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ORIGINAL ARTICLE

The effect of hypertension on the apparent diffusion coefficient values of kidneys

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PURPOSE
The purpose of this study was to diagnose hypertension-induced renal microvascular dysfunction using renal diffusion magnetic resonance imaging (MRI) and to identify any correlation between blood pressure level and apparent diffusion coefficient (ADC) values.

MATERIALS AND METHODS
The study included 77 consecutive patients (41 women and 36 men). The patients were divided into 4 groups according to their blood pressure level. Group 1 consisted of normotensive control patients; group 2, pre-hypertensive patients; group 3, stage 1 hypertensive patients; and group 4, stage 2 hypertensive patients. All patients underwent transverse diffusion-weighted multi-section echo-planar MRI. In the transverse ADC maps, rectangular regions of interest were placed in the cortex at 3 sites (upper, middle, and lower pole) of each kidney. The ADCs of the kidneys were calculated separately for low, average, and high b values to enable the differentiation of the relative influence of the perfusion fraction and true diffusion. In addition, a multi-slab balanced turbo field-echo magnetic resonance angiographic technique (without the use of a contrast agent) was used to exclude renal artery stenosis.

RESULTS
There was no statistically significant difference between the groups in age, and no significant correlation between the ADC values of both kidneys and blood pressure level in each group ($P > 0.05$). In addition, the ADC values of patients with microalbuminuria did not differ from those of the other patients ($P > 0.05$).

CONCLUSION
Despite the end-organ damage caused by hypertension, renal microvascular functions were preserved and hypertension did not affect ADC values.

Key words: • *hypertension* • *diffusion-weighted MRI* • *end-organ damage* • *kidney*

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The apparent diffusion coefficient (ADC), as a quantitative parameter calculated from diffusion-weighted magnetic resonance images, combines the effects of capillary perfusion and water diffusion in the extracellular extravascular space (1). Therefore, diffusion-weighted magnetic resonance imaging (DW-MRI) can be used to differentiate normal from abnormal tissue structure and might be useful in characterizing various renal abnormalities (2). Recently, DW-MRI has been used to perform the functional evaluation of kidneys (3–7). The feasibility and reproducibility of DW-MRI of kidneys in healthy volunteers and in patients with renal abnormalities has been reported by Thoeny et al. (2).

Target organ damage (cardiac, vascular, and renal abnormalities) increases progressively with age in patients with metabolic syndrome. The risk for such damage is particularly pronounced in individuals with hypertension. This damage is usually caused by the alterations in organ structure that are produced by sustained blood pressure (BP) elevation (8, 9).

We hypothesized that hypertension-induced renal microvascular dysfunction might be an early manifestation of hypertensive renal damage, and the microvascular dysfunction, which can impair renal diffusion and perfusion, and it might be detected by renal diffusion MRI. Therefore, the aim of this study was to identify any possible correlation between BP level and ADC values.

Materials and methods

The local ethics committee approved the study protocol and informed consent was obtained from all patients before the study was initiated. The study included 77 consecutive patients (41 women and 36 men) that were divided into 4 groups according to their BP level. Group 1 consisted of normotensive control patients (n = 11); group 2, pre-hypertensive patients (n = 38); group 3, stage 1 hypertensive patients (n = 20); and group 4, stage 2 hypertensive patients (n = 6). The BP level of each patient was measured with a mercury sphygmomanometer in an office setting, and the first and fifth phases of Korotkoff sounds were used for systolic and diastolic BP. Appropriate cuff sizes were chosen for each patient's arm circumference. Trained physicians measured the BP level on 3 different days while each patient was seated with their arm elevated to the level of the heart. Each measurement was performed after 15 min of rest and the average of the 3 measurements was recorded. In accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (10), pre-hypertension was defined as a systolic BP between 120 and 139 mm Hg and/or a diastolic BP between 80 and 89 mm Hg. Patients with a systolic BP of 140–159 mm Hg and/or

