Diffusion-weighted magnetic resonance imaging in cystic renal masses

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Abstract

Introduction: We aimed to introduce the diagnostic value of diffusion-weighted (DWI) magnetic resonance imaging (MRI) for distinguishing benign and malignant renal cystic masses.
Methods: Abdominal DWI-MRIs of patients with Bosniak categories 2F, 3, and 4 cystic renal masses were evaluated retrospectively. Cystic masses were assigned as benign or malignant according to histopathological or followup MRI findings and compared with apparent diffusion coefficient (ADC) values.
Results: There were 30 patients (18 males and 12 females, mean age was 59.23 ± 12.08 years [range 38–83 years]) with cystic renal masses (eight Bosniak category 2F, 12 Bosniak category 3, 10 Bosniak category 4). Among them, 14 cysts were diagnosed as benign and 16 as malignant by followup imaging or histopathological findings. For the malignant lesions, the mean ADC values were lower than for benign lesions (p=0.001). An ADC value of ≤2.28 $x10^{-6}$ mm^2/s or less had a sensitivity of 75% and a specificity of 92.86% for detecting malignancy.
Conclusions: ADC can improve the diagnostic performance of MRI in the evaluation of complex renal cysts when used together with conventional MRI sequences.

Introduction

Cystic renal masses are frequently detected in clinical practice with the increasing use of advanced imaging modalities for intra-abdominal pathologies. Most renal cysts are incidentally discovered simple cysts and do not require treatment or further evaluation. Renal cysts are so common that patients who are over the age of 50 have a 33–50% possibility of having at least one renal cyst.[1] Among these cysts, malignant cysts are very rare and should be characterized accurately for proper treatment and for predicting prognosis. The Bosniak classification is commonly used in the evaluation of renal cysts using either dynamic contrast enhanced (DCE) computed tomography (CT) or magnetic resonance imaging (MRI). The depiction of enhancing solid component or septa is critical for determining the malignancy. However, the Bosniak classification is based on visual assessment of enhancement after contrast material administration, and quantitative parameters are not included.[2]

Diffusion-weighted imaging (DWI), which relies on the random motion of free water molecules, has been widely used for the early diagnosis of acute cerebrovascular ischemia, hematoma, abscess, and the characterization of neoplastic masses.[3] Recently, DWI has become more familiar and has gained a definitive role in the evaluation of abdominal malignancy in lymph nodes, and renal, liver, pancreas, prostate masses.[4] Although recent studies implied that apparent diffusion coefficient (ADC) values derived from DWI could be used for the characterization of solid renal masses, the data about the value of DWI for discriminating malignancy in cystic renal masses are inadequate.[5-9] Here, our objective was to introduce the diagnostic performance of ADC measurements to differentiate malignant from benign renal cysts. For this purpose, Bosniak category 2F, 3, and 4 renal cysts that had malignant potential were evaluated.

Methods

The institutional review board approved a retrospective review of clinical and imaging data and waiving the need for the informed consent.

Patients

The MRI database in our institution was searched for patients who underwent abdominal DCE-MRI, including DWI, to characterize complex renal cystic masses between January 2012 and March 2015. Keywords used to search the radiology information system included: renal cyst, renal cell carcinoma, Bosniak, and renal mass. Patients with Bosniak

category 2F and above cysts were included in the study.[10,11] Small cysts (<1 cm) were excluded from the study due to difficult assessment and to prevent inconsistent measurements on ADC maps and renal cysts that have high signal on T1-weighted images (WI) due to hemorrhagic or high-protein content, which causes very low signal on ADC maps. Also, Bosniak category 1 and 2 renal cysts that have no diagnostic difficulty, Bosniak category 3 and 4 cysts that have no histopathological diagnosis, and Bosniak category 2F cysts without at least two-year followup MRI were excluded. The renal cysts were classified as benign or malignant based on followup imaging or histopathological findings. We summarized the election process of the study and the final diagnosis of the included patients in Fig. 1.

