An exploration into the role of diffusion weighted MRI imaging in the assessment of chronic kidney disease

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Received: September 2018; Accepted: October 2018; Published: November 1, 2018
Citation: Saeed N. Younis, Safa Ezzidin Norouldin Almukhtar, Dendar Khudhur Rashid. An exploration into the role of diffusion weighted MRI imaging in the assessment of chronic kidney disease. World Family Medicine. 2018; 16(10): 33-39. DOI: 10.5742MEWFM.2018.93508

Abstract

Background and objective: Research has shown that diffusion-weighted magnetic resonance imaging (DW-MRI), one of the functional MRI techniques, can be utilized to evaluate renal function; however, more investigation is needed to understand its potential and capacity. The present study was carried out in order to evaluate the relationship between apparent diffusion coefficient (ADC) values of renal parenchyma and different stages of chronic kidney disease and to compare it with serum creatinine and estimated GFR among patients who referred to Rizgary Teaching Hospital in Erbil, the Kurdistan Region of Iraq.

Materials and Methods: The present experiment was an analytic cross-sectional study that was carried out from November 2017 to April 2018. In so doing, 12 individuals (control group) and 38 patients (patient group) diagnosed with known chronic kidney disease (CKD) were selected. After they had undergone magnetic resonance imaging of the upper abdomen, the patient group subjects were classified into different stages of CKD based on estimated glomerular filtration rate (eGFR) calculated using chronic kidney disease epidemiology (CKD-EPI) equation. Both control and patient groups underwent DW-MRI at b values of 40, 400, and 800, and ADC values were calculated for both groups. Afterwards, the control and patient groups were compared regarding their ADC values.

Results: The results of the present study revealed a significant inverse correlation between ADC values and serum creatinine in the patient group. Also, there was a strong positive correlation between ADC and eGFR in the patients with CKD. Moreover, the patient group had a significantly lower mean ADC compared to the control group.

Conclusion: The observed correlation between ADC values and serum creatinine and eGFR in the patients under investigation in the present study indicated that the presence and degree of renal dysfunction can be determined through ADC values.

Key words: chronic kidney disease (CKD), diffusion-weighted magnetic resonance imaging (DW-MRI), apparent diffusion coefficient (ADC), renal dysfunction

Introduction and Background

As one of the leading threats to, and problems in public health all over the world [1], chronic kidney disease (CKD) is increasingly prevalent worldwide and puts a lot of financial pressure on countries [2]. A variety of acute and chronic conditions can cause parenchymal kidney disease resulting in nephron loss followed by adaptive hyperfiltration in the remaining nephrons. This adaptive hyperfiltration in turn leads to long-term glomerular damage causing proteinuria and progressive loss of kidney function [3].

Renal function can be estimated through serum markers like blood urea nitrogen level, creatinine level, and estimated glomerular filtration rate (eGFR) [4]. However, it should be noted that single kidney function cannot be evaluated via blood tests which are significantly affected by the patients' age and body mass index (BMI). Therefore, and given the limitations of serum markers, imaging techniques have recently obtained significance in evaluating renal function and renal parenchymal disease [6].

Although good anatomic images can be obtained through computed tomographic (CT) scan and ultrasonography (USG), the information provided by them is of limited functional value. Moreover, changes in renal echogenicity can be observed through USG; however, the final results lack objectivity and can be significantly influenced by operator dependency. Furthermore, due to using iodinated contrast material in CT scan, its utilization is limited due to the adverse effects of iodinated contrast material on kidneys [6]. Both structure and function can be shown objectively via magnetic resonance imaging (MRI) without exposing the patient to radiation. Renal function can be evaluated through functional MRI techniques like blood oxygen level-dependent (BOLD) imaging, contrast-enhanced MRI renography, and diffusion-weighted imaging (DWI) [6].