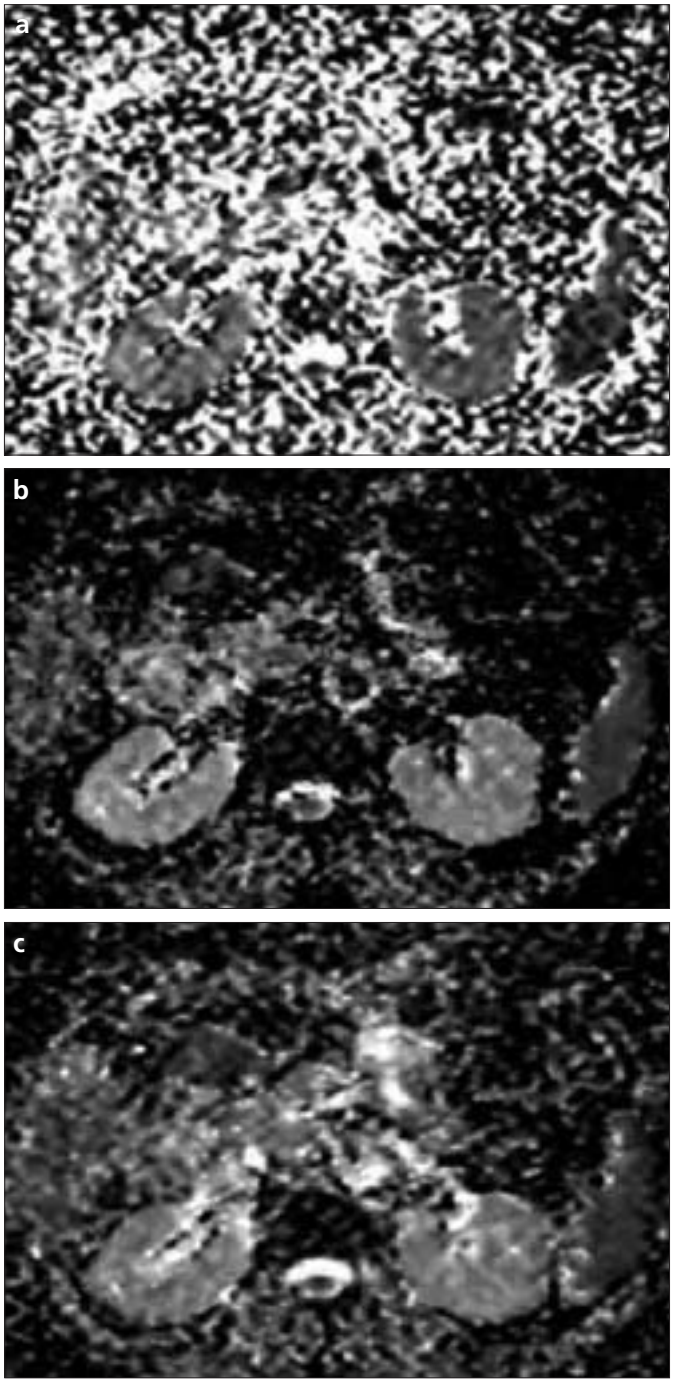

Figure 1. a–c. Apparent diffusion coefficient (ADC) maps **(a-c)** of a normotensive male patient. ADC map with low b values (ADC_{low}) **(a)**. ADC map with all b values ($ADC_{average}$) **(b)**. ADC map with high b values (ADC_{high}) **(c)**.

