

Original Research Article

Role of diffusion weighted MRI in characterization of renal diseases

Pankaj Kumar^{1*}, Yashpaul², P. K. Soni², Dhiraj Kapoor³, Rajesh Kumar¹, Sayan Malakar³, Guriqbal Singh³, Bhagwan Dass³

¹Department of Medicine, SLBSGMC, Mandi, Himachal Pradesh, India

²Department of Radio Diagnosis, ³Department of Medicine, Dr. RPGMC, Kangra, Himachal Pradesh, India

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*Correspondence:

Dr. Pankaj Kumar,

E-mail: pakugu2003@yahoo.co.in

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ABSTRACT

Background: MRI has the unique ability to show both structure and function objectively without any radiation exposure to the patient. Apparent diffusion coefficient (ADC) is a quantitative parameter that combines the effects of capillary perfusion and water diffusion. Renal parameters have shown inverse relationship with the ADC values in these studies. So, ADC values have a potential to serve as a marker of renal function. The aim of the present endeavor was to study the role of DW MRI in characterization of renal function and to find out the clinical use of DW MRI in renal diseases; and establish the relationship between renal function assessed by eGFR and that by DW MRI calculated in terms of ADC values in various renal diseases

Methods: Total 30 patients were included in the study. The study was carried out in department of radiodiagnosis at Dr. RPMGC Kangra. 1.5 Tesla MRI machine was used. The ADC value was calculated at upper, mid and lower pole of each kidney and the mean was taken. Then the mean of right and left kidneys was taken to calculate the mean ADC of the patient.

Results: Serum creatinine in present study ranged from 0.67 to 13.9mg/dl, with mean value of 7.28mg/d. Serum urea ranged from 22 to 293mg/dl with the mean of 119.6mg/dl. There was significant inverse correlation occurred between ADC values and serum urea ($r=-0.43$, $p=0.02$). There was significant inverse correlation between ADC values and serum creatinine ($p=0.01$) and a positive correlation between eGFR and ADC values ($r=0.14$, $p=0.47$).

Conclusions: ADC values consistently decreased with increasing stage of renal failure, so these can be used as an indirect maker of renal function. Authors conclude that lower would be the ADC value more advanced would be the stage of renal failure. DW MRI can also be detect early stages of renal failure even when the serum maker are within normal range.

Keywords: Apparent diffusion coefficient, Diffusion weighted imaging, Gradient echo

INTRODUCTION

Renal failure cases are growing at alarming rate in India, with DM and HTN being the commonest contributory causes. Prevalence of renal disease in India has been found to be 0.79%.¹ Since renal disease is accompanied by renal dysfunction, monitoring of renal function

permits assessment of disease progression, hence periodic assessment of renal function is necessary for optimal management of a patient with renal disease. Serum creatinine (SCr), Serum urea (SU) and estimated glomerular filtration rate (eGFR) are useful for monitoring renal function; however, these are imperfect measures of renal function assessment, as serum

creatinine is affected by muscle mass, type of diet and haemoglobin/bilirubin concentration of blood.² Serum urea is reabsorbed in distal tubule, especially in dehydration so that it does not accurately reflect the renal function.³

Keeping in view the limitations of serum markers, imaging has been found to play an important role in the evaluation of renal diseases. USG depicts echogenicity of renal parenchyma which reflect the changes at the level of interstitium but not those at the level of glomerulus which is more accurate measure of renal function.⁴ USG also suffers from operator dependency and lacks objectivity. In addition to exposure to ionizing radiation, CT scan requires use of iodinated contrast material, which is undesirable in patients with renal dysfunction. Nuclear medicine techniques are generally thought to be the most accurate method for quantification of renal function. However, these methods utilize ionizing radiation and have low spatial resolution.

