malignancy in lymph nodes, and renal, liver, pancreas, prostate masses [10].

Diffusion weighted imaging (DWI) has been applied successively in renal masses; however, its usefulness in cystic masses is not established and a well-known pitfall of DWI is that benign HPC may show restricted diffusion [11].

There are still very limited studies using 3T MRI trying for characterization of cystic renal masses using DW-MRI trying to differentiate benign cysts from the malignant cysts which requires surgical interference and indeterminate cysts (IIF).

Our study aims is to retrospectively evaluation of the efficiency of DWI and ADC values in characterization of benign, indeterminate, and malignant renal masses using 3T MRI.

Patients and Methods

Our retrospective research was approved by Urology and nephrology center board and Benha medical school boards and patient's consents was obtained.

Inclusion and exclusion criteria

We had 73 consecutive patients with 75 cystic renal masses, all the patient underwent MRI scans, malignant lesions underwent biopsy, nephron spring or nephrectomy.

All the scans were obtained prior to biopsy and surgical excision.

In our study we included radiological benign lesions, indeterminate cases which have 2 years follow up, radiologically malignant appearance cases, the scans done before having biopsies or even surgical interference.

The cases with no definitive imaging, clinical diagnosis or no histopathology results were excluded (n=5), patient with no Diffusion MRI sequences were excluded (n=13), lesions with poor quality Diffusion sequences or obvious artefacts are also excluded (n=4).

Our study included finally 51 patients with 51 lesions were included in our study.

MRI Protocol

All images were obtained using a 3T MR system (Signa horizon-General Electric medical systems, Miluakee-USA) equipped with a phased-array coil.

The breath hold DW images were obtained using a customized Black-Blood Spin Echo- Echo Planar Imaging (BB SE-EPI) sequence. An XL TORSO coil was used.

In the coronal T2 TSE Breath Hold (BH) and coronal T2 TSE Free Breathing (FB), two b values (b 800 and b 1600 s/mm²) using the transverse BB SE-EPI sequences were acquired.

The scanning parameters were as follows:

Coronal T2W TSE BH (TR=shortest, TE=80, Slice Thickness=6, Interslice Gap=1, Matrix=312 x 247, FOV FH=405, NSA=1, Sense Factor=P, Reduction (RL)=2, Voxel Size=0.79, Slice Number=74, Scan Time=22-3).

Transverse T2W TSE FB (TR=shortest, TE=80, Slice Thickness=7, Inter- slice Gap=1, Matrix=284 x 194, FOV FH=255, NSA=1, Voxel Size=0.73, Slice Number=32, Scan Time=1-36).

Transverse BB SE-EPI b 800 and b 1600 (Slice Thickness=7, Interslice Gap=1, Matrix=152 x 112, FOV FH=199, RL=450, AP=338, NSA=3, Sense Factor= P, Reduction=2). The DWI acquisition was two minutes and 14 seconds in total.

All of the MR images of the 51 patients were reviewed at the PACS workstation (Philips Workspace, Extended MR Workspace, release 2.6.3. 2009, Philips Medical Systems, The Netherlands).

Image Analysis

Qualitative assessment including DWI and ADC tumor signals

We Compared the signal intensity of the lesions in both ADC and DWI images with the normal renal parenchyma in the contralateral kidney or the same kidney if the patient had previous nephrectomy.

We used a rating scale with 1=hyper intense, 2=hypointense, and 3=mixed signal intensity or isointense.

Quantitative assessment using the ADC map

All the DWI images were transferred for ADC maps reconstruction to an independent workstation for processing. To obtain mean ADCs (\pm standard deviation) of each cyst we measure ADC maps by using average size circular ADC ROI.

For solid masses with cystic necrosis we placed 2 ROIs on the solid part and on the cystic component. For complex cystic masses we placed the ROIs on either the wall nodularity or the thick septations.

Lymphadenopathy

Malignant masses with enlarged lymph nodes we assessed the signal intensity and ADC values of the associated enlarged lymph nodes.

