RESEARCH ARTICLE

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Relationship Between Apparent Diffusion Coefficient and Histologic Grading in Renal Cell Carcinoma *,**

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Objective: Renal cell carcinoma (RCC) is the most common malignant lesion of the kidney. The Fuhrman nuclear grading system is the most widely used system for RCC as an independent predictor of prognosis. In terms of survival, it divided patients into a group with a good prognosis (Grade 1), a group with a poor prognosis (Grade 4) and a group with a prognosis between these two groups (Grades 2 and 3). MRI is the only method currently used to assess the molecular diffusion process in vivo. The aim of this study was to evaluate the relationship between apparent diffusion coefficient (ADC) values and Fuhrman nuclear grading and to investigate whether ADC values can contribute to preoperative prognosis.

Materials and Methods: In this study, we evaluated 30 patients diagnosed with RCC in the Department of Pathology of our hospital who had diffusion weighted magnetic resonance images (DW-MRI) obtained with preoperative b 1000 gradient values. Measurements were made on ADC maps.

Results: Nine of the cases were classified as Grade 1, 11 as Grade 2 and 10 as Grade 3. Mean ADC values according to nuclear grade were $1.68\pm0.64x10^{-3}$ sec/mm^2, $1.16\pm0.20x10^{-3}$ sec/mm^2, $1.35\pm0.45x10^{-3}$ sec/mm^2 for Grade 1-3 respectively. When mean ADC values were compared according to nuclear grades, a statistically significant difference was observed between grades 1 and 2 ($p<0.05$). No significant difference was observed between the other groups ($p>0.05$).

Conclusion: In this study, it was concluded that ADC values may be partially useful in the grading of RCC cases and may contribute to preoperative prognostic evaluation

Key Words: *Apparent diffusion coefficient, diffusion weighted magnetic resonance imaging, fuhrman nuclear grading sistem, renal cell carcinoma*

Böbrek Hücreli Kanserde Görünür Difüzyon Katsayısının Histolojik Derece ile İlişkisi

Amaç: Böbrek hücreli karsinom (RCC) böbreğin en sık görülen malign lezyonudur. Fuhrman nükleer derecelendirme sistemi, prognozun bağımsız bir belirleyicisi olarak RCC için en yaygın kullanılan sistemdir. Sağkalım açısından hastaları iyi prognozlu bir gruba (Grade 1), kötü prognozlu bir gruba (Grade 4) ve bu iki grup arasında bir prognoza sahip bir gruba (Grade 2 ve 3) ayırmıştır. MRG şu anda in vivo moleküler difüzyon sürecini değerlendirmek için kullanılan tek yöntemdir. Bu çalışmanın amacı, görünür difüzyon katsayısı (ADC) değerleri ile Fuhrman nükleer derecelendirmesi arasındaki ilişkiyi değerlendirmek ve ADC değerlerinin preoperatif prognoza katkıda bulunup bulunamayacağını araştırmaktır.

Gereç ve Yöntem: Bu çalışmada Patoloji Anabilim Dalı'nda RCC tanısı alan ve preoperatif b1000 gradient değerleri ile elde edilmiş difüzyon ağırlıklı manyetik rezonans görüntüleri (DW-MRI) olan 30 hasta değerlendirildi. Ölçümler ADC haritaları üzerinde yapıldı.

Bulgular: Olguların dokuzu Grade 1, 11'i Grade 2 ve 10'u Grade 3 olarak sınıflandırıldı. Nükleer dereceye göre ortalama ADC değerleri Grade 1-3 için sırasıyla 1.68±0.64x10-3 sn/mm^2, 1.16±0.20x10-3 sn/mm^2, 1.35±0.45x10-3 sn/mm^2 idi. Ortalama ADC değerleri nükleer derecelere göre karşılaştırıldığında, derece 1 ve 2 arasında istatistiksel olarak anlamlı bir fark gözlenmiştir ($p<0.05$). Diğer gruplar arasında anlamlı bir fark gözlenmedi ($p>0.05$).

Sonuç: Bu çalışmada, ADC değerlerinin RCC olgularının derecelendirilmesinde kısmen yararlı olabileceği ve preoperatif prognostik değerlendirmeye katkıda bulunabileceği sonucuna varıldı.

Anahtar Kelimeler*: Difüzyon ağırlıklı manyetik rezonans görüntüleme, görünür difüzyon katsayısı, fuhrman nükleer derecelendirme sistemi, renal hücreli karsinom*

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Introduction

Renal cell carcinoma (RCC) accounts for 2-3% of adult renal malignancies (1). The incidence of RCC has been gradually increasing over the years. This is attributed to the increasing number of incidentally diagnosed cases of RCC due to the increasing use of imaging modalities such as ultrasonography (US) and computed tomography (CT) (2). Currently, more than 50% of RCC cases are diagnosed incidentally (3). In addition, the rate of diagnosed advanced stage RCC has been decreasing over the years (2). Therefore, it can be said that the actual incidence of RCC has increased over the years

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due to reasons such as environmental factors. There is male gender predominance with a ratio of 3:2 in the incidence of RCC. On average, 20-30% of cases are metastatic at the time of diagnosis (4). 40% of patients die due to RCC (5).