Magnetic resonance imaging protocol

All images were obtained from a 1.5-T MRI system (General Electric, Signa HDxt 1.5 T GE Medical Healthcare, Milwaukee, WI, U.S.) with a 16-channel phased array body coil. T1-WI were obtained before and after administration of an intravenous bolus of 0.1 mmol/kg of gadoteric acid (Dotarem, Guerbet, Roissy, France) at 25, 45, 90, 120, and 180 seconds. Single shot echo planar sequences on the axial plane and tridirectional gradients with breath-hold technique and at two b values (b=0 and 800 s/mm^2) were used for DWI. MRI parameters are summarized in Table 1. ADC maps were generated from DWI using a commercially available software-workstation system (Functool ver. 5x2.1.06, GE Medical Health Care).

Diagnostic criteria

Followup imaging for Bosniak category 2F lesions was performed with the same MRI protocol and cysts were accepted as benign if there was no difference in morphology and no progression in size and contrast enhancement on followup imaging for at least two years. Histopathological diagnosis after surgery was accepted as a reference test for Bosniak category 3 and 4 cysts. The histopathological slides of all tumours stained with hematoxylin-eosin and tumour fragments fixed in paraffin were obtained from the pathology archive and were reviewed under a fluorescence microscope (OlympusBX51-P, polarizing microscope, Olympus Corporation, Tokyo, Japan) retrospectively by the one pathologist with 10 years of experience in urological pathology. Two tumour grading classifications were used in the histopathological analysis (World Health Organization [WHO]/International Society of Urological