As a widely utilized method of neuroimaging, diffusion-weighted magnetic resonance imaging (DW-MRI) can particularly be used to evaluate intracranial tumors, acute cerebral stroke, and demyelinating diseases [7]. Since DW-MRI is extremely sensitive to motion, its application outside the central nervous system is limited [8]; therefore, it cannot be in the abdomen because the effect of diffusion is obscured due to the presence of spontaneous motion such as peristalsis, respiration, and blood flow. However, motion-related problems have recently been overcome and reliable diffusion-weighted images of the abdominal organs can be obtained as a result of advances in ultrafast MRI methods [9].

Changes in the diffusion properties of water molecules in tissues are the basis for diffusion-weighted magnetic resonance imaging (DW-MRI) which is commonly employed in neuroradiology for early diagnosis of cerebral ischemia and characterization of cerebral tumors and infections [10].

Since available techniques are usually inadequate for abdominal imaging especially for focal lesion detection and characterization, and the evaluation of diffuse parenchymal diseases; therefore, diffusion-weighted imaging (DWI) is employed. The potential value of DWI in evaluating different renal diseases, such as renal ischemia, renal infection, diffuse renal disease, and pyonephrosis, has been proved in recent studies [10-14].

Recent studies have pointed out that there is an association between nephrogenic systemic fibrosis (NSF) and the use of gadolinium chelate contrast agents [15-19] in patients with renal failure, especially those with acute on chronic renal disease and glomerular filtration rate (GFR) of lower than 30 mL/min/1.73 m2 [20-21]. Moreover, there has been a relationship between apparent diffusion coefficient (ADC) values and eGFR [22-25].

So far few studies have focused on the relationship between apparent diffusion coefficient (ADC) values and different stages of chronic kidney disease (CKD), and they have suggested various cut-off ADC values [26-30]. In this regard and to fill the research gap, the present study was carried out in order to evaluate the relationship between apparent diffusion coefficient (ADC) values of renal parenchyma and different stages of chronic kidney disease and compare it with serum creatinine and estimated GFR among patients who referred to Rizgary Teaching Hospital in Erbil, the Kurdistan Region of Iraq.

Materials and Methods

Subjects and data collection

The present analytic cross-sectional study was carried out at the Radiology Department of Rizgary Teaching Hospital located in Erbil, the Kurdistan Region of Iraq from September 2017 to April 2018. The statistical population consisted of 62 patients who referred to Rizgary Hospital during the above mentioned period. Out of those 62 patients, 12 were excluded from the study due to severe renal atrophy (3 patients), polycystic kidney disease (3 patients), single kidney (3 patients), hydronephrotic kidneys (2 patients), and claustrophobia (1 patient), which led to a net study population of 50 patients who were divided into two groups.

Group 1 was regarded as the control group and consisted of 12 patients who referred to the radiology department for abdominal MRI for different reasons and were diagnosed with normal renal function parameters. Their serum creatinine level was measured within 1 week before imaging. The second group which was regarded as the patient group consisted of 38 patients who were diagnosed with chronic kidney disease (CKD) with a mean age of 54±15.79 years. All of the patients were informed about the MRI examination to which none of the patients had contraindication. After the subjects were ensured about the privacy of their information, informed consent was obtained from them.

According to K/DOQI CKD (kidney disease outcomes quality initiative) classification [13], the subjects in the patient group were classified into 5 stages of disease severity including Stage 1: eGFR; 90mL/min/1.73m2 (kidney damage with normal or increased eGFR); Stage 2: eGFR; 60–89mL/min/1.73m2 (kidney damage with a mild reduction in eGFR); Stage 3: eGFR; 30–59mL/min/1.73m2 (moderate reduction in eGFR); Stage 4: eGFR; 15–29mL/min/1.73m2 (severe reduction in eGFR); and Stage 5: eGFR; < 15mL/min/1.73m2 (kidney failure).

Chronic kidney disease epidemiology (CKD-EPI) equation was employed to calculate the estimated glomerular filtration rate (eGFR).

