ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

Med J SDU / SDÜ Tıp Fak Derg ▶ 2020:27(2):220-225 doi: 10.17343/sdutfd.687734

EVALUATION OF DISEASE DURATION AND EFFECT OF DIABETES MELLITUS ON RENAL PARENCHYMAL DIFFUSION MRI SIGNALS IN PATIENTS WITH CHRONIC RENAL FAILURE

KRONİK BÖBREK YETMEZLİĞİNDE HASTALIK SÜRESİ VE DİABETES MELLİTUSUN, RENAL PARANKİM DİFÜZYON MRI SİNYALLERİNE ETKİSİNİN DEĞERLENDİRİLMESİ

Hüseyin AYDIN[1], Abdulkerim SALKACI[2], Adnan KARAİBRAHİMOĞLU[3]

[1] Department of Radiology, Faculty of Medicine, S.Demirel University, Isparta, Turkey.
[2] Department of Radiology. Duzici State Hospital, Osmaniye, Turkey.
[3] Department of Biostatistics, Faculty of Medicine, S.Demirel University, Isparta, Turkey.

Cite this article as: Aydin H, Salkaci A, Karaibrahimoglu A. Evaluation of disease duration and effect of diabetes mellitus on renal parenchymal diffusion MRI signals in patients with chronic renal failure.Med J SDU 2020; 27(2): 220-225.

Öz

Amaç
Kronik böbrek yetmezliğinde (KBY), renal parankimin difüzyon ağırlıklı (DW) magnetik rezonans görüntüleme (MRI) ADC değerlerinde azalma olduğu bilinmektedir. Ancak KBY hastalık süresinin renal ADC değerlerine olan etkisi bilinmemektedir. Bu çalışmada KBY hastalık süresi ve eşlik eden diabetes mellitusun (DM) renal parankimal ADC değerlerine olan etkisi araştırılmıştır.

Gereç ve Yöntem
Bu çalışmada 39 KBY ve eGFR'si normal sınırlarda 30 DM hastası ile 59 kişiden oluşan kontrol grubunun abdominal MR tetkikleri, retrospektif olarak değerlendirildi. KBY hastaları, hastalık süresine göre üç gruba ayrıldı (<5, 5>10< ve >10) ve eGFR'ye göre 1-5 olarak evrelendirildi. ADC ölçümleri, fokal küçük bir alan ve tüm parankimi içeren, iki farklı yöntem ile yapıldı. Bulgular KBY hastalık süresi, DM varlığı, insülin kullanımı ve dializ durumuna göre istatistiksel analize tabi tutularak değerlendirildi.

Bulgular
ADC değerleri KBY hastalarında, evre 2'den itibaren kontrol gurubuna göre anlamlı şekilde düşük ($p<0.05$) iken, kontrol grubu ve evre 1 KBY arasında anlamlı fark saptanmadı. Dializ hastalarında ise ADC değerleri oldukça düşüktü ($p<0.001$). Hastalık süresi, diyabeti varlığı ve insülin kullanımının ADC değerlerine anlamlı bir etkisi saptanmadı ($p>0.05$). Hasta gruplarındaki her iki yöntem ile ADC ölçüm sonuçlarında anlamlı farklılık izlenmezken ($p>0.05$), sağlıklı grupta tüm parankimi içeren ROI ölçümleri, istatistiksel olarak anlamlı derecede düşük izlenmiştir ($p<0,05$).

Sonuç
KBY hastalarında KBY hastalık süresi, DM varlığı ve insülin kullanımının renal parankimal ADC değerlerine anlamlı bir etkisi yoktur.

Anahtar Kelimeler: Manyetik rezonanas görüntüleme, böbre yetmezliği, kronik, diabetik nefropati.

Abstract

Objective
It is known that in chronic renal failure (CRF), diffusion weighted (DW) magnetic resonance imaging (MRI) ADC values of the renal parenchyma are reduced.