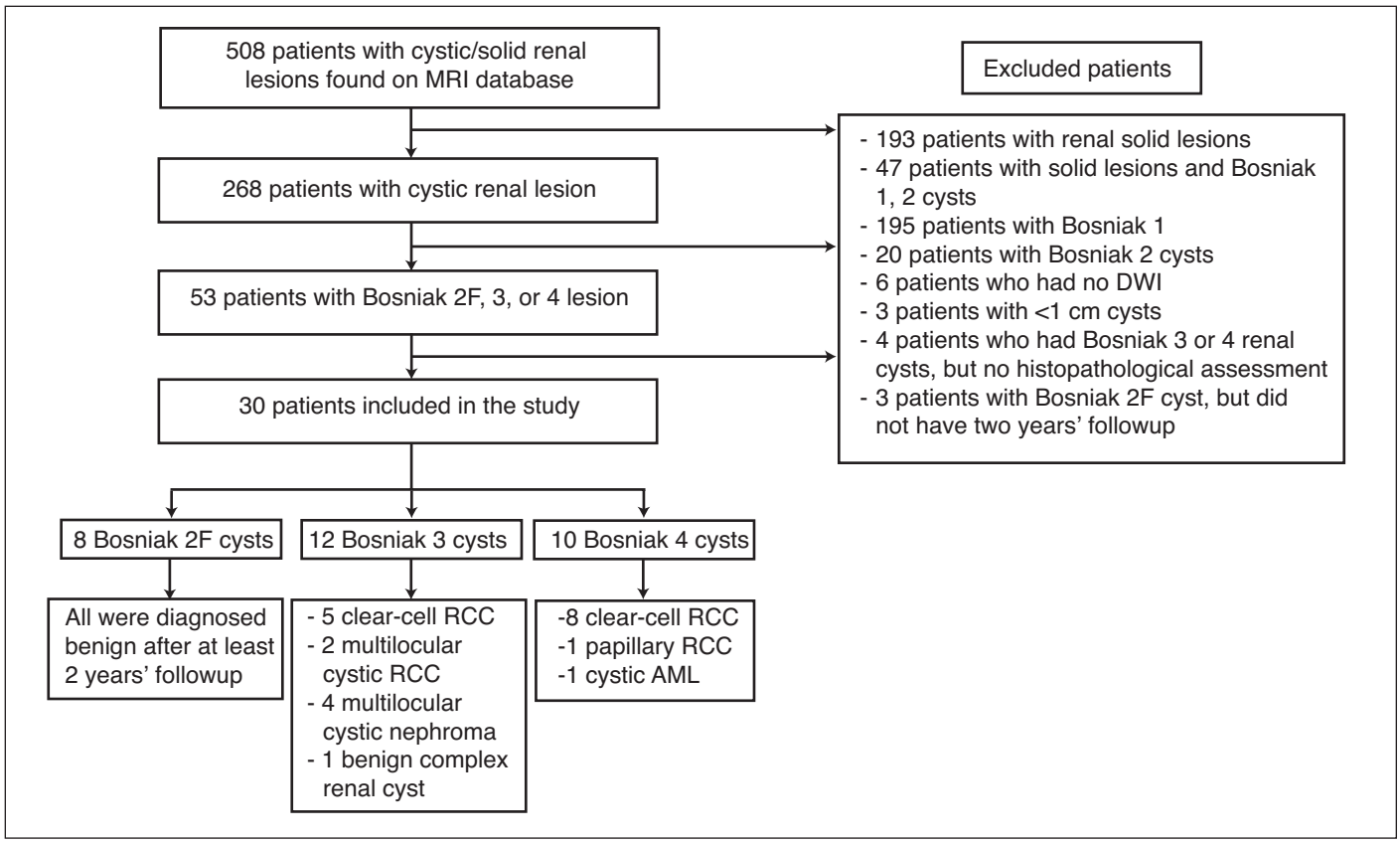

Fig. 1. Diagram of the patient selection in MRI database. AML: angiomyolipoma; DWI: diffusion weighted imaging; MRI: magnetic resonance imaging; RCC: renal cell carcinoma.

Table 1. MR imaging protocol

	T1 FSPGR DE	T2 SS-FSE	DCE 3D GE	DWI (EPI)
Plane	Axial	Axial and coronal	Axial and coronal	Axial
Fat suppression	Chemical shift	+/-	+	+
Time to repeat (msec)	140	17143	6.1	12000
Time to echo (msec)	4.3/2.1	121	3.1	67.2
Flip angle (°)	85	90	12	90
Slice thickness (mm)	6	6	4.8	6
Slice gap	1	1	2.4	1
FOV (mm)	400 x 400	400 x 400	400 x 320	400 x 400
Matrix (mm × mm)	320 x 192	256 x 256	288 x 224	96 x 128
Time of dynamic phases (sec)			0, 25, 45, 90, 120, 180	
NEX	1	1.5	0.7	2
b value (sec/mm^2)				0–800

DCE 3D GE: dynamic contrast-enhanced 3D gradient echo sequence; DWI: diffusion weighted imaging; EPI: echo planar imaging; FOV: field of view; FSPGR DE: fast-spoiled gradient-echo dual echo (in and opposed phase); NEX: number of excitations; SS FSE: single-shot fast-spin echo.

Pathology [ISUP] 2004 grading system for the evaluation of the tumour and the Fuhrman grading system for nuclear grading of tumour cells).[12]

Image analysis

One of the observers searched the MRI database. Patients meeting the inclusion criteria were evaluated by another two observers blinded to the final diagnosis of the cysts. Cysts were categorized as Bosniak category 2F, 3, or 4 according to MRI findings on T2-WI and contrast enhanced fat-suppressed T1-WI. Region of interest (ROI) placement and measurements on ADC maps were made by consensus of observers (Figs. 2 and 3). The largest ROI covering the entire lesion and excluding the normal renal parenchyma and perirenal tissues was placed to measure mean ADC values for