DW-MRI protocol

All MRI examinations were performed using a 1.5-T scanner (MAGNETUM Aera, Siemens Healthcare, Germany). Parameters including repetition time (TR) of 2000ms, echo time (TE) of 65 ms, slice thickness of 6 mm, receiver bandwidth of 1964 Hz/pixel, field of view (FOV) of 380 mm, and matrix size of 164×159 were taken into account in all MRI scans.

All of the images were obtained through respiratory triggering and synchronization with diaphragm motion in order to reduce artefacts from respiratory motion and using parallel imaging based on generalized auto-calibrating partially parallel acquisition (GRAPPA) using a twofold acceleration factor.

It should be noted that all MRI scans were evaluated by the same radiologist. ADC values of the kidneys were calculated with diffusion gradient b-values of 50, 400, and 800 s/mm2. Moreover, the standardized diffusion sequence provided by the manufacturer for abdominal and pelvic scanning was employed in order to obtain DW images and ADC maps of good quality. In addition, no intravenous contrast material was used on the acquisition of DWI-ADC sequences.

Image analysis

The ADC values were measured directly from regions of interest (ROIs) manually outlined in the renal parenchyma. As circular ROIs of size 1 cm2 were taken into account, three such ROIs were placed in each kidney; one at the upper, interpolar, and lower pole in axial imaging. However, it is stated that it can be hard to place ROI cursor accurately in cortex or medulla separately [30]. Afterwards, a total of 6 ROIs were obtained from each individual. Finally, the mean of these six ADC values was calculated. The standard laboratory assay was utilized to calculate serum creatinine. The mean ADC values were recorded for each patient, and the relationship of ADC values with CKD stage and serum creatinine levels were evaluated.

Results

According to the results of descriptive statistics, the patient group included 38 subjects whose mean age was 54±15.79 years with a range of 20 to 70 years. Regarding their gender, 17 were men and 21 were women. The descriptive statistics also showed that none of the 12 subjects in the control group had any known risk factors of kidney disease, and all of them had normal blood urea and serum creatinine level which were tested within the first week of MRI examination. With regard to their gender, half of them (n=6) were women and half men (n=6). Their age ranged from 26 to 59 with a mean of 42.6±9.9 years.

The results of K/DOQI CKD (kidney disease outcome quality initiative) classification indicated that out of the 32 CKD patients, 9 belonged to stage 5, 10 to stage 4, 7 to stage 3, 4 to stage 2, and 2 to stage 1.

According to our result, the mean ADC values of normal individuals and different stages of chronic kidney disease were as follows.

Normal: the mean ADC value in both kidneys ranges (1891-2103) with a mean and SD of 1981±52.1
Stage 1: the mean ADC value in both kidneys' ranges (1972-2103) with a mean and SD of 2015±32.5
Stage 2: the mean ADC value in both kidneys ranges (1818-1980) with a mean and SD of 1849±25.32
Stage 3: the mean ADC value in both kidneys ranges (1750-1865) with a mean and SD of 1800.2± 39.5
Stage 4: the mean ADC value in both kidneys ranges (1654-1735) with a mean and SD of 1677+-0.13
Stage 5: the mean ADC value in both kidneys ranges (1485-1645) with a mean and SD of 1560±45.5

The results of Pearson correlation coefficient in the patient group (n=38) revealed that there was a significant inverse correlation between serum creatinine (eGFR) and ADC value (r=-0.78) (See Figure 1).

The results also showed that in the CKD group (n=32) there was a strong positive correlation between ADC and eGFR (R=0.88) (See Figure 2).

Moreover, the results indicated that the patient group had a significantly lower mean ADC value compared to the control group (1648±115.5(x10-6 mm2/s) vs. 1981 ±135.0(x10-6 mm2/s)). Also, the results of Pearson correlation coefficient test in the CKD group revealed that there was a correlation between mean ADC value and stages of CKD. It was also observed that there was a significant difference among stages of CKD regarding mean ADC value (mean ADC value dropped with advance in CKD stages) (See Figures 3 & 4).