MRI has the unique ability to show both structure and function objectively without any radiation exposure to the patient. Functional MRI techniques such as DWI, blood oxygen level-dependent (BOLD) imaging, and CE MRI renography have potential utility in the evaluation of renal function. DW-MRI is a non-invasive modality to characterize tissues based on Brownian motion of water molecules within them. ADC is a quantitative parameter calculated from DWI that combines the effects of capillary perfusion and water diffusion. It has earlier been used successfully in imaging of various CNS disorders. DW-MRI in kidneys makes sense because of the organ's high blood flow and its role in water filtration. Renal diseases, reflected in the form of elevated serum urea and serum creatinine, have shown inverse relationship with the ADC values in these studies. So, ADC values have a potential to serve as a marker of renal function.⁵

The aim of the present endeavor to study the role of Diffusion Weighted Magnetic Resonance Imaging in characterization of renal function. To find out the clinical use of DW MRI in renal diseases; and establish the relationship between renal function assessed by eGFR and that by DW MRI calculated in terms of ADC values in various renal diseases

METHODS

Total 30 patients were included in the study. Renal function was assessed by eGFR, calculated by Cockcroft Gault formula. Patients having eGFR less than 60ml/min or having known renal pathology even with eGFR >60 ml/min were included. Patients having any MRI incompatible metallic foreign body in their body and patients having claustrophobia were excluded. Study was carried out in department of radiodiagnosis at DR. RPMGC Kangra for one year from January 2014-December 2014. Fifty consecutive patients coming to medicine OPD were taken but 10 patients have

claustrophobia, 5 patients did not consent for study and 5 patients have MRI incompatible metallic foreign body in their body, so they were excluded. Examination of patient was done on 1.5 Tesla MRI machine (Signa Excite, GE Healthcare). The ADC value was calculated at upper, mid and lower pole of each kidney and the mean was taken to be the mean ADC value of that kidney. Then the mean of right and l kidneys was taken to calculate the mean ADC of the patient. P value was calculated for the significance of relation between ADC values and serum creatinine, ADC value and serum urea and ADC value and eGFR. P value less than 0.05 was taken as significant.

RESULTS

ADC values in present study⁵

- CKD - 1.970.35mm²/s
- ARF - 2.190.26mm²/s
- Normal - 2.110.29mm²/s
- for Masses /Cysts -3.430.5mm²/s
- Solid tumours - 2.050.77mm²

In present study, the age range of the patients was 13 to 82 years, with mean age of 52.1 years. The mean age of male patients (18) was 49.4years, while the mean age of female (12) patients was 49.2years. The body weight of the patients in our study ranged from 15kg to 110kg, with mean weight being 54.6kg. In present study, 15 (50%) of the patients were hypertensive with 8 males and 7 females. Two patients in addition to HTN, one 82 years old male and another 55year old female were also having U/L right renal cysts with eGFR being 23.83 and 18.85ml/min respectively. Out of total 30 patients, 6 patients (20%) had DM. Out of these 6 patients, 4 were males and 2 were females

Table 1: ADC values in different stages of renal failure.

Stage of renal failure	Mean ADC ($\times 10^{-3}$ /sec) in stage
Stage 1	-
Stage 2	1.95
Stage 3	1.96 \pm 0.38
Stage 4	1.93 \pm 0.41
Stage 5	1.72 \pm 0.62

Size of kidney was taken as decreased if craniocaudal span less than 7.1cm or width less than 3.1cm. In present study, 7 patients (23.33%), had decreased size of B/L kidneys. 23 patients (76.67%) had B/L normal renal size. Out of 7 patients with decreased renal size 6 (85.7%) had HTN and 1 (14.2%) had DM. In present study authors found HTN to be a major contributing factor for decreased renal size than DM.

ADC values were measured separately in 60 kidneys in 30 patients. Values were taken at upper mid and lower poles without any preference to cortex or medulla and

mean value was calculated by averaging these three values. ADC values in 30 right kidneys ranges from 1.53 to $3.06 \times 10^{-3} \text{mm}^2/\text{sec}$ with ADC for right kidneys being $2.08 \times 10^{-3} \text{mm}^2/\text{sec}$. ADC values in 30 left kidneys ranged from 1.03 to $2.89 \times 10^{-3} \text{mm}^2/\text{sec}$ with mean ADC for left kidney being $2.06 \times 10^{-3} \text{mm}^2/\text{sec}$. Mean ADC values was

calculated by taking the average ADC of the right and left kidneys. In 6 (20%) patients with DM, ADC values ranged between 1.6 to $2.6 \times 10^{-3} \text{mm}^2/\text{sec}$ with mean of $2.16 \times 10^{-3} \text{mm}^2/\text{sec}$. In 15 (50%) patients with HTN, ADC values ranged between 1.1 to $2.86 \times 10^{-3} \text{mm}^2/\text{sec}$ with mean of $1.76 \times 10^{-3} \text{mm}^2/\text{sec}$.