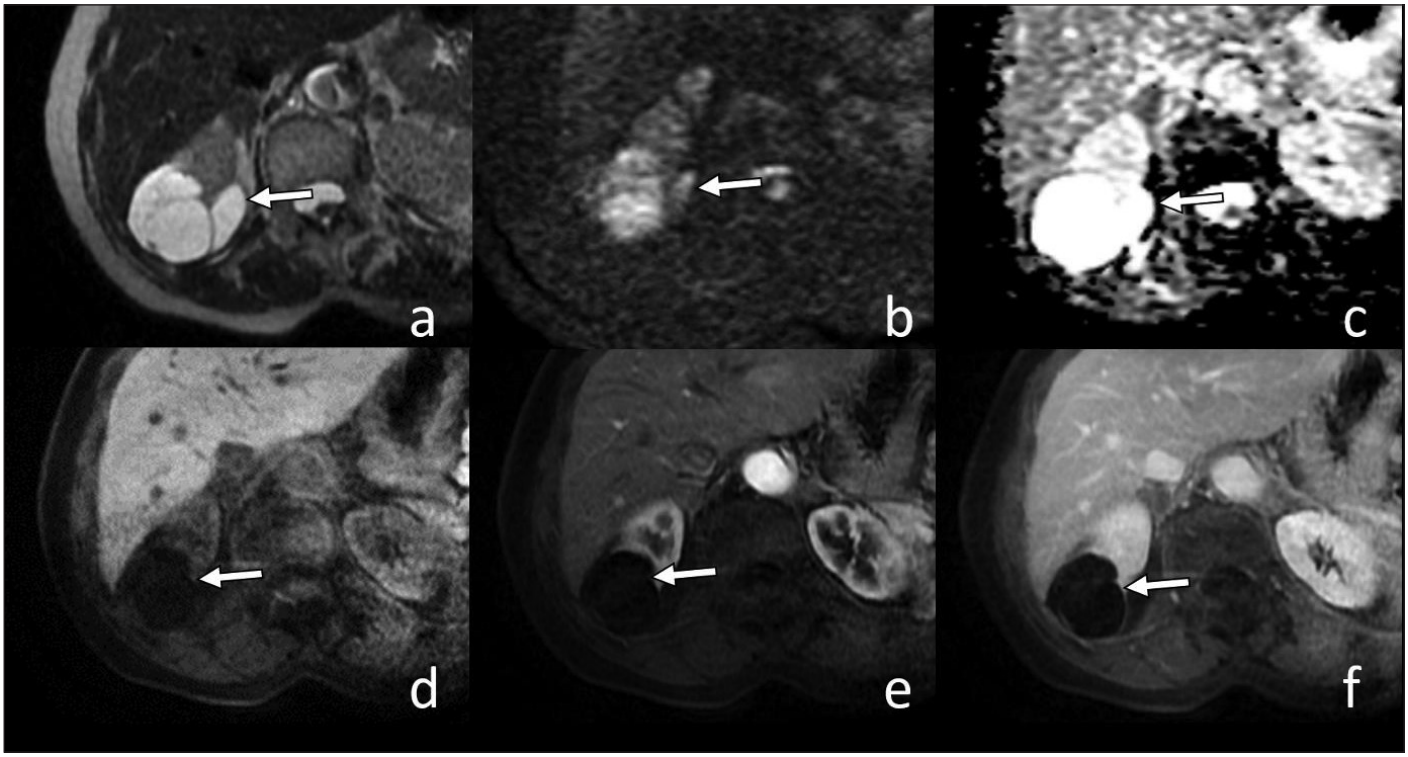

Fig. 2. Magnetic resonance image of a complex cyst of the right kidney. ***(a)*** Hyperintense fluid content of the cyst and a few slightly thick septa within the cyst were observed on T2-weighted image (WI); ***(b,c)*** the cyst had a high signal on both diffusion-weighted imaging and apparent diffusion coefficient map; ***(d)*** precontrast and post-contrast T1-WI obtained in ***(e)*** corticomedullary and ***(f)*** nephrogram phases exhibit slight enhancement on the posterior wall and septation of the cyst. Solid component and measurable enhancement were not identified. The cyst was categorized as Bosniak category 2F.