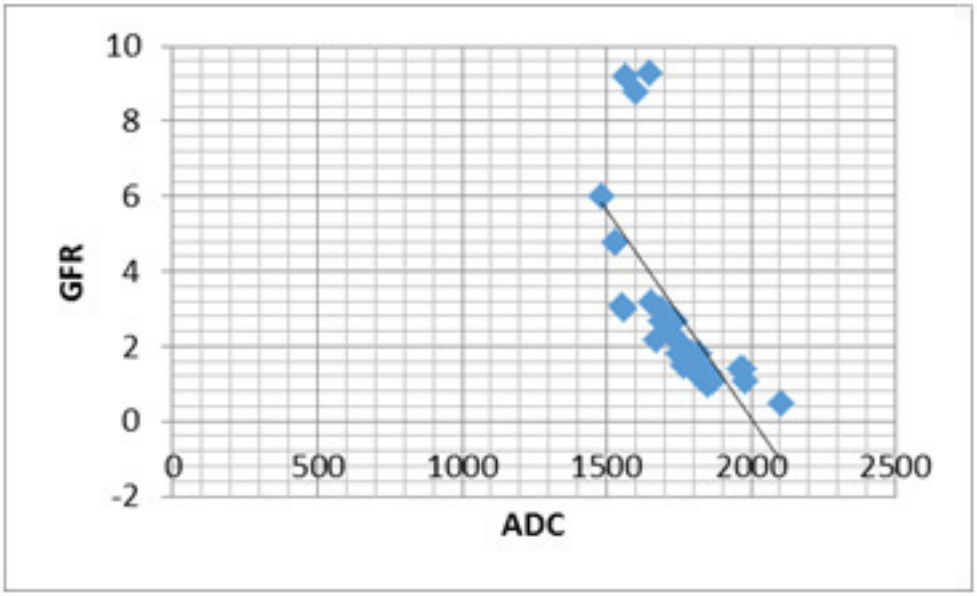


Figure 1: Correlation between ADC value and serum creatinine (eGFR) in the patient group (Stages 1, 2, 3, 4, & 5)