Factors affecting prognosis in RCC can be classified as anatomical, histologic, clinical and molecular (4). Histological factors include histological subgroup, Fuhrman grade, presence of sarcoma-like findings, small vessel invasion, tumour necrosis and collecting system invasion. Fuhrman nuclear grade (FNG) is the most commonly used histologic grading system in RCC (6). Tsui et al. (7) found the five-year cancer-specific survival for grades 1, 2-3 and 4 to be 89%, 65% and 46%, respectively. Although the Fuhrman system shows discrepancies in self-assessment and inter-observer assessment, it still has value as an independent prognostic factor (8).

Diffusion-weighted MRI is a technique based on Brownian motion of water, does not require contrast material and has a short acquisition time. There is an increasing use of MRI in the evaluation of renal lesions. Some studies have investigated the usefulness of ADC in differentiating between benign and malignant renal lesions and in determining subtypes of RCC and have reported that ADC values are useful in differentiating between benign and malignant renal tumours and in determining subtypes (9).

In our study, we compared FNG, which is an independent indicator of prognosis, with ADC values of RCC and investigated the relationship between ADC values and grading and its prognostic significance.

Materials and Methods

Research and Publication Ethics: Since our study, which was approved by the Ethics Committee of Fırat University Faculty of Medicine, was retrospective, no consent form was organised.

Working Group: In our study, we retrospectively reviewed the patients who underwent radiologic imaging with various prediagnoses in the clinics and outpatient clinics of Fırat University Hospital between June 2011 and July 2013 and who were diagnosed with renal mass radiologically and diagnosed with RCC histopathologically by operation or biopsy. 75 cases were identified and 44 of them had preoperative MR imaging.

Cases with poor image quality or artifacts and cases in which biopsy was performed immediately before MRI were excluded. Thirty patients who met the eligibility criteria were included in the study.

Diffusion Weighted Magnetic Resonance Imaging: For magnetic resonance imaging, a 1.5 T (Signa Hi-speed, GE Medical Systems, Milwaukee, Wis) superconductive device was used in the MRI unit of the Radiology Department of Fırat University Hospital. Patients were prepared in supine position with the kidney levels in the centre of the 4-channel coil. The patients were informed about the points to be followed, and communication was established with the patients through an MRI compatible headset system during the examination. No sedation was applied to the patients during the acquisition. Since ADC values are more significant at higher b values, b1000 values were used. T2W fast spin echo, contrast enhanced T1W fast spin echo and DW (b=1000 sec/mm²) echo planar magnetic resonance images were included in the study.

Analysis of Images: Measurements were performed on the workstation with DICOM open image analysis program (Osirix, v. 3.9). During the analysis of the images, simple liver cyst in 6 cases, hemangioma in the liver in 2 cases, simple cyst in the spleen in 1 case, bilateral renal angiomyolipoma in 1 case, stones in the same kidney as the lesion in 1 case, In 9 cases bilateral bosniac type I cysts, in 2 cases hemorrhagic cyst in the same kidney as the lesion, in 1 case bosniac type II cyst in the contralateral kidney, in 2 cases in the same kidney, in 3 cases bosniac type I cysts in the contralateral kidney were detected. Color ADC maps were generated by the device on diffusion weighted images.

ADC measurements were performed using T2-W and contrast-enhanced images. ADC measurements were performed with a region of interest (ROI) standardised to 100 mm^2 and mean values were calculated. Cystic, hemorrhagic and necrotic areas were not measured. Whenever possible, measurements were made from solid areas. For masses below 3 cm, a single measurement was made and for masses above 3 cm, 3 separate measurements were made from different sections and the mean ADC value was used in calculations.

Measurements were also made from the normal renal parenchyma of each patient. Calculations were performed with ROIs placed at the anterior, middle and posterior levels in the section passing through the hilus level of the kidney.

Statistical Analysis: Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 15.0 for Windows). Mean ± standard deviation, median (minimum – maximum), frequency and percentage values were used in the descriptive statistics of the data. The compliance of the variables with normal distribution was evaluated with the Kolmogorov Smirnov test.for each case, b1000 values calculated from renal mass and normal renal parenchyma were entered into the programme. T-test was applied to compare two groups and one-way analysis of variance to compare multiple groups. Tukey test was used to determine the differences between groups. The significance level for all analyzes was $p<0.05$.

Results

We included 30 cases with a histopathologic diagnosis of RCC who underwent preoperative MR imaging in the Department of Pathology of our hospital between 2011 and 2013.

Histopathologic preparations were re-evaluated by a pathologist and classified according to the Fuhrman system. Nine cases were grade 1 (G1), 11 cases were grade 2 (G2), and 10 cases were grade 3 (G3). No Grade 4 (G4) case was encountered.

Eighteen of the patients were male and 12 were female. The mean ages were 55.05±16.54 years (27-82 years) and 58.83±15.32 years (30-75 years) for men and women, respectively.

The mean tumor diameter in the study was 6.06±3.07 cm (2-14 cm) and the mean tumor diameters for G1, G2 and G3 were 4.44 cm, 6.63 cm and 6.9 cm, respectively. A decrease in ADC was observed with increasing tumour diameter. However, this was not statistically. As the diameter of the tumour increased, the nuclear grade also increased, but this did not reach statistical significance.