İletişim kurulacak yazar/Corresponding author: huseyinrady@gmail.com
Müracaat tarihi/Application Date: 11.02.2020 • Kabul tarihi/Accepted Date: 18.02.2020
Available online at http://dergipark.gov.tr/sdutfd
Makaleye http://dergipark.gov.tr/sdutfd web sayfasından ulaşılabilir.

However, the effect of CRF disease duration on renal ADC values is unknown. In this study, the effect of CRF disease duration and accompanying DM on renal parenchymal ADC values was investigated.

Materials and Methods
In this study, abdominal MR examinations of 39 CRF and 30 DM patients (eGFR within normal limits) and 59 control subjects were evaluated retrospectively. CRF patients were divided into three groups according to disease duration (>5, 5-10, and >10) and were staged as 1-5 according to the eGFR results. ADC measurements were made by two different methods, including a focal small area and the entire parenchyma. The findings were evaluated by statistical analysis according to the duration of CRF, presence of DM, insulin use and dialysis status.

Results
ADC values were significantly lower in CRF patients compared to the control group since stage 2 ($p < 0.05$), while there was no significant difference between the control group and stage 1 CRF. ADC values were quite low in dialysis patients ($p < 0.001$). Disease duration, presence of diabetes and insulin use did not significantly contribute to ADC values ($p > 0.05$). While no significant difference was observed in the ADC measurement results with both methods in the patient groups ($p > 0.05$), ROI measurements containing the entire parenchyma in the healthy group were statistically significantly lower ($p < 0.05$).

Conclusion
In CRF patients, the duration of CRF disease, the presence of DM and insulin use have no significant contribution to renal parenchymal ADC values.

Keywords: Diffusion Magnetic Resonance Imaging, Renal Failure, Chronic, Diabetic Nephropathy.

Introduction

Diffusion-weighted imaging (DWI) is a Magnetic Resonance Imaging (MRI) technique based on changes in the diffusion properties of water molecules in the tissue. DWI can be used to assess kidney function, as major renal functions such as glomerular filtration, tubular reabsorption and secretion are associated with the diffusion of water (1–4). Free movement of water in the extravascular space is restricted in chronic renal parenchyma due to chronic tissue hypoxia, cellular edema and cell damage. In many studies, there was a decrease in renal parenchyma ADC values (1,5–8). However, as far as we know, there is no study on the effect of the duration of chronic renal failure (CRF) on ADC values. Similar results are expected with ADC changes in non-diabetic CRF, as diabetes mellitus (DM) patients also experience nephropathic changes resulting in cell edema, cellular damage and atrophy due to hemodynamic disorders and chronic hypoxia. However, the relationship between ADC values in diabetic and non-diabetic CRF patients are also unclear.

In this study, the effect of CRF disease duration, presence of DM and the use of insulin on renal parenchymal ADC values were investigated.

Materials And Methods

Patient selection
Between September 2015 - September 2017, 128 patients with MR images in our hospital's PACS were included in the study. Patient groups (CRF, DM, use of insulin, dialysis) were identified according to laboratory results with patient information and reports registered in PACS. According to the nearest eGFR in the MR examination, CRF patients were staged from 1 to 5. Patients were divided into three groups according to the duration of CRF (0-5 years, Group 1; 5-10 years, Group 2; 10 years and above, Group 3). According to the data in PACS, the control group was made up of individuals who did not have any known diabetes, urinary system disease, malignancy, chronic and systemic diseases, but who had undergone MR for any reason. Approval was obtained from the ethics committee of our hospital for this study (14.02.2018 / 38).

MR Examination Parameters
MRI examinations were performed with a 1.5 Tesla MAGNETOM Avanto (Siemens Medical Solutions, Erlangen, Germany) device. MRI examinations were obtained in a supine position without the need for sedation and using a 16-channel “body coil”. Axial and coronal plane turbo spin-echo T2W without fat saturation, axial plane gradient echo with fat saturation T1 VIBE images and axial plane Dixon imaging and single plane DWI were taken. MR examination parameters are presented in Table 1.