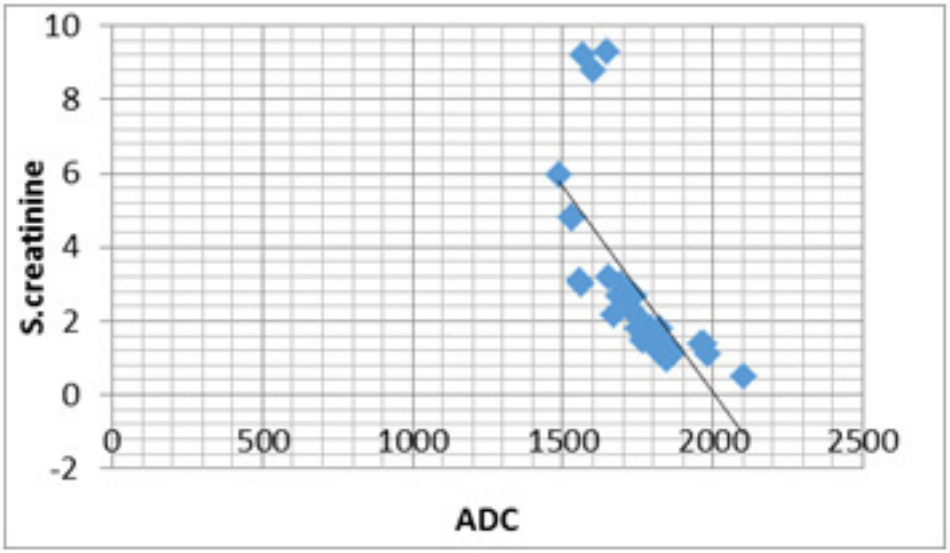


Figure 2: Correlation between ADC and eGFR in the CKD patients

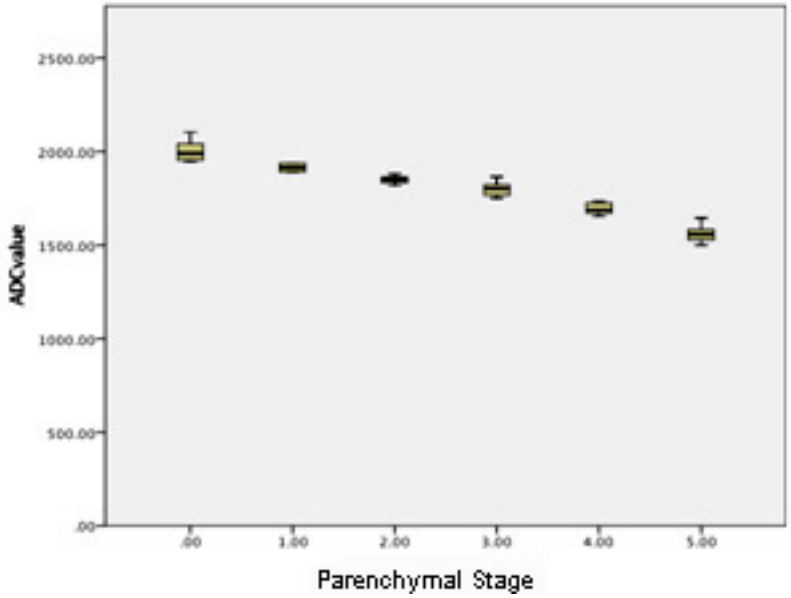
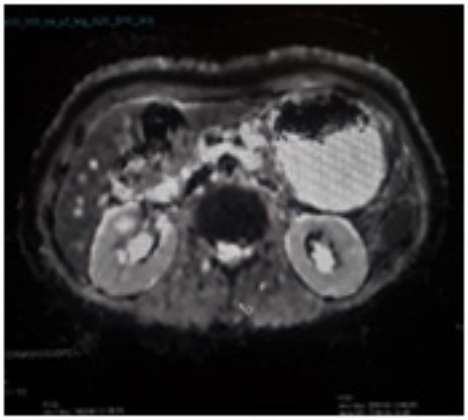
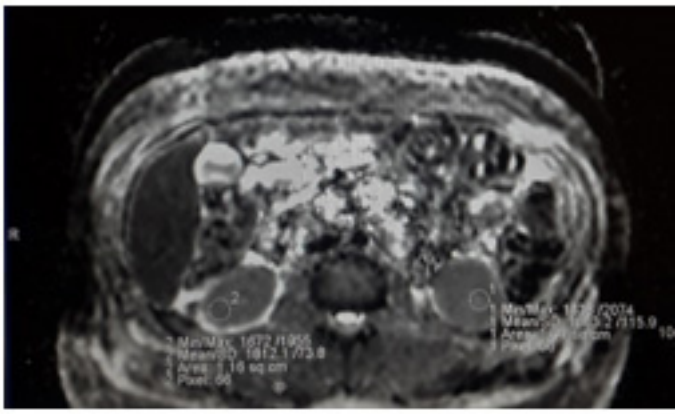


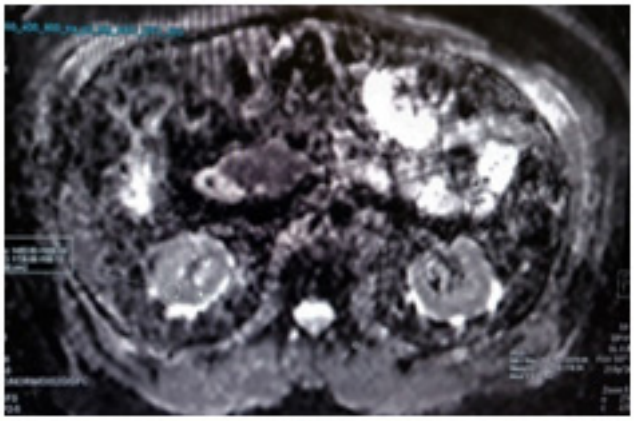
Figure 3: Box plot of mean ADC in different stages of CKD showing decreasing ADC values with increasing stage of CKD