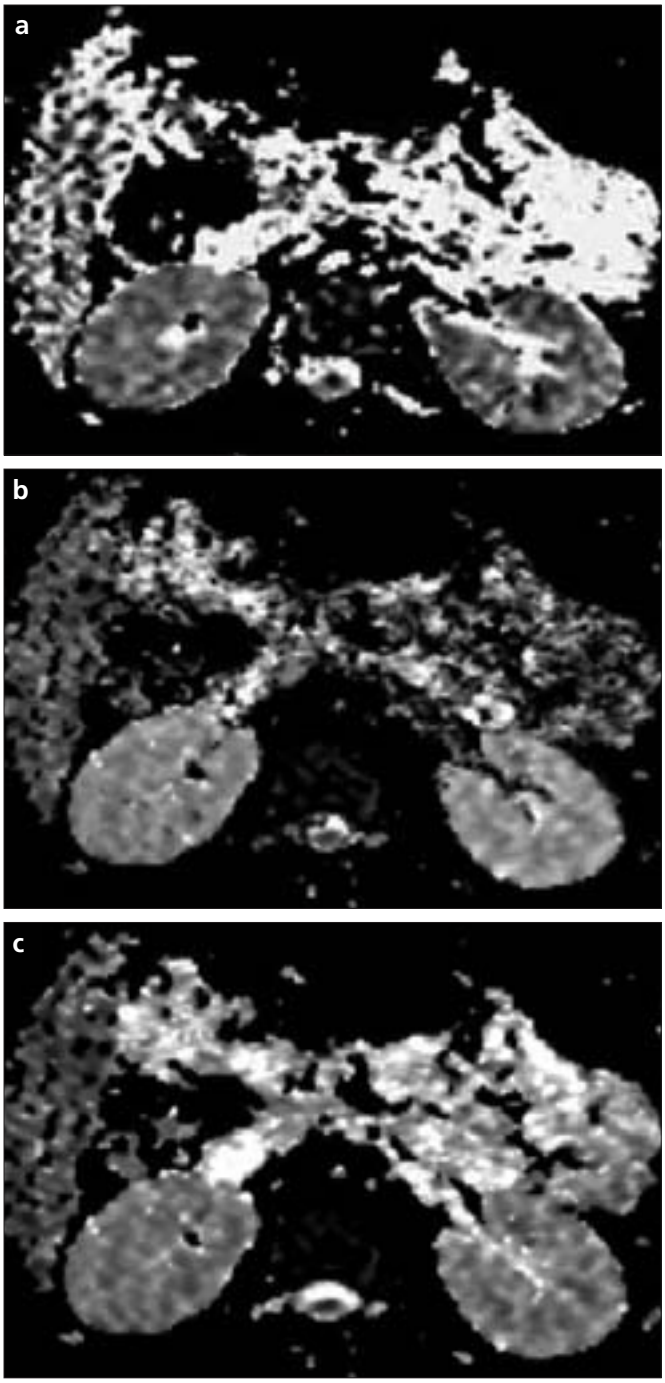

Figure 2. a–c. Apparent diffusion coefficient (ADC) maps **(a-c)** of a pre-hypertensive female patient. ADC map with low b values (ADC_{low}) **(a)**. ADC map with all b values ($ADC_{average}$) **(b)**. ADC map with high b values (ADC_{high}) **(c)**.

a diastolic BP of 90–100 mm Hg were diagnosed as stage 1 hypertensive. Subjects with a systolic BP ≥160 mm Hg and/or a diastolic BP ≥100 mm Hg were diagnosed as stage 2 hypertensive. Subjects with a systolic BP <120 mm Hg and a diastolic BP <80 mm Hg were diagnosed as normotensive (controls). Exclusion criteria included any systemic disease, such as diabetes mellitus, systemic lupus erythematosus, and obstructive nephropathy of any etiology, as well as smoking and any history of anti-hypertensive drug usage. Subjects using any vasoactive drug were also excluded.

Laboratory tests for secondary hypertension were performed for any patient if clinically appropriate. To screen for microalbuminuria, 24-h urine was collected in 55 patients. Target organ damage was considered in patients with microalbuminuria.

MRI was performed with a 1.5-T MR imager (Philips Gyroscan, Intera, The Netherlands). Transverse DW multi-section echo-planar MRI was