Evaluation of Images
The images were transferred from our hospital's

Table 1 Magnetic resonance examination parameters.

Turbo Spin Echo T2W		**GRE Fat Saturated T1W VIBE**	
Voxel (mm)	1 x 1 x 6	Voksel size (mm)	0,6 x 0,6 x 3
FOV (mm)	320	FOV (mm)	380
Slice Thickness (mm)	6	Slice Thickness (mm)	3
Phase direction	R L	TR (msec)	5.03
TE (msec)	93	TE (msec)	2,41
Matrix (mm)	195 x 320	Matrix (mm)	240 x 320
Avarage(Next)	1	Avarage (Next)	1
Bandwidth (Hz/Px)	260	Band width (Hz/Px)	350
SNR	1.0	Paralel Imaging (PAT)	Off
Diffusion Weighted Imaging (DWI)		**DIXON**	
Voxel size (mm)	1 x 1 x 0,6	Voksel size (mm)	0,6 x 0,6 x 3
FOV(mm)	400	FOV (mm)	380
Slice Thickness (mm)	6	Slice Thickness (mm)	3
Phase direction	A P	TR (msec)	7.1
TR (msec)	5200	TE (msec)	2,39
TE (msec)	72	Matrix (mm)	240 x 320
Matrix (mm)	128 x 192	Avarage (Next)	1
Avarage (Next) (b1, b2)	3,6	Band width (Hz/Px)	490
b1, b2 (sec/mm^2)	50, 800	Paralel Imaging (PAT)	Off

PACS to FDA approved Mac OS X radiology workstation. Measurements were performed in one go by a single radiologist (AŞ) with four years of abdominal MR experience. Firstly, morphological evaluation of the area to be measured in terms of an artifact, cyst, mass foreign body and vascular structure was performed in both kidney T2W axial MRI sections. Then, measurements were made using two different methods in the section through the renal hilus level from ADC images obtained by using 800 sec/mm2 b value. In the first method, the region of interest (ROI) was drawn by hand to cover the entire renal parenchyma. In the second method, three measurements were made, averaged using a 30 mm2 circular ROI from the areas where the corticomedullary junction was best tracked, and ADC values were automatically obtained in mm^2/s.

Statistical Evaluation

The descriptive statistics were presented as frequency (percentage) and mean±SD. Continuous variables were checked by the Kolmogorov-Smirnov test for normality. Mann-Whitney U test and Kruskal-Wallis test was preferred for independent group comparisons due to non-normal distribution. The chi - square test was used to determine the relations between categorical, and Spearman's Rho correlation analysis for numerical variables. For a 5% Type-I error, $p<0.05$value was considered a statistically significant result.

Results

A total of 128 individuals were included in the study. Sixty-one of the subjects were female (47.66%), 67 were male (52.34%) and the mean age of the patients was 53.46 ± 14.99 years, respectively. The patient with CRF was 30.47% (n = 39) and the rate of diabetic patients was 40.6% (n = 52). The clinical status of the individuals constituting the study group is shown in Table 2. The rate of patients using insulin was 7% (n = 9) and the rate of patients undergoing dialysis was 3.9% (n = 5). According to the duration of diagnosis of CRF, 46.2% (n = 18) of the patients were Group 1, 20.5% (n = 8) were Group 2 and 33.3% (n = 13) were Group 3.

According to gender, right and left kidney ADC measurement values did not differ significantly in either method. The differences between both kidney ADC measurements were not statistically significant in all

groups (p> 0.05). Although ADC measurements were lower in patients using insulin than those who did not use insulin, this difference was not statistically significant.

