MAJOR PAPER

Correlation between Estimated Glomerular Filtration Rate (eGFR) and Apparent Diffusion Coefficient (ADC) Values of the Kidneys

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Purpose: Study of the kidney by apparent diffusion coefficient (ADC) measurements is interesting because of the organ's high blood flow and water transport functions. We investigated the relationship between ADC values of the kidney and the estimated glomerular filtration rate (eGFR).

Methods: We retrospectively evaluated 180 patients (113 men, 67 women, aged 20 to 89 years, mean age, 61.06 years) who underwent abdominal magnetic resonance (MR) imaging at 1.5 tesla. Transverse multisection echo-planar diffusion-weighted imaging (DWI) was performed using diffusion gradient b-values of 50 and 1000 s/mm². Regions of interests (ROIs) were manually delineated in the parenchyma as large as possible at the level of the middle portion of the bilateral kidneys. For each kidney, 2 nonoverlapping ROIs were placed at different locations; 4 total ROIs from the bilateral kidneys were averaged for each patient. ADC values were measured directly from the ROIs. The eGFR was calculated by an equation based on serum creatinine level. The patients were divided into 3 groups: eGFR < 30 mL/min/1.73 m²; 30 ≤ eGFR < 60; and 60 ≤ eGFR.

Results: The mean ADC values of the 3 groups were 1.71 ± 0.18 for the group with eGFR < 30 mL/min/1.73 m²; 1.87 ± 0.11 for those with eGFR ≥ 30; and 1.88 ± 0.12 × 10⁻³ mm²/s for those with eGFR ≥ 60. The mean ADC values were significantly lower in the patients with eGFR < 30 than in the other groups (*P* < 0.05); no difference was found between the other groups; and there was no statistically significant correlation between mean ADC and eGFR values.

Conclusion: Patients with low eGFR tended to have lower ADC values. However, this study failed to show significant correlation between mean ADC values and eGFR.

Keywords: *ADC, GFR, kidney, MRI*

Introduction

Diffusion-weighted magnetic resonance (MR) imaging (DWI) is used to show Brownian motion of the water molecules of tissue,¹ can be used to differentiate normal and abnormal structures of tissues, and may help characterize various abnormalities. The apparent diffusion coefficient (ADC) is a quantitative parameter calculated from MR DWI, a noninvasive technique, that combines the effects of capillary perfusion and water diffusion in the extracellular extravascular space.¹

Recently, nephrogenic systemic fibrosis (NSF) has been associated with the use of gadolinium che-

late contrast agents,²⁻⁷ and such association has been reported in patients with renal insufficiency, particularly those with acute or chronic renal disease and glomerular filtration rate (GFR) lower than 30 mL/min/1.73 m².^{2,8,9} Thus, GFR is an important consideration when contemplating use of these contrast media. A relationship has also been noted between ADC values and GFR.¹⁰⁻¹³

We aimed to investigate the relationship between ADC values of the kidney and eGFR.

Materials and Methods

Patients

Between February 2008 and January 2009, 305 patients underwent upper abdominal MR imaging using the scan parameters shown below. 203 of 305

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had blood test containing serum creatinine level within 2 weeks from MR imaging. From the 203, we excluded 23 patients with acute renal failure ($n=3$), large mass lesion of the kidney ($n=3$), a single kidney ($n=6$), strong parenchymal atrophy ($n=3$), autosomal dominant polycystic kidney disease ($n=2$), or severe distortion artifact due to metallic objects or gas ($n=6$). Thus, the final study population comprised 180 patients (113 men, 67 women; aged 20 to 89 years, mean age, 61.06 years) who had undergone abdominal MR imaging for abdominal screening ($n=46$), characterization of liver mass ($n=77$), adrenal mass ($n=5$), mass of other abdominal organs ($n=5$), investigation of bile duct or pancreatic duct ($n=42$), adenomyomatosis of the gallbladder ($n=1$), or abdominal aortic stenosis ($n=2$). Three of the 180 had IgA nephropathy, and 32 had hypertension. Six of 24 patients with diabetes mellitus also had diabetic nephropathy. Previous study reported that hydration state did not significantly influence mean ADC values under normal conditions.^{14,15} In this study, patients underwent imaging after more than 4 hours' fasting.