There were 19 right kidney lesions and 11 left kidney lesions. Total nephrectomy was performed in 23 cases, partial nephrectomy in 2 cases and tru-cut needle biopsy was performed in 5 cases. The mean tumor diameter was 2.5 cm in partial nephrectomy cases and 5.8 cm in total nephrectomy cases.

Eighty percent (n= 24) of the cases were diagnosed as clear cell RCC (ccRCC), 13.4% (n= 4) as chromophobe RCC (crRCC) and 6.6% (n= 2) as papillary RCC (pRCC).

When the groups were classified according to their histologic subtypes, 33% of ccRCC were G1, 33% were G2, 33% were G3, 25% of crRCC were G1, 50% were G2, 25% were G3, 50% of pRCC were G2 and 50% were G3.

Median ADCs for ccRCC were significantly higher than those for other histological types. Furthermore, there was statistically significant difference between mean ADC values for each subtype (p=0.032). The mean ADC values ($x10^{-3}$ sec/mm^2) and standard deviations of histologic subtypes are shown in Table 1.

ADC measurements of clear cell and non-clear cell RCCs (nccRCC) were compared. The mean ADC value was higher in ccRCC and the difference was statistically significant (p= 0.01). The mean ADC values and standard deviations of clear cell and nccRCCs are shown in Table 2.

When the mean ADC values of the groups were examined, it was found as $1.68±0.64x10^{-3}$ s/mm^2 for G1, $1.16±0.20x10^{-3}$ s/mm^2 for G2, and $1.35±0.45x10^{-3}$ s/mm^2 for G3 (Table 3, Figure 1-3).

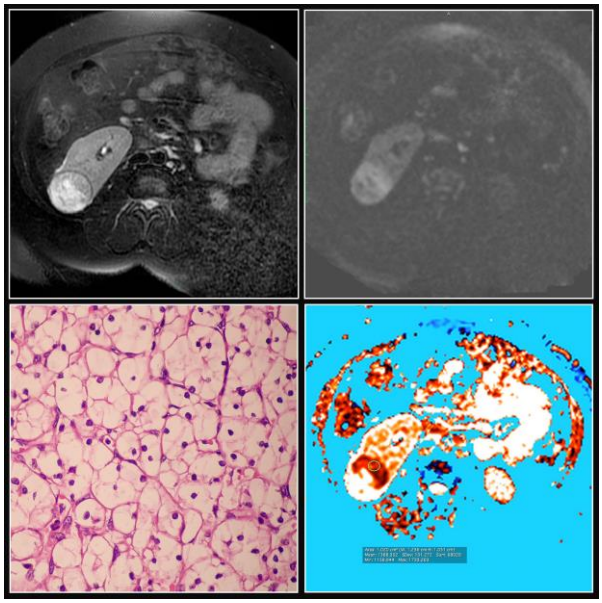

Figure 1. Grade 1 ccRCC. (A) axial T2 MRI, (B) diffusion MRI, (C) histopathologic image (H&E, X400) and (D) ADC map of the same case

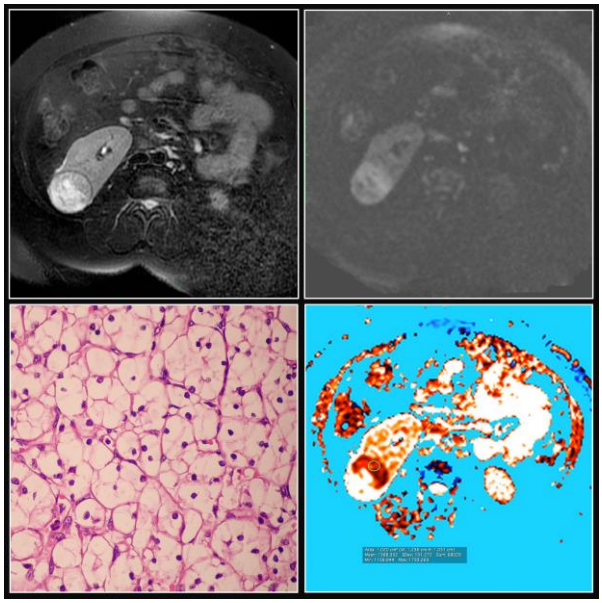

Figure 2. Grade 1 ccRCC. (A) axial T2 MRI, (B) diffusion MRI, (C) histopathologic image (H&E, X400) and (D) ADC map of the same case.