There was no significant difference between stage 1 CRF and control group ADC mean values (p> 0.05). However, in other CRF stages, ADC values were significantly lower in both methods compared to the control group (p <0.05). No statistically significant difference was found in ADC values between stage 2, 3 and 4 CRF patients (p>0.05). ADC measurements were quite low in a small number of dialysis patients (p <0.001). In ADC values between stage 1 and stage 2 CRF, a significant difference was found in the right kidney, and in stage 2 CRF, the right kidney ADC values were significantly lower. Accordingly, ROC analysis of ADC measurements was performed between 1st and 2nd stage CRF patient groups. As a result of the analysis, only the area under the curve for right kidney 1st and 2nd method ADC measurements was found significant. For the first method, the ADC cut-off value measured in the right kidney was 1.82 mm2 / sec, and the sensitivity and the specificity ratios were 68% and 67%, respectively. The cut-off value obtained by the second method was 1.85 mm2 / s and the sensitivity and the specificity ratios were calculated as 71.5% and 70.8%, respectively (Table 3). ADC measurements obtained for the left kidneys did not have a significant ROC curve, but since the significance values were very close to the type-I error rate, it was thought that meaningful results could be obtained if the number of patients increased.

The effect of the duration of CRF on the measurements was investigated. ADC measurements fell slightly, as disease duration increased. However, this was not statistically significant (p> 0.05) (Table 4).

The presence of DM and insulin use in CRF patients did not lead to a significant difference in ADC measurements (p> 0.05) (Table 2). All ADC measurements were significantly lower in dialysis patients than in other CRF patients.

Comparisons were made between ADC measurement methods in groups with and without CRF. In the non-CRF group, all ADC measurements were higher with the 2nd method and this was statistically significant (p <0.05) However, there was no statistically significant difference between the measurement methods results in CRF patients.

Table 2 ADC values for both kidneys in the study groups.

	Methods			
	1st		2nd	
Groups (n)	**Right**	**Left**	**Right**	**Left**
Control (59)	1,8 ±0,1	1,8 ±0,1	1,8 ±0,1	1,8 ±0,1
CRF (17)	1,7 ±0,2	1,7 ±0,2	1,7 ±0,1	1,7 ±0,2
CRF+DM (52)	1,7 ±0,2	1,7 ±0,1	1,7 ±0,2	1,7 ±0,2
DM (30)	1,8 ±0,1	1,7 ±0,1	1,7 ±0,2	1,8 ±0,1
DM+Insuline (9)	1,7 ±0,1	1,7 ±0,1	1,7 ±0,2	1,7 ±0,1
Dialyse (5)	1,4 ±0,2	1,5 ±0,1	1,4 ±0,1	1,4 ±0,1

Table 3 Results of right and left ADC measurements in first and second stage CRF patients.

	Methods			
CRF	**1st**	**2nd**	**1st**	**2nd**
	Right		**Left**	
Stage 1 (n=24)	1,8 ±0,1	1,8 ±0,2	1,8 ±0,1	1,8 ±0,2
Stage 2 (n=30)	1,7 0,2*	1,7±0,1**	1,7 ±0,1	1,7 ±0,1

* significant in P < 0.05 level according to Mann-Whitney U test
** Significant at P < 0.05 level according to ROC analysis

Table 4 Descriptive measurements of measurement results according to the duration of CRF

	Methods			
CRF duration year (n)	**1st**	**2nd**	**1st**	**2nd**
	Right		**Left**	
0-5 (18)	1,7 ±0,2	1,7 ±0,2	1,7 ±0,2	1,7 ±0,2
5-10 (8)	1,7 ±0,1	1,7 ±0,1	1,7 ±0,1	1,7 ±0,1
10+ (13)	1,7 ±0,2	1,7 ±0,2	1,6 ±0,2	1,7 ±0,2
p	0,871	0,972	0,573	0,996

Discussion

As far as we know, this study is the first study to investigate the effect of the duration of CRF disease on renal parenchyma ADC values. According to our findings, the duration of CRF did not cause a significant change in ADC measurements in both kidneys. There was also no significant relationship between the duration of CRF and e-GFR.