Reference standard

For benign lesions and indeterminate lesions 2 years follow up were obtained to confirm patient stability. For malignant lesions we had either post biopsy or post nephrectomy histopathology results (Figures 1 and 2).

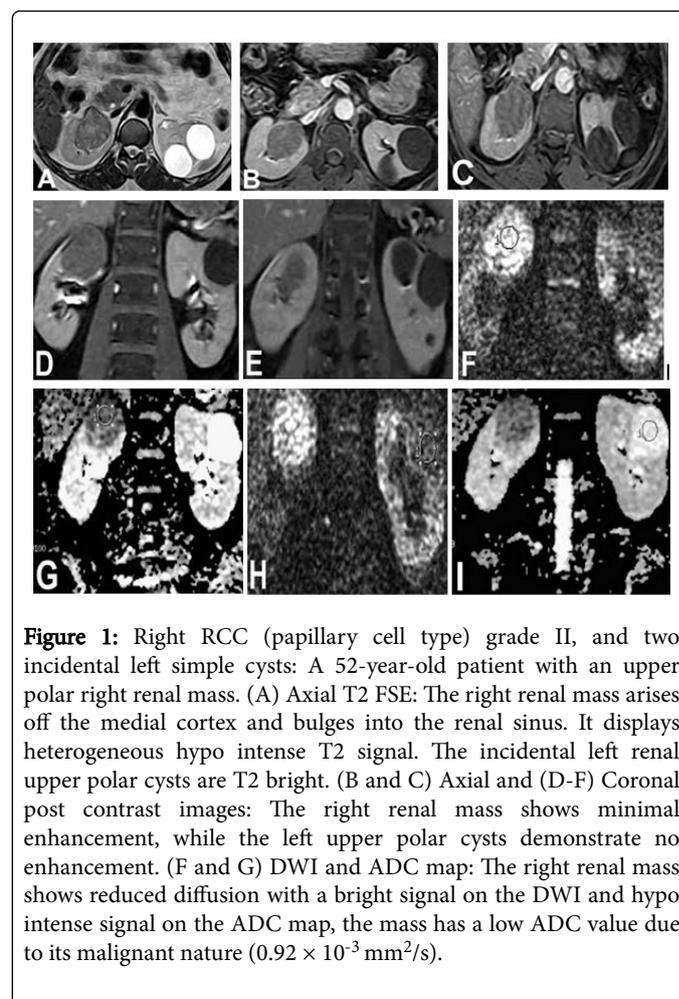


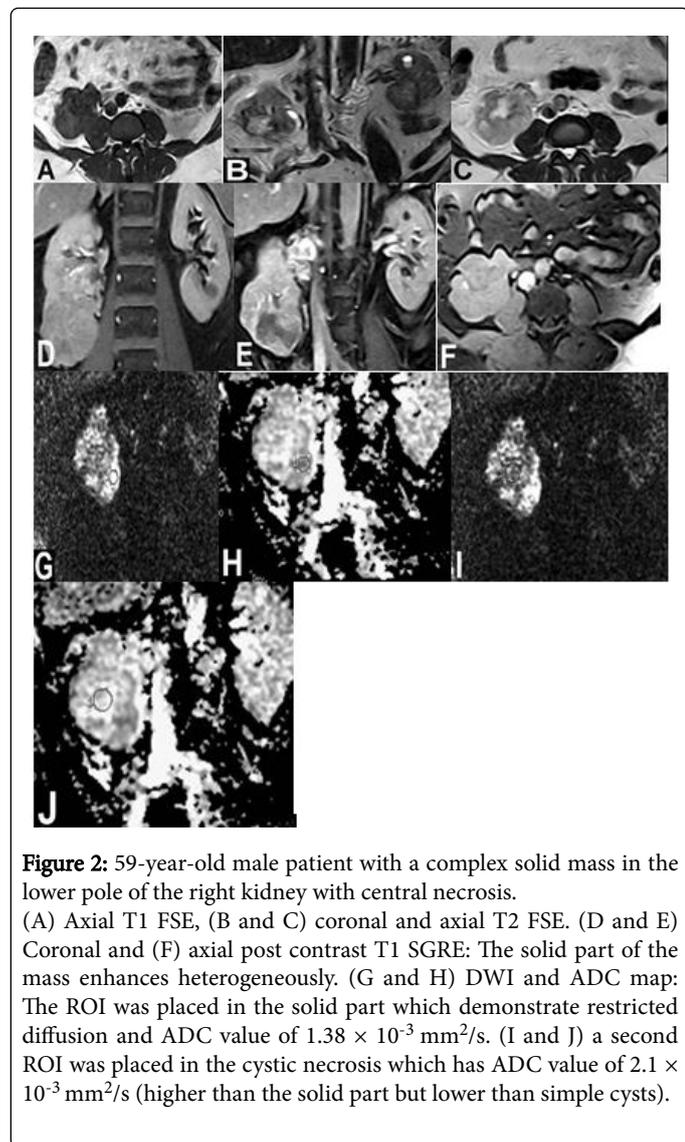
Figure 1: Right RCC (papillary cell type) grade II, and two incidental left simple cysts: A 52-year-old patient with an upper polar right renal mass. (A) Axial T2 FSE: The right renal mass arises off the medial cortex and bulges into the renal sinus. It displays heterogeneous hypo intense T2 signal. The incidental left renal upper polar cysts are T2 bright. (B and C) Axial and (D-F) Coronal post contrast images: The right renal mass shows minimal enhancement, while the left upper polar cysts demonstrate no enhancement. (F and G) DWI and ADC map: The right renal mass shows reduced diffusion with a bright signal on the DWI and hypo intense signal on the ADC map, the mass has a low ADC value due to its malignant nature (0.92×10^{-3} mm²/s).