Table 2. Relationship of eGFR, urea and creatinine with ADC values.

Patients	Decreased eGFR with assoc. co morbidity (if any)	Creatinine	UREA	Body weight (kg)	eGFR	Avg ADC right kidney	Avg ADC left kidney	Avg ADC of patients
1	HTN	10	293	50	7.47	1.74	1.03	1.36
2	HTN	2.9	51	58	17.9	1.81	1.99	1.9
3	DM	2.5	115	60	30	2.09	1.62	2.35
4	B/L cysts	1.3	37	32	29.56	2.39	2.65	2.52
5	HTN	6.1	148	40	9.56	1.17	2.54	2.3
6	HTN	6	156	15	12.22	1.06	1.14	1.1
7	DM	4.5	190	60	13.33	1.17	2.63	1.9
8	HTN	10	163	35	3.89	1.7	1.7	1.7
9	HTN	9.9	235	38	4.85	0.84	2.89	1.86
10	U/L right renal mass	0.67	22	49	80.24	1.68	2.21	1.95
11	HTN	5.8	148	33	6.7	0.83	2.6	1.71
12	HTN	2.6	71	64	29.4	1.53	1.63	1.58
13	HTN	2.7	76	62	24.7	2.09	2.44	2.26
14	HTN	13.9	248	64	5.4	1.73	1.77	1.75
15	DM	8.3	255	80	13.6	2.26	1.56	1.91
16	-	3.5	235	80	26.4	1.96	2.24	2.1
17	DM	2.8	92	50	33.3	2.14	2.15	2.14
18	-	1.8	46	45	24.62	1.42	1.62	1.52
19	-	2.2	50	31	15	1.98	2.7	2.34
20	DM	3.6	50	59	26.67	1.57	1.62	1.6
21	-	2.5	53	82	37.17	2.23	2.37	2.3
22	HTN	1.3	43	23	17.9	2.08	2.33	2.21
23	HTN+U/L cysts	1.8	97	55	23.43	2.56	1.86	1.94
24	-	3.2	74	105	30	2.2	2.5	2.35
25	DM	1.2	25	20	13	2.67	2.06	2.34
26	HTN+ U/L cysts	4.7	162	110	18.85	2.62	1.47	1.59
27	HTN	2.9	48	65	30.6	2.5	2.6	2.55
28	-	2.7	48	47	22.7	1.9	2.04	1.97
29	HTN	13.9	248	65	5.45	1.8	1.7	1.75
30	-	3	96	62	20.3	2.17	2.14	2.15

ADC values with in one (3.33%) patient with B/L renal cysts was $2.52 \times 10^{-3} \text{mm}^2/\text{sec}$ and in two patients with U/L right renal cysts the ADC values in the were 2.62 and $2.56 \times 10^{-3} \text{mm}^2/\text{sec}$ respectively, while the left non-cystic kidneys the ADC values were 1.86 and $1.47 \times 10^{-3} \text{mm}^2/\text{sec}$. In one (3.33%) patient with U/L right renal mass the ADC value was $1.69 \times 10^{-3} \text{mm}^2/\text{sec}$, whereas the ADC value in the normal left kidney was $2.21 \times 10^{-3} \text{mm}^2/\text{sec}$ (Table 1). On applying stastical tests of significance, authors found that a positive correlation between eGFR and ADC values ($r=0.14$, $p=0.47$)

Serum creatinine in present study ranged from 0.67 to 13.9mg/dl, with mean value of 7.28mg/dl. 4 (13.33%) patients had S Cr <1.5mg/dl. Rest 26 (86.66%) patient had S Cr >1.5mg/dl. 5 (83.33%) out of 6 patients with DM had raised S Cr 14 (93.33%) out of 15 patients with DM has raised S Cr, including 2 (6.67%) hypertensive patients with U/L cystic disease. Authors had 9 (30%) patients with S Cr $\leq 2.5 \text{mg/dl}$ and 21 (70%) patients with S Cr >2.5 mg/dl.