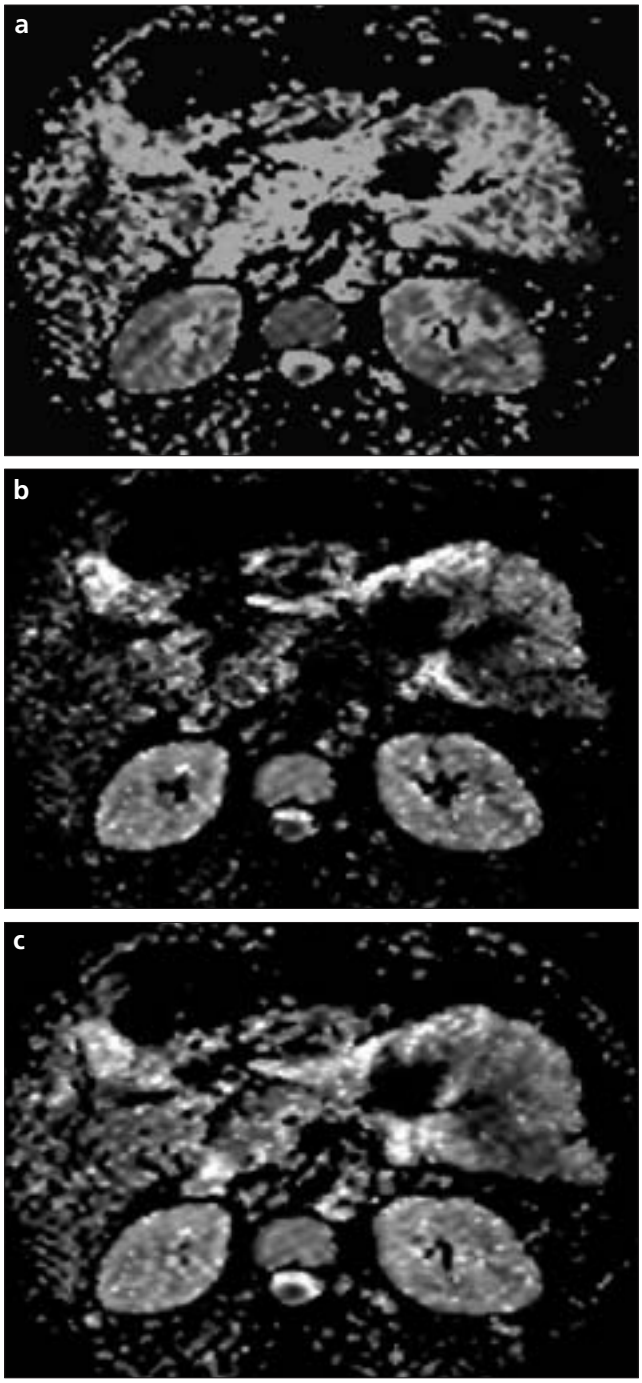

Figure 3. a–c. Apparent diffusion coefficient (ADC) maps **(a-c)** of a stage 1 hypertensive male patient. ADC map with low b values (ADC_{low}) **(a)**. ADC map with all b values ($ADC_{average}$) **(b)**. ADC map with high b values (ADC_{high}) **(c)**.