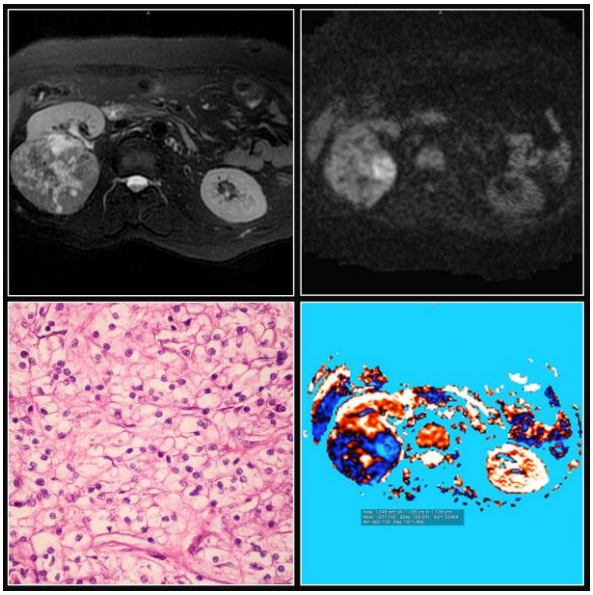

Figure 3. Grade 2 ccRCC. (A) axial T2 MRI, (B) diffusion MRI, (C) histopathologic image (H&E, X400) and (D) ADC map of the same case.

Parenchymal ADC values of the opposite normal kidney were analysed. It was calculated as $2.22\pm0.24x10^{-3}$ sec/mm^2 for G1, $2.01\pm0.28x10^{-3}$ sec/mm^2 for G2, and $2.09\pm0.18x10^{-3}$ sec/mm^2 for G3. No statistically significant difference was observed between the groups.

When compared with normal renal parenchymal ADC values ($2.10\pm0.25x10^{-3}$ s/mm^2), the mean ADC values of RCC cases ($1.38\pm0.48x10^{-3}$ s/mm^2) were statistically significantly lower (p=0.002) (Table 4).

There was a significant difference between G1 and G2 when comparing the mean ADC values (p<0.05). Between G1 and G3 and between G2 and G3, there was no statistically significant difference (p>0.05) in the mean ADC values (Table 3).

When pathologic and normal renal parenchymal ADC values were compared for each group, statistically significant decreases were observed.

Table 1. ADC values of RCC histologic subtypes

	n	Minimum ADC Value ($x10^{-3}$ sec/mm^2)	Maximum ADC Value ($x10^{-3}$ sec/mm^2)	Average ADC Value ($x10^{-3}$ sec/mm^2)	Standard Deviation ($x10^{-3}$ sec/mm^2)
ccRCC	24	0.74	2.46	1.49	0.47
crRCC	4	0.79	1.20	1.02	0.17
pRCC	2	0.74	0.78	0.76	0.03

cc: clear cell, cr: chromophobe, p: papillary

Table 2. Comparison of ADC values of clear cell and non-clear cell RCCs

	n	Average ADC Value ($x10^{-3}$ sec/mm^2)	Standard Deviation ($x10^{-3}$ sec/mm^2)	p <0.05
Clear Cell	24	1.49	0.47	0.01
Non Clear Cell	6	0.94	0.18	

Table 3. ADC values of patients according to grades in RCC. Comparison of mean ADC values according to the grades of RCC.

	n	Minimum ADC Value ($x10^{-3}$ sec/mm^2)	Maximum ADC Value ($x10^{-3}$ sec/mm^2)	Average ADC Value ($x10^{-3}$ sec/mm^2)	Standard Deviation ($x10^{-3}$ sec/mm^2)	Between ADC averages difference ($x10^{-3}$ sec/mm^2)	P<0.05
G1	9	0.74	2.46	1.68	0.64-0.20[a]		
G2	11	0.78	1.53	1.16	0.20-0.20[b]		
G3	1	0.74	2.08	1.35	0.45-0.19[c]		
G1-G2						0.51	0.049
G1-G3						0.32	0.280
G3-G2						0.18	0.633

G: Grade

a: G1-G2 Standard Deviation b: G1-G3 Standard Deviatio c: G3-G2 Standard Deviation

Table 4. Comparison of normal parenchymal ADC values with RCC ADC values

	n	Average ADC Value ($x10^{-3}$ sec/mm^2) (Normal)	Average ADC Value ($x10^{-3}$ sec/mm^2) (RCC)	P<0.05
G1	9	2.22±0.24	1.68±0.64	0.003
G2	11	2.01±0.28	1.16±0.20	0.485
G3	10	2.09±0.18	1.35±0.45	0.006
G1+G2+G3	30	2.10±0.25	1.38±0.48	0.002

Discussion

RCC, the most common malignant tumour of the kidney, consists of different subtypes (10). Malignant tumors of the kidney constitute approximately 2-3% of all malignant tumors and tumor-related deaths, with the highest incidence in developed countries. Male/female=2/1. RCC is a tumor of adulthood and accounts for 85% of all primary renal malignancies (11). It is frequently observed after the age of 40. Although its incidence is highest between 60-70 years of age, the mean age at which it is most common is 55 years. However, it can also be observed rarely in childhood (12, 13). An annual increase of approximately 2% is observed in the incidence of the disease worldwide and in Europe, while a decline has been observed in Denmark and Sweden for the last two decades (14). Diagnosis rates increase with developing imaging methods and this leads to a relative increase in incidence. However, it is thought that there is no change in the actual incidence of the tumor (13).