(a)



(b)



(c)

Figure 4. (a) ADC map in a 40-year-old female with normal kidney function (healthy individual), showing no restriction of diffusion, and mean ADC value was 2085 (x10-6 mm2/s). (b) ADC map in a 45-year-old male with CKD (stage 2), showing restricted diffusion in the kidney parenchyma bilaterally with a mean ADC value of 1845 (x10-6 mm2/s). The circles show examples of ROI placement. (c) ADC map in a 62-year-old male with CKD (stage 5), showing restricted diffusion in the kidney parenchyma bilaterally with more decrease in mean ADC value of 1636 (x10-6 mm2/s). It also shows decrease in parenchymal thickness.

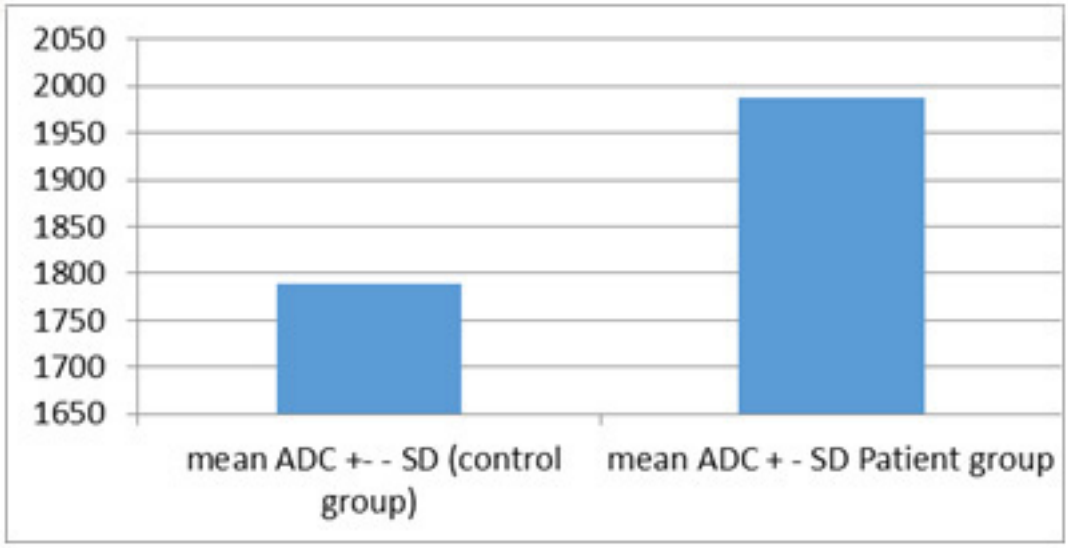


Figure 5. Difference between mean ADC values in the control and patient groups

The results of the present study also indicated that there was a strong positive significant relationship between serum creatinine level and chronic kidney disease stages (r=8.3; p<0.05). There was also a strong positive significant correlation between eGFR and mean ADC value in the patients with CKD at all stages from 1 to 5 (r=0.88; p<0.05) (See Table 1). The results also proved that there was a significant difference between the control and patient groups in terms of their mean ADC values (See Figure 5).

According to the results, there was a moderate negative correlation between serum creatinine level and ADC value in the CKD subjects (r=-0.78), while there was a very weak positive correlation between serum creatinine level and ADC value in the control group (r=0.18), and this difference between the two groups was statistically significant (P<0.05) (See Figures 2 and 3 above).