Each GFR was calculated using an equation recently reported by the Japanese Society of Nephrology for estimating GFR (eGFR) in Japanese patients based on serum creatinine level (Cr): $\text{eGFR (mL/min/1.73 m}^2\text{)} = 194 \times \text{Cr}^{-1.094} \times \text{Age}^{-0.287}$ (if female, $\times 0.739$). Serum Cr within 2 weeks from the MR imaging examination was used (mean interval, 0.417 day). The patients were divided into 3 groups, $\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$ ($n=5$); $30 \leq \text{eGFR} < 60$ ($n=47$); and $60 \leq \text{eGFR}$ ($n=128$). In the 5 patients with $\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$, renal insufficiency resulted from unknown reasons in 2 patients and from both diabetic nephropathy and hypertension in three.

MR imaging

Patients underwent transverse multisection single shot spin-echo echo-planar DWI with diffusion gradient b-values of 50 and 1000 s/mm^2 on a 1.5-tesla MR imager (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) with 16 channel-body matrix phased-array coil. The scan parameters were: repetition time (TR)=1500 to 3000 ms; echo time (TE)=75 ms; bandwidth=1158 kHz/pixel; 6 excitations (NEX); 8.0-mm slice thickness; 1-mm intersection gap; field of view (FOV)= $400 \times 320 \text{ mm}$; matrix size= 160×92 ; phase partial Fourier factor=6/8; and imaging time, about 180 to 420 s. Sequences were performed along the 3 orthogonal directions to minimize the effects of anisotropy. Generalized auto-calibrating partially parallel acquisitions (GRAPPA) tech-

nique was applied with an acceleration factor of 2. All images were obtained by respiratory triggering and synchronization with diaphragm motion to reduce artifacts from respiratory motion.

Image analysis

ADC maps were calculated automatically by the following equation using 2 b-values, 50 s/mm^2 (b_0) and 1000 s/mm^2 (b_1): $\text{ADC} = (\log \text{SI}_0 - \log \text{SI}_1) / (b_1 - b_0)$, where SI_0 and SI_1 are the signal intensities measured on the images corresponding to diffusion factors b_0 and b_1 . The ADC values were measured directly from regions of interest (ROIs) manually delineated in the parenchyma as large as possible at the level of the middle portion of the bilateral kidneys in axial imaging; the ROIs were outside cysts. The ROI cursors were placed at the approximate level of the corticomedullary junction, not separately at the renal cortex and medulla. The circular ROIs measured no less than 200 mm^2 . For each kidney, 2 nonoverlapping ROIs were placed at different locations; 4 total ROIs from the bilateral kidneys were averaged for each patient (Fig. 1). The relationship between ADC values and GFR were evaluated.

Statistical analysis

We evaluated all statistics using Statcel 2 software package (OMS Publishing, Tokorozawa, Japan) and analyzed the differences in ADC values among the 3 groups by Bonferroni/Dunn test. $P < 0.05$ was considered statistically significant. We assessed the relationship between ADC values and eGFR with Pearson's correlation coefficient test.

Fig. 1. Apparent diffusion coefficient (ADC) map. Regions of interest (ROIs) were placed in the central portion of the bilateral kidneys in axial imaging. Two ROIs were placed on each kidney, and the ADC was averaged from 4 ROIs for each patient.

Results

Figure 2 shows the relationship between age and eGFR of sample data. The mean ADC values of the 3 groups were 1.71 ± 0.18 for those with $\text{eGFR} < 30$ mL/min/1.73 m²; 1.87 ± 0.11 for those with $30 \leq \text{eGFR} < 60$; and $1.88 \pm 0.12 \times 10^{-3} \text{mm}^2/\text{s}$ for those

with $60 \leq \text{eGFR}$. The mean ADC values of the patients with $\text{eGFR} < 30$ group were significantly lower than those of the other groups ($P < 0.05$). However, no difference between the other groups was found (Fig. 3). There was no statistically significant correlation between mean ADC values and eGFR ($P = 0.643$) (Fig. 4).

Fig. 2. Plots show age and estimated glomerular filtration rates (eGFR) in this study, which included 180 patients aged 20 to 89 years (mean age, 61.06 years).