Statistical analysis

Statistical analyses were performed by SPSS version 18.0 (statistical package for social sciences). Data are presented as the mean and

standard deviation or n (%). The one-sample Kolmogorov-Smirnov test was used to evaluate the distribution of data.

An unpaired Student's t-test was used to compare the mean ADC values between suspicious lesions and normal renal parenchyma after ensuring normal distribution by Shapiro-Wilk test.



The Mann-Whitney U or Kruskal-Wallis tests were performed to compare the mean ADCs and histopathological variables.

A p value of less than 0.05 was considered to be a statistically significant difference. Receiver operating characteristic (ROC) analysis was done to evaluate the diagnostic performance of the ADC for differentiating benign and malign lesions.

The significant cut-off value was determined to be the value that best discriminated between benign and malignant in terms of maximum sensitivity and specificity.

Results

We had 51 patients with 51 renal masses finally, all are enrolled with 31 male patients with 31 lesions and 20 female patients with 20 lesions).

The range of patients age was 24-84 years, the median age was 63 years (Table 1).

The final diagnosis was confirmed either by stability for 2 years with typical benign radiological features (n=32) or by histopathology examination for malignant lesions.

| | Benign n=20 | Malignant n=28 | Indeterminate n=3 | P Value |
|---------------|----------------|-------------------|----------------------|---------|
| Age mean (SD) | 59.8 (11.3) | 59.5 (12.9) | 28.0 (13.7) | 0.001* |
| Sex no% | | | | |
| 1 | 10 (50) | 8 (28.6) | 2 (66.7) | 0.1 |
| 2 | 10 (50) | 20 (71.4) | 1 (33.3) | |

Table 1: Demographic characteristics of studied cases.

Study groups

We divided the lesions into 3 categories according to radiological features as follows:

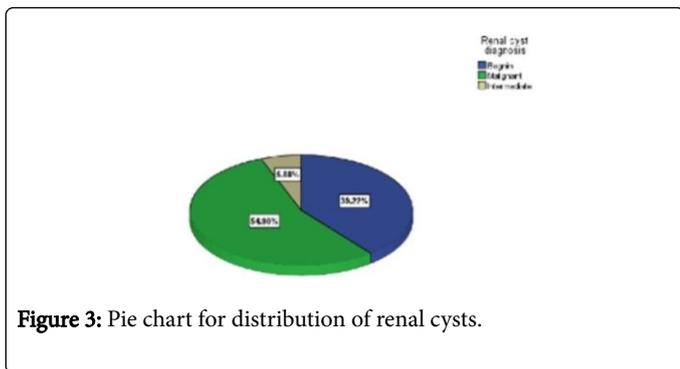
- **Group 1: Benign cystic renal parenchymal masses**
This group includes 20 lesions.
- **Group 2: Indeterminate cystic parenchymal masses**
This group includes 3 lesions (N=3).
- **Group 3: Malignant cystic renal masses**
This group includes 28 lesions.