Various grading systems have been developed for RCC (15). Firstly, in 1971, Skinner et al. created a grading system evaluating only the shape of the nucleus (16). Fuhrman et al. made a new proposal in 1982 to classify RCC according to its nuclear grade. The best single indicator of postoperative metastasis is tumour stage and size. FNG, which later became the most widely recognised grading system for RCC, assuming the role of an independent predictor for prognosis with numerous additional studies. (6,17). In the Fuhrman study, he divided the patients into three groups based on survival: the good prognostic group (grade 1), the poor prognostic group (grade 4) and the group in between (grades 2 and 3) (18).

Most investigators report that nuclear grading has prognostic validity only in classical and pRCC (19).

However, the nuclear grading system has been adopted for the strongest ccRCC and is now applied for this type of tumour in the clinical setting (17).

In 2006, Rioux-Leclercq et al. (20) tested the accuracy of various Fuhrman grading schemes to predict survival due to RCC. As a result, the nuclear grading system was accepted as an independent predictor of survival in patients with RCC. FNG system should be taken into consideration when evaluating survival in RCC. However, no difference was observed between modified or traditional Fuhrman grading schemes.

Diffusion-weighted imaging is a functional MRI sequence whose image contrast is based on microscopic movements of water and can be obtained in a very short time using mainly echo planar imaging technique. This sequence does not require the use of contrast agents. In conventional MRI, the diffusion motion of water molecules in the tissue contributes very little to the magnetic resonance signal obtained. In DWI, on the other hand, the movement of water molecules in biological tissues can be measured by applying very strong magnetic field gradients to the area to be imaged. In this way, information can be obtained at the cellular level from the tissue under investigation and important contributions can be made to diagnosis and differential diagnosis by determining the signal characteristics of free or restricted water molecules that change with pathologies. In addition, the fact that it allows quantitative evaluation by ADC measurements is an important superiority over other methods (21-24).

Indeed, a strong correlation between ADC and grade has been shown in two tumors. These are gliomas and prostatic adenocarcinomas and tumor cellularity is an important determinant. ADC should be considered as a complex variable reflecting tissue characteristics as well as cellularity (17).

Magnetic resonance imaging is the only method available today for the assessment of molecular diffusion processes in vivo. The kidney is an organ of interest for ADC study due to its high blood flow rate and its role in water transport (25).

The basic scale defining diffusion sensitivity in diffusion-weighted imaging is the b value. It is known that examinations performed with a high b value (1000-1200 sec/mm^2) increase the sensitivity to diffusion by minimizing the T2 effect in tissues (26).

At high b values (800 or 1000 sec/mm^2), images are obtained with more signal loss from water molecules. Tissues with a high degree of diffusion restriction show bright signal areas in the images at high b values, and low signal intensity in the corresponding ADC map. Diffusion MRI can help to characterize renal lesions in a

non-invasive manner. In the characterisation of renal masses, diffusion MRI has a promising role to play. Solid RCC is a highly cellular tumour and usually has a high signal intensity compared to normal parenchyma on high b-value images. Conversely, benign cysts and low cellularity masses usually show low diffusion restriction and low signal intensity on high b-value images. However, RCC may have various diffusion MR appearances due to variable degree of cellularity, cystic change, necrosis and presence of hemorrhagic elements (27).

In addition, ADC was shown to correlate with cellular diversity in benign and malignant tissue. ADC may therefore play a role in predicting RCC grade. If this is confirmed, ADC may be effective in determining the most appropriate treatment option to use with pre-operative imaging in a given case (17).

Recent studies have revealed the potential of ADC in the assessment of various conditions such as pionephrosis, infection, renal ischaemia and diffuse renal disease. (25).

In a meta-analysis conducted by Lassel et al. in 2013, 17 studies with 764 patients were included and according to this study, ADC values of RCCs were significantly lower than normal parenchyma. Uroepithelial cancers could be differentiated with low ADC values. ADC values differed significantly between RCC and oncocytoma. It was concluded that ADC values may help to differentiate malignant and benign renal tumors and may reduce inappropriate nephrectomies by differentiating oncocytoma from malignant tumors (28).

In our study using high b (b 1000) values, the mean ADC values of RCCs ($1.38x10^{-3}$ sec/mm^2) were found to be lower than the mean ADC values of normal renal parenchyma ($2.10x10^{-3}$ sec/mm^2) in accordance with the literature (p=0.002).

In a study by Sasamori et al. (29) in 2014, 31 patients with renal mass underwent diffusion imaging with preoperative 50, 500 and 1000 b values. It was observed that the mean ADC values were significantly higher in RCC compared to urothelial carcinoma ($p<0.05$) and the mean ADC value was lower in angiomyolipoma compared to RCC ($p<0.01$). In the differentiation of solid renal tumours, ADC values generated by 3T diffusion MRI may be useful.

Paudyal et al. (30) evaluated diffusion MRI for the characterisation of renal carcinoma. In this study of 47 cases, ADC values were found to be significantly higher in RCCs compared to urothelial carcinomas (p=0.022). In histologic subtype analysis, a significant difference in ADC values was observed between clear cell ($1.59x10^{-3}$ sec/mm^2) and non-clear cell ($6.72x10^{-3}$ sec/mm^2) RCC (p=0.0004). Similarly, while there was a significant difference between ADC values in RCC lesions with and without metastases (p=0.0004), no difference in intensity was observed in T1 and T2 weighted images.