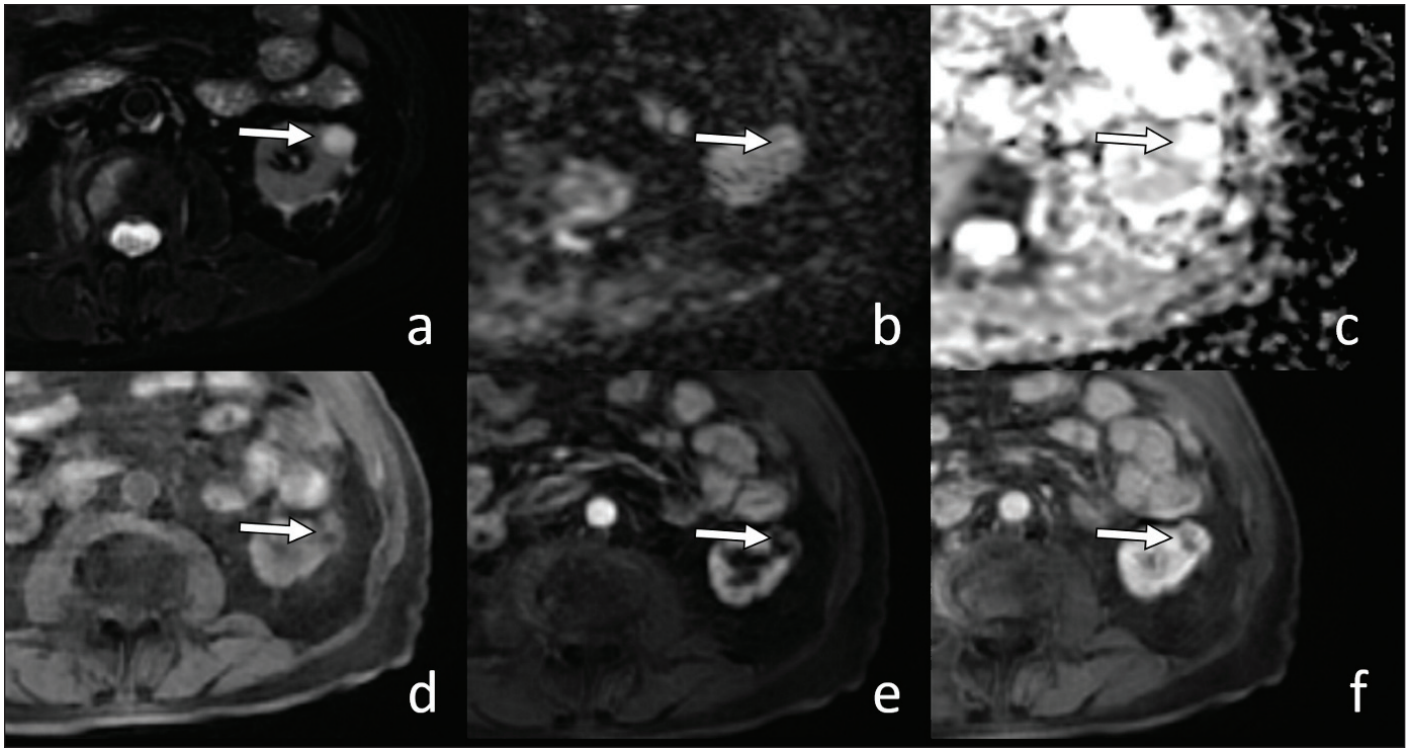

Fig. 3. A small cystic renal cell carcinoma on the left kidney. ***(a)*** The lesion had a high signal on fat-suppressed T2-weighted image; ***(b)*** isointense signal on diffusion-weighted imaging; and ***(c)*** hyperintense signal on apparent diffusion coefficient were observed; ***(d, e, f)*** significant contrast enhancement of the solid component of the cyst was observed. Findings were compatible with Bosniak category 4.

each cyst (Fig. 4). Post-contrast T1-WI were used for orientation and optimal anatomic placement of the ROIs on ADC maps and the mean value of three ROIs were recorded.