Diffusion weighted MRI

The quality of DWI images of 51 lesions were reviewed, all had good quality. 12 patients had metastatic renal hilar and para aortic lymph nodes, all showed bright signal intensity in DWI images.

We had 27 malignant lesions out of 28 lesions demonstrated low signal intensity on the DWI images at b 800, only one showed low signal intensity on both DWI and ADC images.

4 lesions showed heterogeneous signal intensity on both DWI and ADC images, due to mixed solid and cystic components. 3 cysts were clear renal cell carcinoma and 1 lesion was unclassified renal cell carcinoma (Figure 3).



ADC values

The normal renal parenchyma showed mean ADC values was 2.07×10^{-3} and $1.56 \times 10^{-3} \text{ mm}^2/\text{s}$ at b800 and 1600 s/mm², respectively.

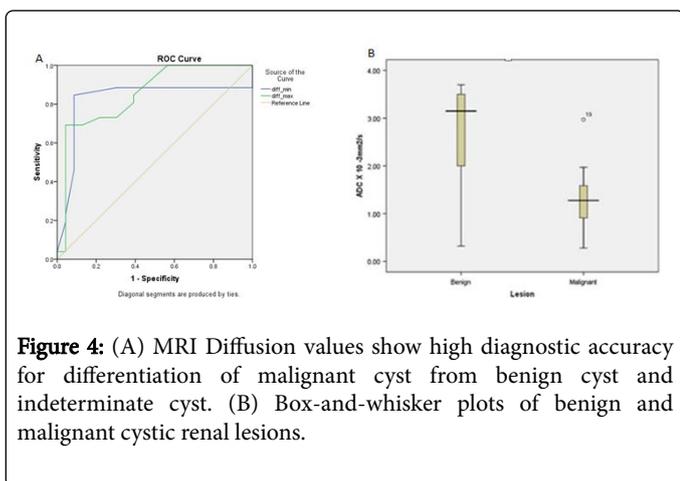
We found that the benign cystic lesions were significantly high compared to malignant cystic lesions $3.03 \times 10^{-3} \text{ mm}^2/\text{s}$ (0.75) ($1.67 \times 10^{-3} \text{ mm}^2/\text{s}$) (0.61) 10^3 versus 1.9 (0.59) $10^3 \text{ mm}^2/\text{s}$ (0.59) ($1.12 \times 10^{-3} \text{ mm}^2/\text{s}$) (0.61) [Median (Min–Max)] respectively (Tables 2,3 and Figure 4).

| | Benign mean (SD) | Malignant mean (SD) | Indeterminate mean (SD) | P value |
|--------------------------------|--------------------------|---------------------------|-------------------------|---------|
| b value 800 s/mm ² | 1.67 (0.36) ^A | 1.12 (0.61) ^{AB} | 2.00 (0) ^B | 0.001* |
| b value 1600 s/mm ² | 3.03 (0.75) ^A | 1.9 (0.59) ^A | 2.37 (0.15) | <0.001* |

Table 2: Comparison of MRI diffusion in diagnosis of renal cyst. (A,B): Indicate statistically significant differences.

| Test Result Variable(s) | AUC | Std. Error | P value | Asymptotic 95% Confidence Interval | |
|--------------------------------|-------|------------|---------|------------------------------------|-------------|
| | | | | Lower Bound | Upper Bound |
| b value 800 s/mm ² | 0.824 | 0.071 | 0 | 0.685 | 0.962 |
| b value 1600 s/mm ² | 0.849 | 0.057 | 0 | 0.738 | 0.961 |

Table 3: Diagnostic accuracy of MRI diffusion for renal cysts cases.