Maruyama et al. (31) evaluated the usefulness of tumor size and ADC/dimension ratio in differentiating low and high grade tumors in a study of 49 cases, 34 of 49 ccRCCs were low grade and 15 were high grade tumours. There were significant differences in ADC values, tumour size and ADC/size ratio between high and low grade tumours ($p<0.05$). There was also a correlation between tumour size and ADC value ($p<0.01$). There was statistically significant difference between high-grade ccRCC and low-grade ccRCC by tumor size and ADC/size ratio.

In our study, although a decrease in ADC value was observed with increasing tumor diameter, it was not statistically significant. Again, an increase in nuclear grade was found with increasing tumor diameter, which was not statistically significant. We attributed this to our low number of cases.

Cogley et al. (27) examined diffusion MRI of RCC, urothelial carcinoma and renal infections in 2013. ADC values were lower for solid components than for necrotic or cystic areas in complex renal masses. Restricted diffusion areas in complex solid and cystic renal masses were found to be helpful in differentiating complicated cysts, cystic or necrotic areas and RCC with MRI without contrast agent.

Doğanay et al. (32) investigated the role and dependability of DW-MRI in the differentiation of malignant and benign renal lesions. In this study, DW-MRI was used to differentiate angiomyolipoma and oncocytoma from RCC and malignant lesions from benign lesions. Higher b values (b 600 and b 1000) were found to have higher sensitivity and specificity values.

Sandrasegaran et al. (33) examined the role of DWI in differentiating renal mass subtypes in 42 patients with renal masses. Benign lesions were found to have a higher mean ADC than malignant lesions in this study. ADC measurements have been used for the differentiation of benign cystic lesions from cystic kidney cancer.

Goyal et al. (34) in a study of 33 cases with 36 RCCs in 2012, histologic subtype, nuclear grade and cell count were performed for each lesion, and the relationship between ADC values and cell count of different grades and subtypes was investigated. Out of 23 low grade (grade 1 and 2) and 13 high grade (grade 3 and 4) tumors, 32 were clear cell and 4 were nccRCC. It was observed that the grade increased with decreasing ADC values. Mean ADC values were significantly higher for ccRCC ($1.62x10^{-3}$ sec/mm^2) than for nccRCCs ($1.04x10^{-3}$ sec/mm^2) (p=0.005). Only low-grade RCCs and ccRCC were found to have higher ADC values.

In a study by Wang et al. (35), diffusion imaging was performed with 3T MRI using 500 and 800 b values in 83 patients with 85 kidney masses. It was found that 49 of the cases were ccRCC, 22 were pRCC and 14 were crRCC. At 500 b values, ADC values of ccRCC were significantly higher than other subtypes (p=0.001). The difference between pRCC and crRCC was not significant (p=0.68). At 800 b values, ccRCC showed the

highest mean ADC value of the subtypes and the difference with each of the subtypes was statistically significant (p<0.001). The mean ADC at 800 b values was more effective in differentiating ccRCC and nccRCC (ROC= 0.973). $1.281x10^{-3}$ sec/mm^2 was the threshold value that allowed differentiation with a sensitivity of 95.9% and specificity of 94.4%.

In our study, the average ADCs were higher in ccRCC than in other subgroups, which is consistent with the literature. Contrary to the literature (27), a statistically significant difference was observed when comparing subtype mean ADCs individually in our study (p=0.032).

Yu et al. (36) In a study consisting of diffusion MR images obtained with 800 b values on 137 RCC patients, ADC values taken from the solid parts of the tumors and the normal parenchyma of the opposite kidney were measured and statistically analyzed. Mean ADC values were significantly lower for RCC than normal renal parenchyma (p<0.001). A significant difference in ADC values was observed between clear cell and non-clear cell RCCs, and a significant difference was also observed between G1 and G2 and between G3 and G4 of RCCs. ADC was found to be useful in the characterization of subtypes and nuclear grades of RCC.

Rosenkrantz et al. (17) retrospectively evaluated the usefulness of ADC in differentiating low and high grade ccRCC in 57 ccRCC patients with pathological diagnosis and preoperative DW MRI. A total of 31 low-grade (1 G1 and 30 G2) and 26 high-grade (20 G3 and 6 G4) RCCs were analysed. In both low-grade and high-grade ccRCCs, ADC values at 400 and 800 b were significantly lower in high-grade ccRCCs (p<0.001), demonstrating its effectiveness in detecting high-grade ccRCCs compared with conventional MRI features alone. This study showed that the average lesion size in high-grade ccRCC was larger than in low-grade ccRCC (p<0.006).

In our study, we compared the ADC values of the patients who were grouped according to their histopathologic nuclear grades. Although the literature generally focuses on ccRCC, in our study, subtypes of RCCs were included in different numbers in the groups. As a result of the statistical comparison between the three groups (G1, G2 and G3), a significant difference was found between G1 and G2 in accordance with the study of Yu et al. (36). However, we observed no significant difference between other groups. In this study, we compared RCC ADC values with normal kidney ADC values for each group. We found a statistically significant decrease in ADC values of RCC compared to normal kidney parenchyma.