Statistical analysis

Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software

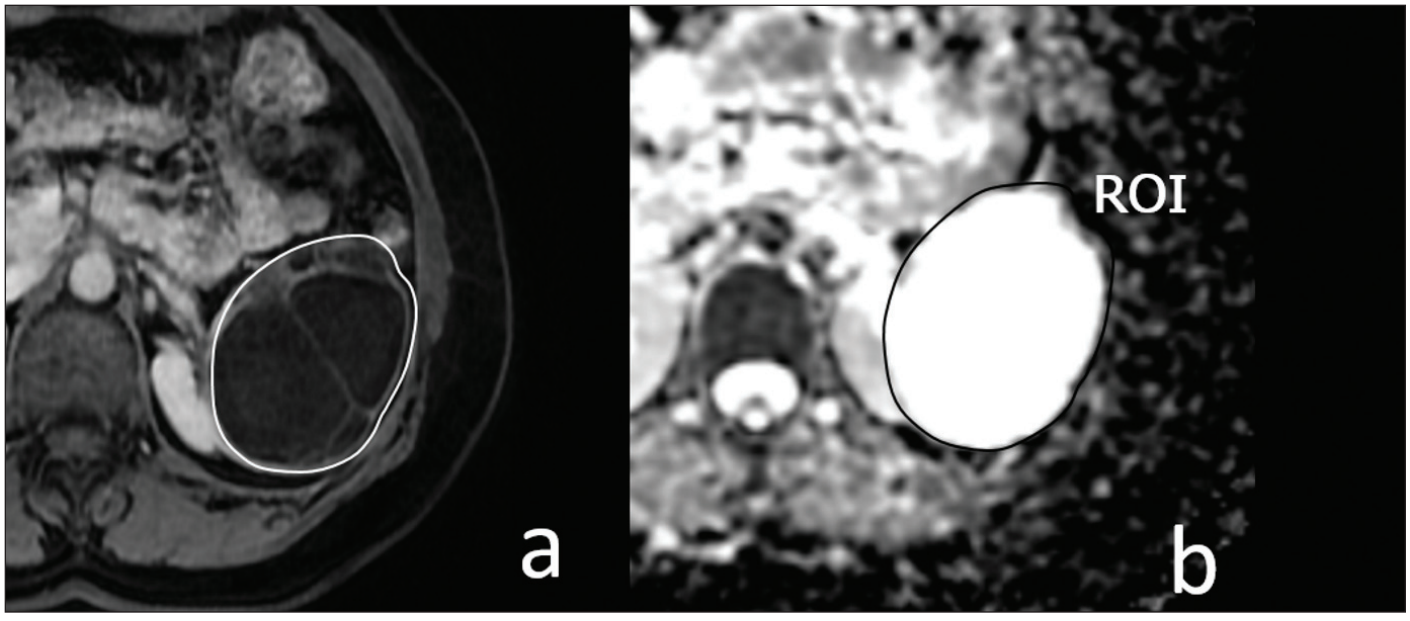

Fig. 4. A demonstration of region of interest (ROI) replacements on a Bosniak category 3 renal cyst on images of ***(a)*** nephrogram phase and ***(b)*** apparent diffusion coefficient (ADC) map were demonstrated. The largest ROI, including the entire cyst but not including the adjacent tissue and renal parenchyma, was replaced. ROI measurements were obtained from ADC maps and the mean value of three measurements was calculated.

(Utah, U.S.) programs were used for statistical analyses. Descriptive data were provided for continuous variables. Shapiro-Wilk's test was used to search the normality of ADC values and showed skewed distribution. Non-parametric statistical method (Mann-Whitney U test, Kruskal-Wallis test) was used for comparing mean ADC values. Receiver operating characteristic (ROC) analysis was used to determine an optimal cutoff value for significantly different quantitative data indicating malignancy. Statistical significance was set at $p<0.05$.

Results

Eight Bosniak category 2F, 12 Bosniak category 3, and 10 Bosniak category 4 cysts fitting the inclusion criteria were found and included in the study (Fig. 1). Among these patients, 18 (60%) were male, and 12 (40%) were female. Seven patients had an additional cyst that was categorized as Bosniak category 1 and these cysts were not included. The mean patient age was 59.23 ± 12.08 years (range 38–83). Patient data according to Bosniak classification are summarized in Table 2.

All of the Bosniak category 2F cysts were diagnosed as benign after at least a two-year followup because no radiological progression was observed. Bosniak category 3 and 4 cysts were diagnosed according to histopathological assessment after surgery. Out of 12 Bosniak category 3 cysts, seven cysts were malignant and five were benign. Histopathological diagnosis of these cysts was clear-cell renal cell carcinoma (cRCC) in five patients, multilocular cystic RCC in two patients, multilocular cystic nephroma (MCN) in four patients, and benign complex renal cyst in one patient. Nine of the 10 Bosniak category 4 cysts were malignant. Eight patients were diagnosed with cRCC, one patient with papillary RCC, and one patient with cystic angiomyolipoma in Bosniak category 4 after histopathological assessment (Fig. 1). In total, fourteen benign cysts (46.7%) and sixteen malignant cysts (53.3%) were evaluated in the study.