In this study, in accordance with the literature, a significant decrease was found in ADC values from stage 2 in CRF patients compared to the control group ($p < 0.05$). The 1.82 mm2 / sec ADC cut-off value obtained by the first method from the right kidney separated stage-1 from stage-2, with 68% sensitivity and 67% specificity rates. These ratios are 71.5% and 70.8%, respectively, according to the ADC cut-off value of 1.85 mm2 / s in method 2. It is understood that there is a tendency for the left kidney close to the right kidney measurements. According to these results, statistically significant ADC changes in CRF begin at stage 2 and distinguish stage1 from stage 2. However, since there was no significant correlation between ADC measurement values and e-GFR in stages 2, 3, and 4 CRFs, ADC values separating these stages could not be defined.

In studies conducted to date, the decrease in renal parenchymal ADC values in CRF patients is a common opinion, but different results have been reported about ADC changes according to clinical stages. Li et al found a negative correlation between ADC values and histopathological score in patients classified according to renal biopsy, but could not show the same correlation (as in our study) between GFR and ADC (9). Unlike these studies, however, many recent studies have reported a positive correlation between GFR and ADC values (1,4,6–8,10–12). Two studies involving stage 1 and stage 2 CRF patients, a gradual decrease in CRF stage and ADC values, and a positive correlation between ADC values and GFR (4,11). Toya et al. reported a significant difference in ADC measurements between stage 4 and stage 5 CRF values of b = 50 and b = 1000 s / mm2. (8). According to the results of renal biopsy, Xu et al. found that while ADC values found a negative correlation with tubulointerstitial diseases, there was no correlation in glomerular lesions (13). The most important reasons for reporting different ADC values in these studies are the use of different b values and ROI techniques. For this reason, it has become difficult to catch a certain standard and determine the cut-off value in the numerical values measured.

There was no significant correlation between e-GFR and ADC values in patients with DM in this study. There was no significant correlation between kidney ADC values and e-GFR in diabetic CRF patients. In other words, accompanying DM in patients with CRF did not affect ADC values. Chronic hypoxia, edema and cell damage due to vascular circulatory disorders are common physiopathological changes in both diabetic and non-diabetic CRF. Therefore, it was thought that there was no significant difference between these two groups' ADC values. Similarly, the use of insulin did not cause any change in ADC values in both DM patients and DM patients with CRF. One study reported a negative correlation between ADC and the clinical stage of nephropathy in diabetic nephropathy patients (14). In another study, it was reported that diffusion restriction started in diabetic nephropathy before microalbuminuria developed (15).

Another important finding in this study is that in the patient group with CRF, close values are calculated for all ADC measurements between both measurement methods, while all measurements made with the 2nd method in the healthy group are statistically significantly higher. Since the diameter of the ROI (30 mm2) used in the second method is quite small, it cannot represent the entire parenchyma. In the

healthy population or early-stage renal parenchymal injury, the presence of areas of focal involvement, as well as intact parenchyma, causes an error in focal ROI measurements. Therefore, we suggest that parenchymal ADC measurement should be performed in healthy individuals or early-stage CRF patients using the ROI containing the entire parenchyma in a single section.

There were some limitations to this study. 1) Since measurements were made by one radiologist at a time, intra-observer and intra-observer compliance could not be evaluated. However, for the second method, at least three measurements were made from each kidney, averaged, and the error rate was tried to be reduced. 2) Since there is no biopsy in patients, the relationship between disease severity and ADC is not clear.

In conclusion, the duration of CRF disease, the presence of diabetes mellitus, and insulin use have no significant effect on renal parenchymal ADC values in CRF patients. However, there is a negative correlation between the severity of the CRF and the ADC values. Also, according to ADC values, stage 1 CRF can be distinguished from stage 2. In early-stage CRF, it is more appropriate to use ROI with all parenchyma in ADC measurement.