Out of total 4 patients with S Cr <1.5mg/dl) 1 (3.33%) each had renal mass (S Cr -0.67mg/dl), 1 (3.33%) had

B/L renal cysts (S Cr -1.3 mg/dl) and 2 (6.67%) had decreased eGFR (17 and 13ml/min) respectively.

Table 3: Detailed distribution of S Cr in different groups of patients with their corresponding ADC values.

S Cr level	Associated condition(s)	No. of patients	Range of ADC ($\times 10^{-3}$ mm ² /sec)	Mean ADC ($\times 10^{-3}$ mm ² /sec) in subgroup	Mean ADC ($\times 10^{-3}$ mm ² /sec) in group	Total
S Cr >1.5 mg/dl	With DM	5	1.60-2.35	1.98±0.38	1.82±0.72	26
	With HTN+U/L cysts	2	1.59-1.94	1.76±0.17		
	With HTN	12	1.10-2.55	1.82±0.72		
	With renal failure	7	1.53-2.35	1.77±0.24		
S Cr ≤1.5 mg/dl	With DM	1	-	2.34	2.23±0.29	4
	With HTN	1	-	2.21		
	With Renal Mass	1	-	1.95		
	With B/L cysts	1	-	2.52		
	With HTN+U/L cysts	1	-	1.94		
Total						30

On applying statistical tests of significant inverse correlation between ADC values and serum creatinine ($p=0.01$).

Serum urea ranged from 22 to 293 mg/dl with the mean value of 119.6mg/dl. 3 (10%) patients had SU <40 mg/dl. 27 (90%) patients had SU >40mg/dl, out of which maximum 9 (33.33%) patients had SU in the range 40 to 60mg. 15/15 patients (100%) with HTN had raised SU. 5/6 (83.33%) patients with DM had raised SU. Patients with normal serum urea were included because one had renal mass (SU- 22mg/dl), one had decreased eGFR (13ml/min) (SU- 25mg/dl) and one had renal cysts (SU- 37mg/dl) with eGFR 29.56ml/min. respectively (Table 2).

On applying statistical tests of significant inverse correlation between ADC values and serum urea ($r=-0.43$, $p=0.02$).

Table 4: Relationship of albuminuria with ADC value.

Urine Albumin level (mg/dl)	eGFR (ml/min)	Mean ADC ($\times 10^{-3}$ mm ² /sec)
≤1	15.4	2.09±0.38
1.1-2	26.8	1.78±0.68
>2	16.93	1.73±0.63

A total of 13 patients (43.33%) showed presence of urine albumin while in remaining 17(57.67%) patients, urine was negative for albumin. Albuminuria with hypertension was present in (7/15=46.67%) patients and urine Albumin with diabetes mellitus was present in (3/6=50%). On applying statistical tests of significant inverse correlation

between ADC values and serum urea ($r=-0.43$, $p=0.02$) (Table 4).

DISCUSSION

DW MRI for assessment of renal function was first done by Siegel et al, by using ADC values.⁶ Since then, several studies have been conducted by various investigators to find out the role of DW MRI in renal function assessment.

DW-MRI is a novel method of assessment of renal function. Expressed in quantitative terms as apparent diffusion coefficient. In general, with decrease in renal function the diffusion of water molecules decreases, reflected in quantitative decrease in ADC values. Most patients in present study with decreased eGFR also showed a corresponding decreased in ADC values.

Number of patients in the different stages of renal failure in our study were: stage 1 none; stage 2 -1 (3.33%); stage 3- 5(16.67%); stage 4-13 (43.33%); stage 5 -11 (36.67%)

Overall age range of the study population was 13 to 82years with mean age of 52.1years. Mean age of presentation in present study was higher as compared to that of Goyal et al (45.1 years) and lower as compared to Cova et al, (62 years) and Namimoto et al, (59.4 years). The age range in present study was similar to that of nominated et al (13 to 81 years).^{5,6}

The male to female sex ratio in our study of 30 patient was 1.5:1(18 males and 12 female). Similar sex ratio of 1.6:1 and 1.2:1 have been reported by Goyal et al, and Cova et al, in their studies.^{5,7}