Silva et al. (37) tried to differentiate benign and malignant tumors with ADC values in a study of 66 patients with renal tumors. Oncocytoma was found to have the highest ADC value. The ADC value decreased in the order of ccRCC (1.5033±0.1328), crRCC (1.1075±0.1034), pRCC (0.7611±0.0942) and angiomyolipoma. ADC values of RCC subtypes were very close to the values in our study and showed a similar ranking.

Sharma and et.al. (38) investigated the utility of chemical shift imaging and DW/ADC maps in differentiating renal tumors. In their study, they measured the ADC values of patients with 15 ccRCC, 1 crRCC, and 3 pRCC as $1.29x10^{-3}mm^2$, $0.80x10^{-3}mm^2$, $0.68x10^{-3}mm^2$, respectively. They found no correlation between ADC values and tumor subtypes. This may be due to the small sample size. In our study, despite a similar sample size, there was a statistically significant difference between the subtypes (p=0.032).

Li and et.al. (39) calculated ADC values in a study group consisting of 68 ccRCC (clear cell renal cell carcinoma) and 32 nccRCC patients (21 crRCC and 11 pRCC). The mean ADC values for ccRCC, crRCC, and pRCC were $2.85±1.35x10^{-3}mm^2$, $1.42±0.78x10^{-3}mm^2$, $1.34±0.52x10^{-3}mm^2$, respectively. As in our study, they found a statistically significant difference between ccRCC and nccRCC (p<0.001). However, they were unable to distinguish between crRCC and pRCC using ADC values. In contrast, our study was able to differentiate between the subtypes using ADC values.

The unequal number of cases in the groups, the inhomogeneous distribution of histologic subtypes within the groups, and the absence of a G4 group were the shortcomings of our study. In addition, since DWI was obtained without breath holding, motion artifacts affected the image quality.

In conclusion, preoperative DWI holds promise in contributing to abdominal MRI data and prognostic evaluations due to its ability to detect histologic subtypes of RCCs. This technique offers advantages such as rapid acquisition, ease of use without the need for contrast material, and the potential to differentiate cases based on their nuclear grades. Integrating DWI into clinical practice may enhance our ability to stratify RCC patients prognostically, leveraging its non-invasive nature and capability to provide valuable histological insights. However, we concluded that our findings should be supported by larger and multicenter studies.

References

1. Turgut AT, Gündoğdu E. Ürogenital sistem radyolojisi. İn: Sancak İT, (Editor). Temel Radyoloji. 1st Edition, Ankara: Güneş Tıp Kitapevleri, 2015: 1032-1033.

2. Chow WH, Devesa SS, Warren JL, Fraumeni JF Jr. Rising insidence of renal cell cancer in the United States. JAMA 1999; 281: 1628-1631.

3. Patard JJ, Rodriguez A, Rioux-Leclercq N, Guille F, Lobel B. Prognostic significance of the mode of detection in renal tumours. BJU Int 2002; 90: 358-363.

4. Lam JS, Shvarts O, Leppert JT, Figlin RA, Belldegrun AS. Renal cell carcinoma 2005: New frontiers in staging, prognostication and targeted molecular therapy. J Urol 2005; 173: 1853-1862.

5. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. CA Cancer J Clin 2005; 55: 10-30.

6. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. Am J Surg Pathol 1982; 6: 655-663.

7. Tsui KH, Shvarts O, Smith RB, et al. Prognostic indicators for renal cell carcinoma: A multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. J Urol 2000; 163: 1090-1095.

8. Lang H, Lindner V, de Fromont M, et al. Multicenter determination of optimal interobserver agreement using the Fuhrman grading system for renal cell carcinoma: Assessment of 241 patients with >15-year follow-up. Cancer 2005; 103: 625-629.

9. Chandarana H, Kang SK, Wong S, et al. Diffusion-weighted intravoxel incoherent motion imaging of renal tumors with histopathologic correlation. Invest Radiol 2012; 47: 688-696.

10. Kovacs G, Akhtar M, Beckwith BJ, et al. The Heidelberg classicification of renal cell tumors. J Pathol 1997; 83: 131-133.

11. Konety BR, Vaena DA, Williams RD. Renal parenchymal neoplasms. In: McAninch JW, Lue TF, (Editors). Smith's & Tanagho's General Urology. 18. Baskı, San Francisco: McGraw-Hill Companies, 2013: 332-333.

12. Ordonez NG, Rosai J. Urinary tract. Kidney, renal pelvis and ureter. In: Rosai J. (Editor). Rosai and Ackerman's Surgical Pathology. 9th Edition, 2nd Volume. Philadelphia: Mosby Elsevier, 2004: 1163-316.

13. Chow W, Devesa SS, Fraumeni J. Epidemiology of renal cell carcinoma. In: Vogelzang NJ, Scardino PT, Shipley WU, et al. (Editors). Genitourinary Oncology. 3rd Edition, Philedelphia: Lippincott Williams and Wilkins, 2000: 101-110.