The mean ADC value was 2.75 ± 0.43 $x10^{-6}$ mm^2/s for Bosniak category 2F cysts, 2.34 ± 0.35 $x10^{-6}$ mm^2/s for Bosniak category 3 cysts, and 2.29 ± 0.54 $x10^{-6}$ mm^2/s for Bosniak category 4 cysts. Lower ADC values were obtained with higher Bosniak categories, but the difference was not statistically significant (p=0.075).

The mean ADC values of malignant renal cysts were significantly different from the benign renal cysts (2.72 ± 0.35 $x10^{-6}$ mm^2/s and 2.18 ± 0.43 $x10^{-6}$ mm^2/s, retrospectively; p=0.001). A cutoff value of ≤2.28 $x10^{-6}$ mm^2/s for mean ADC gave 75% specificity and 92.86% sensitivity. We summarized the ROC analysis for ADC values in Table 3.

Cysts that had histopathological results were evaluated and among 12 Bosniak category 3 and 10 Bosniak category 4 cysts, there was a significant difference between malignant and benign cysts (p=0.006).

In the comparison of the mean ADC values of malignant and benign Bosniak category 3 cysts, a significant difference was found between subgroups (p=0.007). The comparison of benign and malignant Bosniak category 2F lesions and Bosniak category 4 lesions could not be performed since there was an insufficient number of malignant Bosniak category 2F and benign Bosniak category 4 cysts to be evaluated.

Discussion

Ultrasonography (US), CT, and MRI are the most favoured tools for defining renal tumours.[13,14] After a first-line evaluation with US, DCE-MRI or CT can be preferred for further assessment. Evaluation of contrast enhancement on a calcified renal lesion on CT is insufficient due to high density, and MRI can be problem-solving for such lesions.[13,15] Recent studies showed that MRI is more favourable than CT because of improved soft tissue contrast resolution, avoidance of ionizing radiation, and the use of functional imaging techniques, such as diffusion and perfusion imaging.[13,15,16] In addition to conventional abdominal MRI sequences, DWI is part of abdominal MRI protocol in most centres and may have a role in the differentiation of malignant and benign renal masses.[14,17] In our centre, MRI is the preferred method for evaluation of renal cysts and DWI is routinely used in abdominal imaging as well. We found in our study that ADC is convenient for the assessment of malignant renal cysts.

While there are many reliable tools for the evaluation of solid renal tumours, many questions in the assessment of cystic renal lesions still exist. It is known that less than 5% of RCCs are cystic. It is important to assess renal cysts carefully to decide on surgery.[13,18] The Bosniak classification, used with CT or MRI, has solved this problem almost entirely by forming a communication between radiologists and urologists;[10,13] however, there are still unsolved issues.

Table 2. Descriptive data of renal cysts according to Bosniak classification

	Bosniak category 2F (n=8)	Bosniak category 3 (n=12)	Bosniak category 4 (n=10)	Total (n=30)
Age (year)	65.63 ± 11.19	54.42 ± 11.13	59.9 ± 12.4	59.23 ± 12.08
Size (mm)	47.63 ± 26.43	63.17 ± 35.65	42.3 ± 20.85	52.07 ± 29.58
Mean ADC (mm^2/s)	2.75 ± 0.43	2.34 ± 0.35	2.29 ± 0.54	2.43 ± 0.47
Malignancy (%)	0	58.33	90	53.33

ADC: apparent diffusion coefficient.

Table 3. Comparison of ADC value for differentiating malignancy in a cystic renal mass

Parameters	ADC	p
AUC (CI)	0.857 (0.681–0.957)	0.001
Optimal cutoff	≤2.28 x10-6 mm²/s	
Sensitivity (% CI)	75 (47.6–92.7)	
Specificity (% CI)	92.86 (66.1–99.8)	
PPV (% CI)	91.30 (83.22–95.69)	
NPV (% CI)	78.78 (70.56–85.19)	
(+) likelihood ratio (CI)	10.5 (1.6–70.9)	
(-) likelihood ratio (CI)	0.27 (0.1–0.6)	
Accuracy (%)	83.93	

ADC: apparent diffusion coefficient; AUC: area under the curve; CI: confidence interval; DWI: diffusion-weighted imaging; NPV: negative predictive value; PPV: positive predictive value.