ADC value distribution

Since authors did not had any control case in present study, for the purpose of comparison normal value of ADC would be taken as suggested by Goyal et al.⁵

The mean ADC value of Rt sided kidneys was $1.81 \pm 0.98 \times 10^{-3} \text{mm}^2/\text{s}$, while that of Lt sided kidney was $2.06 \pm 1.0 \times 10^{-3}$. The ADC value range in hypertensive patients was $1.10-2.55 \times 10^{-3} \text{mm}^2/\text{s}$, with mean ADC value of $1.82 \pm 0.72 \times 10^{-3} \text{mm}^2/\text{s}$, while range in DM patient was $1.60-2.35 \times 10^{-3} \text{mm}^2/\text{s}$ with mean ADC value of $1.97 \pm 0.37 \times 10^{-3} \text{mm}^2/\text{s}$. In 4 kidneys of 3 patients with renal cysts the ADC value range was $2.52-2.62 \times 10^{-3}$ with mean ADC value of $2.56 \pm 0.04 \times 10^{-3} \text{mm}^2$. There was one case who had eGFR 80.24ml/min (stage 2 renal failure). Authors have found decreasing ADC value with increasing stages of renal failure (1.960.38 for stages 3, 1.930.41 for the stage 4 and $1.72 \pm 0.62 \times 10^{-3} \text{mm}^2/\text{s}$ for stage 5)

Similar result have been reported by Goyal et al, in their study where they found that the mean ADC values of different stages of CKD were significantly different from each other ($p=0.001$) and showed decreasing trend with increasing stage 3: $2.964 \pm 0.1243 \times 10^{-3} \text{mm}^2/\text{s}$ for stage -4 $1.8413 \pm 0.2117 \times 10^{-3} \text{mm}^2/\text{s}$ and for stages-5: $1.5218 \pm 0.1853 \times 10^{-3} \text{mm}^2/\text{s}$ and $1.59 \pm 0.79 \times 10^{-3} \text{mm}^2/\text{s}$ for cortex and medulla respectively. Their ADC value were different from present study because they took separate values of cortex and medulla and dehydrated their patients before study. They got increased values in medulla as compared to that of cortex because they conducted the study among dehydrated patients who have more fluid in medulla due to physiological adaption by the body and corresponding decrease in ADC values was not noted.

In present study the ADC value range in patients with eGFR 10-25ml/min was $1.93 \pm 0.57 \times 10^{-3} \text{mm}^2/\text{s}$ and in the patients with eGFR less than 10ml/min was $1.77 \pm 0.67 \times 10^{-3} \text{mm}^2/\text{s}$. Lower ADC values were obtained in our study with increasing stage of renal failure and similar results have been reported by Toyoshima et al.⁸

In present study, the patients were categorized in 2 groups based on their S Cr level as :S Cr <mg/dl and S Cr >1.5mg/dl. The corresponding ADC values in these groups were $1.82 \pm 0.72 \times 10^{-3} \text{mm}^2/\text{s}$ (S Cr >1.5mg/dl) and $2.23 \pm 0.29 \times 10^{-3} \text{mm}^2/\text{s}$ (S Cr <1.5mg/dl). In present study, there were 21 patients with S Cr >2.5mg/dl and their mean ADC value was $1.82 \pm 0.72 \times 10^{-3} \text{mm}^2/\text{s}$, while their patients with S Cr $\leq 2.5 \text{mg/dl}$ and their mean ADC value was $2.16 \pm 0.22 \times 10^{-3} \text{mm}^2/\text{s}$. Similar trend of result have been reported in study by Theony et al.⁹

Serum urea level in present study ranged from 22 to 293 mg/dl with the mean value of 119.6mg/dl. 3 (10%) patients in present study had SU <40 mg/dl, rest 27

(90%) patients had SU >40mg/dl, with 8 (26.84%) patients having SU levels between 41 to 60mg/dl. On comparing the SU levels with corresponding ADC values we found decreasing trend of ADC values with increasing SU level. On applying stastical tests of significance, authors found a significant increase correlation between the 2 variables: SU and ADC ($r=-0.43$, $p=0.02$)