Fig. 3. Graph illustrates mean apparent diffusion coefficients (ADC) in the 3 groups, with estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m² ($n = 5$); $30 \leq \text{eGFR} < 60$ ($n = 47$); and $60 \leq \text{eGFR}$ ($n = 128$). The mean ADC values of the 3 groups were 1.71 ± 0.18 for those with $\text{eGFR} < 30$ mL/min/1.73 m²; 1.87 ± 0.11 for those with $30 \leq \text{eGFR} < 60$; and $1.88 \pm 0.12 \times 10^{-3} \text{mm}^2/\text{s}$ for those with $60 \leq \text{eGFR}$. There were significant differences in ADC values between the group with $\text{eGFR} < 30$ and the others. However, the ADCs were not significantly different between the group with $30 \leq \text{eGFR} < 60$ group and that with $60 \leq \text{eGFR}$. (※: $P < 0.05$, n.s.: not significant)

Fig. 4. The relationship between apparent diffusion coefficient (ADC) values of the kidney and the estimated glomerular filtration rate (eGFR). There was no significant correlation. ($P=0.643$, $r=0.032612$)

Discussion

DWI allows noninvasive measurement of ADC values and, in a clinical setting, provides simultaneous information on diffusion and perfusion. When applying high b-values, the influence of perfusion is largely cancelled out, and the ADC value approximates diffusion. On the other hand, low b-values are influenced by both perfusion and diffusion. In the present study, by applying b-values of 50 and 1000 s/mm² rather than 0 and 1000 s/mm², we could somewhat reduce the contribution of the vascular signal of large vessels.

Recently, DWI has been used to assess extra-cranial organs, such as for functional evaluation of kidneys.¹⁶ The kidney is an interesting organ to study by ADC measurements because of its high blood flow and water transport functions. The microscopic structure and function of the kidney are closely linked.^{17,18} Chronic renal failure (CRF) is characterized by loss of the nephron and by fibrosis, which reduce water transport functions and thereby restrict molecular motion. ADC values in the kidneys of patients with CRF and acute renal failure (ARF) have been reported to be significantly lower than those of normal kidneys using b-values of 30 and 300 s/mm².¹⁰ Toyoshima and associates reported significantly lower mean values for ADC for dysfunctioning than normal functioning hydro-nephrotic kidneys using b-values of 30, 90, and 300 s/mm².¹² Xu and colleagues reported significantly lower ADCs in impaired than normal kidneys and observed a positive correlation between the ADCs and GFR using b-values of 0 and 500 s/mm².¹¹

Previous studies of the relationship between kidney ADC values and eGFR used lower b-factors. Use of lower b-factors than that in our study might have resulted in significant correlation between mean ADC values and eGFR because of the dominant contribution of perfusion effects to the ADC values of the kidney with lower b-values.

It is also important to choose ROIs in the proper portion of the kidney. Evaluation of ADC values in the middle portion of the kidneys is suggested to be less influenced by the perfusion effect.¹⁹ Furthermore, previous reports indicated difficulty and inaccuracy in placing the ROI cursor separately on the thin cortex and small medulla area of the kidney.^{20,21} Therefore, we placed ROI cursors in the middle portion and at the approximate level of the corticomedullary junction, not separately at the renal cortex and medulla.

As mentioned, Xu and colleagues reported a positive correlation between ADCs and GFR. Their study differed from ours by the portion or area of ROI placement and calculation of GFR as well as by b-factor used. They used the entire renal parenchyma at each kidney as the ROI. They focused each kidney separately, using each unilateral GFR by renal scintigraphy. In contrast, our study designated ROIs in only parts of each kidney, irrespective of site, and we used the mean ADC of 4 ROIs from the bilateral kidneys. We investigated eGFR by the individual patient, not by each kidney, employing the eGFR equation using serum creatinine level. From the results of the present study, it is considered that it may be difficult to predict eGFR in individual patient from ADC of kidney.

Race or body surface area may influence some GFR-estimating equations based on serum creatinine level. Recently, data were collected regarding inulin clearance and serum creatinine level in Japanese, and the Japanese Society of Nephrology examined the estimated GFR equation for Japanese, an equation applied only to adults.²² The Japan Radiological Society recommends this equation to estimate GFR when gadolinium chelate contrast agents are used.

Our study has some limitations, including the small number of cases and small variety of renal dysfunctions represented, limited position for each kidney measurement, and placement of ROIs that covered only a part of each kidney. Furthermore, MR images are influenced by respiration motion; ADC values are not stable; and the difference in ADC values may not always be significant. We eliminated patients with acute renal failure because of the instability of the level of serum creatinine in this condition. Serum creatinine levels can also be affected by factors such as dehydration, muscle atrophy, and edema. Thus, estimating GFR using only Cr may be a limitation. Further, the b-value should be optimized before performing prospective study in the future.

Conclusions

Patients with low eGFR tended to have lower ADC values. However, this study failed to show significant correlation between mean ADC and eGFR values using b-values of 50 and 1000 s/mm². It may be difficult to estimate eGFR only from renal ADC values.

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