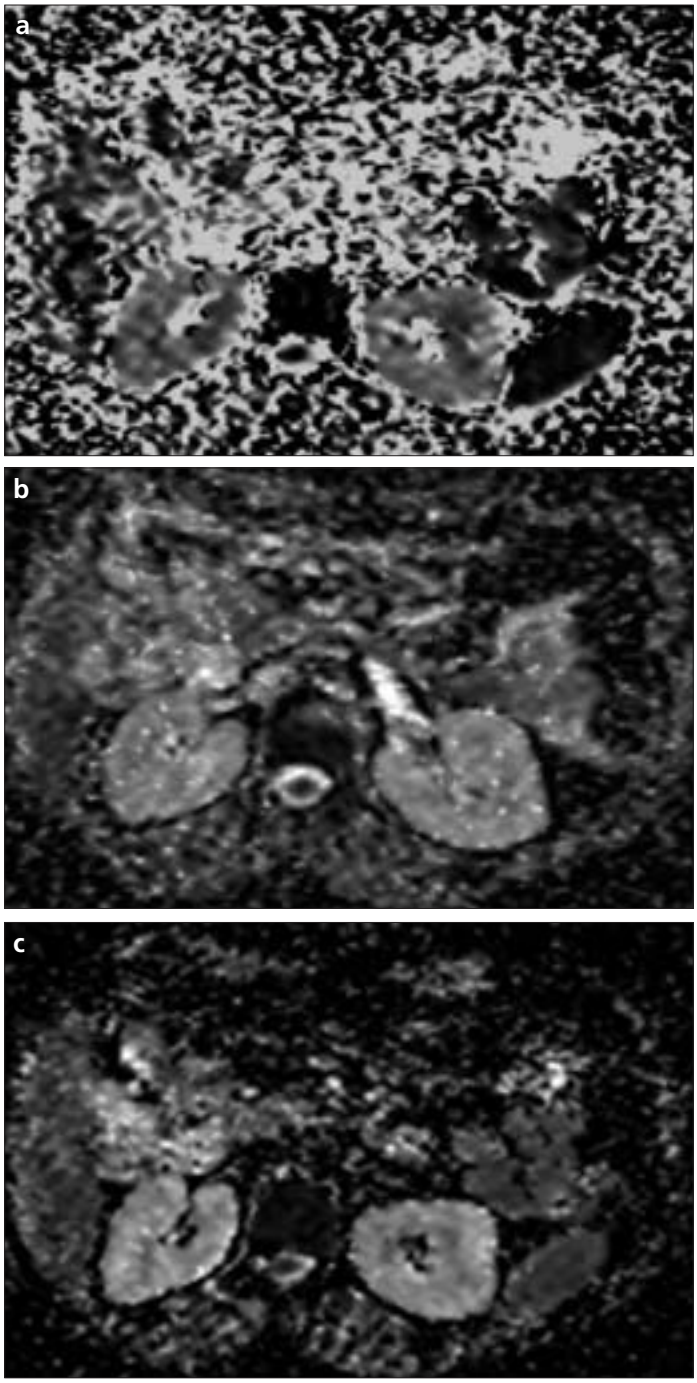

Figure 4. a–c. Apparent diffusion coefficient (ADC) maps **(a-c)** of a stage 2 hypertensive female patient. ADC map with low b values (ADC_{low}) **(a)**. ADC map with all b values ($ADC_{average}$) **(b)**. ADC map with high b values (ADC_{high}) **(c)**.

performed with the following diffusion gradient *b* values: 0, 111, 222, 333, 444, 556, 667, 778, 889, and 1000 s/mm^2. These were applied in 3 orthogonal directions and were subsequently averaged to minimize the effects of diffusion anisotropy and a body coil was used. The following parameters were used for this sequence: parallel imaging reduction factor of 2, 3100/74; section thickness, 5 mm; intersection gap, 1 mm; flip angle, 75°; NEX, 1; matrix size, 128 × 128; field of view, 380 × 380 mm; and rectangular field of view, 100. Fat saturation was used to avoid chemical shift artifacts. Pre-saturation slabs were not used. The entire sequence consisted of 20 sections (acquisition time: 142 s). The study was performed during normal respiration. ADC maps were calculated automatically with the MR system (Figs. 1–4).

In the transverse ADC maps, rectangular regions of interest (105 mm^2) were placed in the cortex on 3 parts (upper, middle, and lower pole) of each kidney