14. Lindblad P. Epidemiology of renal cell carcinoma. Scan J Surg 2004; 93: 88-96.

15. Medeiros LJ, Jones EC, Aizawa S, et al. Grading of renal cell carcinoma. Cancer 1997; 80: 990-991.

16. Kontak JA, Campbell SC. Prognostic factors in renal cell carcinoma. Urol Clin North Am 2003; 30: 467-480.

17. Rosenkrantz AB, Niver BE, Fitzgerald EF, et al. Utility of the apparent diffusion coefficient for distinguishing clear cell renal cell carcinoma of low and high nuclear grade. AJR Am J Roentgenol 2010; 195: W344-351.

18. Novara G, Martignoni G, Artibani W, Ficarra V. Grading systems in renal cell carcinoma. J Urol 2007; 177: 430-436.

19. Ficarra V, Martignoni G, Maffei N, et al. Original and reviewed nuclear grading according to the Fuhrman system: A multivariate analysis of 388 patients with conventional renal cell carcinoma. Cancer 2005; 103: 68-75.

20. Rioux-Leclercq N, Karakiewicz PI, Trinh QD, et al. Prognostic ability of simplified nuclear grading of renal cell carcinoma. Cancer 2007; 109: 868-874.

21. Sener RN. Maple syrup urine disease: Diffusion MRI, and proton MR spectroscopy findings. Comput Med Imaging Graph 2007; 31: 106-110.

22. Luypaert R, Boujraf S, Sourpron S, Osteaux M. Diffusion and perfussion MRI: Basic physics. European Journal of Radiology 2001; 38: 19-27.

23. Schaefer PW. Applications of DWI in clinical neurology. J Neurol Sci 2001; 186: 25-35.

24. Provenzale JM, Sorensen AG. Diffusion-weighted MR imaging in acute stroke: Theoretic considerations and clinical applications. AJR Am J Roentgenol 1999; 173: 1459-1467.

25. Squillaci E, Manenti G, Cova M, et al. Correlation of diffusion-weighted MR imaging with cellularity of renal tumours. Anticancer Res 2004; 24: 4175-4179

26. Ciçekçi M, Onur MR, Aydin AM, et al. The role of apparent diffusion coefficient values in differentiation between adrenal masses. Clin Imaging 2014;38(2):148-153.

27. Cogley JR, Nguyen DD, Ghobrial PM, Rakita D. Diffusion-weighted MRI of renal cell carcinoma, upper tract urothelial carcinoma, and renal infection: A pictorial review. Jpn J Radiol 2013; 31: 643-652.

28. Lassel E, Rao R, Schwenke C, Schoenberg SO, Michaely HJ. Diffusion-weighted imaging of focal renal lesions: A meta-analysis. Eur Radiol 2014; 24: 241-249.

29. Sasamori H, Saiki M, Suyama J, et al. Utility of apparent diffusion coefficients in the evaluation of solid renal tumors at 3T. Magn Reson Med Sci 2014; 13: 89-95.

30. Paudyal B, Paudyal P, Tsushima Y, et al. The role of the ADC value in the characterisation of renal carcinoma by diffusion-weighted MRI. Br J Radiol 2010; 83: 336-343.

31. Maruyama M, Yoshizako T, Uchida K, et al. Comparison of utility of tumor size and apparent diffusion coefficient for differentiation of low- and high-grade clear-cell renal cell carcinoma. Acta Radiol 2014; pii: 0284185114523268.

32. Doğanay S, Kocakoç E, Ciçekçi M, et al. Ability and utility of diffusion-weighted MRI with different b values in the evaluation of benign and malignant renal lesions. Clin Radiol 2011; 66: 420-425.

33. Sandrasegaran K, Sundaram CP, Ramaswamy R, et al. Usefulness of diffusion-weighted imaging in the evaluation of renal masses. AJR Am J Roentgenol 2010; 194: 438-445.

34. Goyal A, Sharma R, Bhalla AS, et al. Diffusion-weighted MRI in renal cell carcinoma: a surrogate marker for predicting nuclear grade and histological subtype. Acta Radiol 2012; 53: 349-358.

35. Wang H, Cheng L, Zhang X, et al. Renal cell carcinoma: diffusion-weighted MR imaging for subtype differentiation at 3.0T. Radiology 2010; 257: 135-143.

36. Yu X, Lin M, Ouyang H, Zhou C, Zhang H. Application of ADC measurement in characterization of renal cell carcinomas with different pathological types and grades by 3.0T diffusion-weighted MRI. Eur J Radiol 2012; 81: 3061-3066.

37. de Silva S, Lockhart KR, Aslan P, et al. The diagnostic utility of diffusion weighted MRI imaging and ADC ratio to distinguish benign from malignant renal masses: Sorting the kittens from the tigers. BMC Urol 2021; 21: 67.

38. Sharma S, Gupta R, Bhalla V, Aggarwal P, Gulati M. Utility of Chemical Shift Imaging and Diffusion-weighted Images/Apparent Diffusion Coefficient Maps as a Tool for Evaluation of Solid Renal Tumors. J Assoc Physicians India 2024;72(3):18-23.

39. Li X, Xiang X, Lin HT. Differential diagnostic value of magnetic resonance diffusion-weighted imaging and apparent diffusion coefficient for renal clear cell carcinoma and non-clear cell carcinoma. Oncol Lett 2022; 25(2): 60.