As indicated in Table 1, an increase in parenchymal stages leads to a rise in the coefficient of the correlation between eGFR and ADC value from 0.22 in the normal group to 0.92 in the worst CKD group (stage 5). Similarly, the coefficient of the correlation between serum creatinine level and ADC value rises from 0.18 in the normal group to 0.87 in the worst CKD group (stage 5). Therefore, it can be concluded that ADC value is a useful diagnostic factor to detect and staging of CKD. As the difference was statistically significant between mean ADC value in patients with stage 3 versus stage 4 and between stage 4 versus 5 because there is a strong significant correlation between ADC in these groups of CKD and both eGFR and serum creatinine level (p<0.05). However, we failed to find significant difference regarding mean ADC values between patients with stage 2 and stage 3. And there was overlap in ADC values between stage 1 and 2 which may be attributed to small number of patients in stage 1 (2) and stage 2 (4) (See Table 1).

Discussion

The results of the present study indicated that there was a significant inverse correlation between serum creatinine (eGFR) and ADC value (r=-0.78) in the patient group, which is in line with the results of previously conducted studies [14, 27, 29]. A strong positive significant relationship between ADC and eGFR (R=0.88) was observed in the CKD group. This finding was also reported by another study [26], while another experiment [28] reported an opposite finding, i.e. lack of significant relationship between eGFR and ADC values.

Furthermore, as the results of the present study indicated, the subject of the patient group with renal dysfunction had a significantly lower mean ADC value compared to the control subjects with normal kidney function. This finding is in agreement with the results of other studies [14, 25, 26, 27, 29]. In justifying this finding, it can be stated that decreased water diffusion and reduced perfusion in renal parenchymal disease lead to a drop in mean ADC value. According to this finding, cut-off ADC values can be used to identify renal dysfunction.

Moreover, different mean ADC values were observed in different stages of CKD, with a decrease in mean ADC value with increase in CKD stages. A similar finding was reported in another study [29]. It should be stated that the obtained cut-off ADC values were similar to those of previously conducted studies [26-30]; therefore, these values can be employed to diagnose stages of CKD.

Also, the results of the present study showed a moderate negative correlation between serum creatinine level and ADC value in the CKD subjects, a very weak positive correlation between serum creatinine level and ADC value in the control group, and a strong significant correlation between ADC and both eGFR and serum creatinine level in the patient group; therefore, ADC values can be employed to distinguish between different stages of CKD. This finding was also reported by another study [29].

Conclusion

In short, ADC values can be employed to examine the degree of renal inefficiency and distinguish different stages of chronic kidney disease (CKD). Therefore, ADC values taken from ADC images can increase the accuracy of examination results and be used as a valuable investigation for assessment of renal function along with serum markers of renal function.

Limitations of the study

The present study had several limitations which should be dealt with in future similar studies. First, the study sample was small; therefore, there were very few patients with stage-1 and stage-2 CKD (n=2 and n=4, respectively) which restricted the possibility of comparing cut-off ADC values in

Table 1. Correlation between ADC value and eGFR and serum creatinine

Chronic kidney disease stages	eGFR-ADC correlation coefficient	P-value	serum creatinine-ADC correlation coefficient	P-value
Normal 0	0.22	0.001	0.18	0.003
Stage 1	0.41	0.0002	0.39	0.001
Stage 2	0.48	0.0001	0.34	0.0003
Stage 3	0.56	0.00007	0.59	0.0002
Stage 4	0.72	0.00006	0.65	0.00003
Stage 5	0.92	0.00004	0.87	0.00002

different stages. Second, the function of each kidney was not evaluated separately, and the correlation between mean ADC values and eGFR was investigated in individual patients. Third, the study did not include acute renal failure cases. Fourth, ADC values were measured manually, which may have involved a degree of subjectivity. Therefore, utilization of computerized ROI demarcation methods with better accuracy are recommended in future studies. Finally, standardized protocol for renal DW-MRI has not been established by manufacturers yet, and this contributes to variation in the absolute ADC values with some changes in expression in different studies including the present research.

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