Acknowledge: We are grateful to Associate Professor Ugur Toprak, M.D. for his careful reading of the manuscript and helpful comments and suggestions.

References

1. Goyal A, Sharma R, Bhalla AS, Gamanagatti S, Seth A. Diffusion-weighted MRI in assessment of renal dysfunction. Indian J Radiol Imaging. 2012;22(3):155.
2. Mahmoud H, Buchanan C, Francis ST, Selby NM. Imaging the kidney using magnetic resonance techniques: structure to function. Curr Opin Nephrol Hypertens. 2016;25(6):487–93.
3. Namimoto T, Yamashita Y, Mitsuzaki K, Nakayama Y, Tang Y, Takahashi M. Measurement of the apparent diffusion coefficient in diffuse renal disease by diffusion-weighted echo-planar MR imaging. J Magn Reson Imaging An Off J Int Soc Magn Reson Med. 1999;9(6):832–7.
4. Albayrak E, Altunkaş A. Kronik Böbrek Hastalığında Böbrek Fonksiyonlarının Difüzyon Ağırlıklı Manyetik Rezonans Görüntüleme ile Değerlendirilmesi. Çağdaş Tıp Derg. 7(4):300–5.
5. Thoeny HC, De Keyzer F, Oyen RH, Peeters RR. Diffusion-weighted MR imaging of kidneys in healthy volunteers and patients with parenchymal diseases: initial experience. Radiology. 2005;235(3):911–7.
6. Xu Y, Wang X, Jiang X. Relationship between the renal apparent diffusion coefficient and glomerular filtration rate: preliminary experience. J Magn Reson Imaging An Off J Int Soc Magn Reson Med. 2007;26(3):678–81.
7. Xu X, Fang W, Ling H, Chai W, Chen K. Diffusion-weighted MR imaging of kidneys in patients with chronic kidney disease: initial study. Eur Radiol. 2010;20(4):978–83.
8. Toya R, Naganawa S, Kawai H, Ikeda M. Correlation between estimated glomerular filtration rate (eGFR) and apparent diffusion coefficient (ADC) values of the kidneys. Magn Reson Med Sci. 2010;9(2):59–64.
9. Li Q, Li J, Zhang L, Chen Y, Zhang M, Yan F. Diffusion-weighted imaging in assessing renal pathology of chronic kidney disease: A preliminary clinical study. Eur J Radiol. 2014;83(5):756–62.
10. Zhao J, Wang ZJ, Liu M, Zhu J, Zhang X, Zhang T, et al. Assessment of renal fibrosis in chronic kidney disease using diffusion-weighted MRI. Clin Radiol. 2014;69(11):1117–22.
11. Yalçin-Şafak K, Ayyildiz M, Ünel SY, Umarusman-Tanju N, Akca A, Baysal T. The relationship of ADC values of renal parenchyma with CKD stage and serum creatinine levels. Eur J Radiol open. 2016;3:8–11.
12. Carbone SF, Gaggioli E, Ricci V, Mazzei F, Mazzei MA, Volterrani L. Diffusion-weighted magnetic resonance imaging in the evaluation of renal function: a preliminary study. Radiol Med. 2007;112(8):1201–10.
13. Xu X, Palmer SL, Lin X, Li W, Chen K, Yan F, et al. Diffusion-weighted imaging and pathology of chronic kidney disease: initial study. Abdom Radiol. 2018;43(7):1749–55.
14. Çakmak P, Yağcı AB, Dursun B, Herek D, Fenkçi SM. Renal diffusion-weighted imaging in diabetic nephropathy: correlation with clinical stages of disease. Diagnostic Interv Radiol. 2014;20(5):374.
15. Chen X, Xiao W, Li X, He J, Huang X, Tan Y. In vivo evaluation of renal function using diffusion weighted imaging and diffusion tensor imaging in type 2 diabetics with normoalbuminuria versus microalbuminuria. Front Med. 2014;8(4):471–6.