On comparing the ADC values with the corresponding eGFR of the patient, authors found that with decreasing eGFR, the ADC values decrease signifying decreased diffusion of water molecules with increased stage of renal failure. The eGFR range in present study was 3.89-80.24ml/min. we found a positive relationship between ADC and eGFR. Similar results have been found by Goyal et al, who found that with decreasing eGFR the corresponding ADC values also decrease. On applying the stastical tests we found that there was a positive correlation but not signify ($r=0.14$, $p=0.47$). There could be many explanation for this: present sample size was small ($n=30$); eGFR depends on many variables, other than serum creatinine, like the body weight age and sex; accurate assessment of GFR is by radioucleotide studies, whereas creatinine based equations give only approximate value; present study patients of CRF were referred mostly from dialysis unit who have mostly advanced stages of renal failure. So, present study sample group had limited range of GFR. Similar findings have been reported by Toyoshima et al, Yufeng et al, Lan Lu et al, and in their studies.^{8,10,11}

In present study we had 4 (10%) patients with 5 renal lesions: 4 (80%) lesions were cysts and 1 (3.33%) was U/L right renal mass. In the cysts, authors found increased ADC values consistent with increased diffusion of water molecules in these lesions and decreased ADC value in solid renal lesions.

The mean ADC value in the renal cysts were $2.56 \pm 0.46 \times 10^{-3} \text{mm}^2/\text{sec}$, while 1 (3.33% patient with renal mass had mean ADC value of $1.95 \times 10^{-3} \text{mm}^2/\text{sec}$, with the ADC value in the renal mass being $1.69 \times 10^{-3} \text{mm}^2/\text{sec}$ which was almost replacing the whole of right kidney, while the contralateral relatively normal left kidney showed ADC value of $2.21 \times 10^{-3} \text{mm}^2/\text{sec}$. The ADC values of our study are similar to those of Kim S et al, who found mean ADC value of simple renal cysts to be $2.50 \pm 0.53 \times 10^{-3} \text{mm}^2/\text{sec}$ and of renal carcinoma to be $1.35 \pm 0.55 \times 10^{-3} \text{mm}^2/\text{s}$.¹² Cova et al, studied 29 patient with known renal lesions, of whom 13 (44.8%) had simple cysts and 7 (24.1%) had solid tumour (3 histologically proven cell carcinomas, 1 histologically proven oncocyoma 3 angiomyolipomas).⁷

They found mean ADC value of simple cysts $3.65 \pm 0.09 \times 10^{-3} \text{mm}^2/\text{sec}$, solid begin and malignant values were significantly different from their mean ADC value of renal parenchyma diffusion in solid renal mass. Their results are in harmony with our result of increased

mean ADC value of cystic lesions than those of solid masses.

CONCLUSION

The eGFR range in our study was 3.89 to 80.24ml, with mean value of 21.14ml/min. There were more males in our study than females. 50% of the patient in present study were Hypertensive and 20% were diabetic. Decreased size of kidney was seen in 7 (23.3%) of patients and was etiologically more related to HTN than DM (85% v/s 14%).

Positive correlation was seen between size of kidney and ADC values but not significant ($p=0.41$). ADC values in present study showed decreasing trend with decrease in eGFR or increase in stage of renal failure but not significant ($p=0.47$). ADC values showed significant Inverse relationship with biochemical markers of renal function serum urea ($p=0.02$) and serum creatinine ($p=0.01$). Urine albumin was present in 13 (43.13%) of the patient and was showing stronger relation with HTN than DM (20% v/s 10%) which was not significant ($p=0.32$). Authors found that ADC values consistently decreased with increasing stage of renal failure, so these can be used as an indirect maker of renal function. However due to inconsistent values at different stages of renal failure it is difficult at present to set cut off values for different stages of renal failure. Authors conclude that lower would be the ADC value more advanced would be the stage of renal failure. Considering the inverse correlation of serum urea and serum creatinine with ADC and positive correlation with eGFR, authors endorse the earlier fact that ADC values could be used as a useful adjacent for assessment of renal function. DW MRI can also detect early stages of renal failure even when the serum maker is within normal range. However, due to inconsistent values we would not recommend it as a sole maker of renal function. DC values could also be used for assessment of renal masses, but it is difficult at present to set off values of renal masses as our sample size for renal masses was small ($n=4$).

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