Benign renal cysts categorized as Bosniak category 3 and 4, treated surgically due to insufficient preoperative diagnosis, which causes unnecessary interventions. Additionally, some studies have shown incompatible interobserver agreement in the Bosniak classification, particularly for Bosniak category 2F and 3 cysts.[19-22] At this point, advanced diagnostic methods are needed in making precise judgments about cystic renal lesions.

DWI is now widely used as a diagnostic method for intra-abdominal lesions, such as malignancies, abscesses, and hematomas. Recent studies showed that DWI also supplies propitious knowledge for the differentiation of malignant and benign solid and cystic renal masses.[8] Goyal et al revealed that DWI is a reliable method to distinguish pseudotumours from RCCs in patients with chronic kidney disease. They claim that pseudotumours of the kidney do not show restricted diffusion, in contrast to RCC.[23] Another study performed by Zhang et al showed that benign cystic lesions had higher ADC values than malignant cystic lesions, but this was not statistically significant.[9]

A study carried out by Inci et al showed a significant difference in ADC values between Bosniak category 1, 2, and 3 cysts at a b factor of 1000 s/mm²; however, cysts were not grouped according to histopathological results in this study.[8] Hence, it is not helpful for verification of ADC values in the differentiation of malignancy ratio in renal cysts. We did not include Bosniak category 1 and 2 cysts in our study because it is known that these cysts are benign and do not need further evaluation, followup, or treatment.[8] Diffusion restriction in a renal cyst represents high cellularity, hemorrhagic or high protein content of the cyst. In Bosniak category 1 and 2 cysts, cellularity is not expected because they do not include septation or a solid component that forms a cellular part of the cysts. They may have low ADC values due to hemorrhage or high protein content, and they may cause false-positive results. Additionally, these cysts do not have a histopathological diagnosis, nor followup imaging in our archive to establish whether they are benign or malignant. For these reasons, unlike the study of Inci et al, we did not evaluate Bosniak category 1 and 2 cysts.

Even though Bosniak category 2F cysts had no histopathological diagnosis, they were included in the study since these cysts have malignant potential that has to be evaluated with followup imaging. Surgery is not suggested for treatment of these cysts, so we included Bosniak category 2F cysts that had at least a two-year followup. It is known that approximately 10% of Bosniak category 2F cysts have progression in followup.[24] Eight Bosniak category 2F cysts included in our study had no progress. Between the malignant and benign cysts, we found statistically significant differences between subgroups.

We also evaluated the Bosniak category 3 and 4 cysts for which we had a histopathological diagnosis and found that mean ADC values were different between the subgroups. Moreover, between benign and malignant Bosniak category 3 cysts, we encountered a similar result, which was statistically significant. We also compared the mean ADC values of Bosniak category 2F, 3, and 4 cysts, and found higher mean ADC values of Bosniak category 2F and 3 cysts compared to Bosniak category 4 cysts; however, this difference was not significant.

In another study performed by Goyal et al, ADC values of renal abscess and cystic renal cell carcinomas was evaluated and they found that while both renal abscess and cystic renal cell carcinomas have lower ADC values compared to normal renal parenchyma, abscesses had significantly lower ADC values than cystic renal cell carcinomas.[25] Additionally, cystic RCC has higher ADC values in contrast to renal abscess, which has a fluid component with very low ADC values.[7]

Our study had some limitations. The first one is that the series in our study was retrospective and this may have caused bias in patient selection. Secondly, the number of benign-malignant renal cysts was relatively small. Thus, we could not compare the malignant and benign Bosniak category 2F and 4 cysts. Lastly, all Bosniak category 2F lesions had only two years' followup, which may not exclude the possibility of slow-growing RCC.

Conclusion

DWI can predict malignancy in cystic renal masses when used together with conventional MRI sequences and can be helpful in decision-making for management of the disease.

Competing interests: The authors report no competing personal or financial interests.

This paper has been peer-reviewed.

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