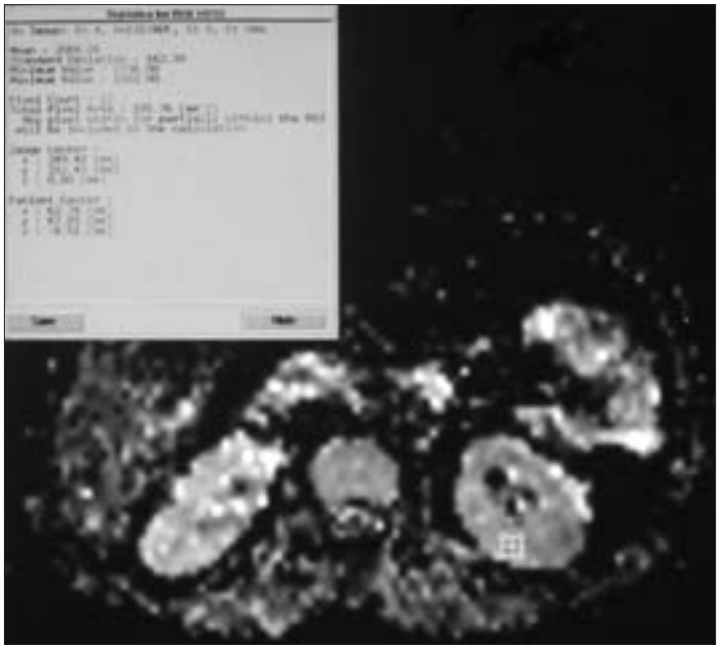

Figure 5. Calculation of apparent diffusion coefficient values. Regions of interest were placed on the cortex of the left kidney.

(Fig. 5). ADCs of the kidneys were calculated separately for low (ADC_{low}: b = 0, 111, 222, and 333 s/mm^2), average, and high (ADC_{high}: b = 889 and 1000 s/mm^2) b values to enable the differentiation of the relative influence of the perfusion fraction and true diffusion. In addition, a multi-slab balanced turbo field-echo MR angiographic technique (without a contrast agent) was used to exclude renal artery stenosis (11) and a body coil was used. A balanced fast field-echo sequence was applied in the coronal plane to identify the origin of the main renal arteries and in the sagittal plane to identify the origin of the superior mesenteric artery. A balanced turbo field-echo sequence was then applied with the following parameters: repetition time/echo time, 6.5/3.3 ms; and flip angle, 75°. The 240 × 240 matrix was reconstructed to a 512 × 512 matrix. A field of view of 300 mm and a rectangular field of view of 35% were used. Water-selective excitation was performed for fat suppression. Phase wrapping was eliminated in the anteroposterior direction. Before each balanced turbo field-echo shot, 3 saturation pulses were applied to provide venous signal suppression. The hilum of each kidney was covered by 2 saturation slabs. A third saturation slab was positioned parallel and caudal to the 3-dimensional imaging volume at a distance of 10 mm to suppress the signal from the inferior vena cava. Breath holding was not performed. Imaging time was 1.07 min/patient. One radiologist, who was blinded to the BP level of each patient, evaluated the results of renal MR angiography and calculated the ADC value for each kidney.

Statistical analyses

Statistical analyses were performed with SPSS v.9.0 software (Statistical Package for the Social Sciences, SPSS Inc, Chicago, IL, USA). The ADC values of the kidneys in the 4 groups were compared with the Mann-Whitney U test. The correlations between ADC values, BP levels, and other study variables were tested with Spearman's correlation analysis. The ADC values of patients with or without microalbuminuria were compared with the t-test. A P value < 0.05 was considered significant.

Results

Two hypertensive patients with renal artery stenosis that were identified with MR angiography were excluded from the study. There was no statistically significant difference between the groups in age (group 1: 45.6 ± 9.3 years; group 2: 45.7 ± 9.2 years; group 3: 43.4 ± 11.2 years; group 4: 48.7 ± 7.4 years; P = 0.748). Serum blood urea nitrogen and creatinine levels were within the normal range in all patients. In all, 27 patients had microalbuminuria (13 prehypertensive, 12 stage 1 hypertensive, and 2 stage 2 hypertensive patients), and the results of 24-h urine collection were negative for microalbuminuria in 28 patients. There was no statistically significant relation between (low, average, or high) ADC values of both

Table 1. Comparison of the apparent diffusion coefficient (ADC) (low, average, and high) values of kidneys in the 4 groups