We assumed that our study have more population data than this limited cases study, and the results are similar to Inci et al with mean ADC value of $3.09 \pm 0.14 \times 10^3 \text{ mm}^2/\text{s}$ in benign renal cysts (Bosniak I) and close to study of Zhang et al. who reported $3.269 \pm 0.61 \times 10^3 \text{ mm}^2/\text{s}$ for simple renal cysts.

The ADC value of indeterminate cystic lesions at b value 800 s/mm² 1600 s/mm² are $2.00 \times 10^{-3} \text{ mm}^2/\text{s}$ and $2.37 \times 10^{-3} \text{ mm}^2/\text{s}$ ($0.15 \times 10^{-3} \text{ mm}^2/\text{s}$) respectively, it was lower than the study of Balyemez et al. Who reported The mean ADC value was $2.75 \pm 0.43 \times 10^{-6} \text{ mm}^2/\text{s}$ for indeterminate cysts, but this results was limited due to small number of indeterminate cases.

Benign lesions showed significant ADC value difference compared to high malignant renal cysts at b values of 800 s/mm², 1600 s/mm² (p<0.001), respectively These results are concordant with the study of Goya et al. [12].

Still there is no significant ADC values difference between indeterminate lesions and low malignant lesions (had a low Fuhrman grade (1 or 2) at b values of 800 s/mm² 1600 s/mm² (p=0.001) and these results were similar to Balyemez et al.

ROC analysis and cut-off levels

We found that cut off values for malignant lesions is $1.5 \times 10 \text{ mm}^2/\text{s}$ (p 0.001) for the ADC with b values of 800 s/mm² with sensitivity and specificity 84% and 92%, respectively and $2.35 \times 10^{-3} \text{ mm}^2/\text{s}$ for the ADC with b values of 1600 s/mm² with sensitivity and specificity of DWI were 73% and 79%, respectively (Table 4).

Discussion

In our study we used DW-MRI trying to characterize the cystic renal masses using ADC values. We found that the ADC values of normal renal parenchyma, benign and malignant renal cysts differ significantly.

Benign cystic renal masses showed high significant values compared to malignant cysts were $3.03 \times 10^{-3} \text{ mm}^2/\text{s}$ ($0.75 \times 10^{-3} \text{ mm}^2/\text{s}$) 10^3 versus 1.9 (0.59) $10^3 \text{ mm}^2/\text{s}$ respectively, and also higher to the normal renal parenchyma which was 2.09×10^{-3} at b value 1600 s/mm², and these values are lower than the study done by Goya et al.

| Test variable | Cut off | Sensitivity | Specificity |
|--------------------------------|---------|-------------|-------------|
| b value 800 s/mm ² | 1.5 | 0.84 | 0.92 |
| b value 1600 s/mm ² | 2.35 | 0.73 | 0.79 |

Table 4: Validity of MRI diffusion according to ROC curve.

Bosniak criteria have stood the test of time as Radiologists and Urologists still primarily rely on these guidelines for cystic renal mass evaluation in clinical practice [13]. However recent studies showed that malignancy rates were only 72% for Bosniak category III lesions and 86% for Bosniak category IV lesions [14].

DWI MRI in cystic renal masses has been applied successfully for characterization with promising results, still there is limitation for hemorrhagic and proteinaceous cysts with false lower values which may affect both sensitivity and specificity of the ADC measurements. Still post contrast enhanced MRI with subtraction has an important role in this category.

Conclusion

In conclusion, MRI still have advantages over CT for evaluation of cystic renal masses [15]. The use of 3T MRI is particularly advantageous when parallel imaging is employed (due to higher base line SNR). Increasing fear of post Gadolinium nephrogenic systemic fibrosis makes the radiologist looking for alternative sequences.

DWI-MRI with ADC values as a routine sequence could be useful in characterization of cystic renal masses to avoid unnecessary surgeries as well as a safe sequence for surveillance and follow up. Still more studies are needed for indeterminate renal lesions and benign lesions which are characterized by Bosniak classification as Bosniak III and IV and had unnecessary nephrectomies.

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