Patients	$ADC_{low}R$ (× 10^{-3} mm^2/sec)	P	$ADC_{avg}R$ (× 10^{-3} mm^2/sec)	P	$ADC_{high}R$ (× 10^{-3} mm^2/sec)	P	$ADC_{low}L$ (× 10^{-3} mm^2/sec)	P	$ADC_{avg}L$ (× 10^{-3} mm^2/sec)	P	$ADC_{high}L$ (× 10^{-3} mm^2/sec)	P
Normotensive	2.3 ± 0.3		1.9 ± .09		2.0 ± 0.09		2.3 ± 0.3		1.9 ± 0.09		2.0 ± 0.06	
Pre-hypertension	2.3 ± 0.2	0.91	1.9 ± 0.1	0.44	2.0 ± 0.1	0.90	2.3 ± 0.2	0.88	1.9 ± 0.1	0.27	2.0 ± 0.1	0.93
Stage 1 hypertension	2.3 ± 0.2		1.9 ± 0.1		2.0 ± 0.1		2.3 ± 0.2		1.9 ± 0.1		2.0 ± 0.1	
Stage 2 hypertension	2.3 ± 0.3		2.0 ± 0.05		2.0 ± 0.1		2.3 ± 0.2		1.9 ± 0.03		2.0 ± 0.08	

avg: average

Table 2. Comparison of the apparent diffusion coefficient (ADC) (low, average, and high) values of kidneys with and without microalbuminuria

Patients	$ADC_{low}R$ ($\times 10^{-3}$ mm^2/sec)	$ADC_{avg}R$ ($\times 10^{-3}$ mm^2/sec)	$ADC_{high}R$ ($\times 10^{-3}$ mm^2/sec)	$ADC_{low}L$ ($\times 10^{-3}$ mm^2/sec)	$ADC_{avg}L$ ($\times 10^{-3}$ mm^2/sec)	$ADC_{high}L$ ($\times 10^{-3}$ mm^2/sec)
Microalbuminuria (+)	2.3 ± 0.2	1.9 ± 0.1	2.0 ± 0.1	2.3 ± 0.2	1.9 ± 0.1	2.0 ± 0.1
Microalbuminuria (-)	2.3 ± 0.9	1.9 ± 0.1	2.0 ± 0.1	2.4 ± 0.2	1.9 ± 0.1	2.0 ± 0.1
P	0.45	0.68	0.42	0.07	0.51	0.06

avg: average

kidneys and BP level in any group ($P > 0.05$) (Table 1). In addition, the ADC values of the patients with microalbuminuria did not differ from those of the patients without microalbuminuria ($P > 0.05$) (Table 2).

Discussion

The feasibility of DW-MRI of the kidneys by using different technical approaches has been reported in several previously published articles (4–7, 12, 13); however, only a few of those studies were performed in humans (3, 5). The reproducibility of DW-MRI of the kidneys in healthy volunteers was investigated by Thoeny et al. (2). In a small group, Namimoto et al. (3) reported that the ADC values of kidneys with renal artery stenosis were lower than those of the contralateral kidneys. That finding may indicate reduced blood perfusion, especially in the cortex. Although Muller et al. (13) reported a significant increase in ADC values in subjects whose test status progressed from a dehydrated to a hydrated state, Thoeny et al. (2) showed that under normal conditions the hydration status of study volunteers did not seem to significantly influence the results. In the present study we did not consider hydration status.

After having reviewed the literature, we concluded that many pathological renal conditions, such as chronic renal failure, pyelonephritis, or obstructive disorders, decrease the ADC values of kidneys (2). Yet, to the best of our knowledge, the effect of hypertension on the ADC values of kidneys has not been reported. In the present study there was no statistically significant difference between the ADC values of pre-hypertensive, hypertensive (stage 1 or stage 2 hypertension), or normotensive patients. In addition, there was no statistically significant correlation between ADC values and BP level. All patients were newly diagnosed with hypertension; therefore, we did not know the duration of the condition in the studied individuals. This is the major limitation of the study. However, microalbuminuria is a late effect of hypertension on the kidneys. The ADC values of patients with microalbuminuria (which is a predictor of target organ damage) did not differ from those of patients without microalbuminuria. This means that although target organ damage occured due to hypertension, perfusion and diffusion of kidneys did not change. We think that the microvascular function of kidneys is preserved in the early phase of renal damage. According to our results, DW-MRI of the kidneys is not a useful method for evaluating end-organ damage in hypertensive patients.

In conclusion, hypertension did not affect the ADC value, even if it caused end-organ damage; however, faster and newer imaging sequences may change these results.

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