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Diffusion-weighted imaging in assessing renal pathology of chronic kidney disease: A preliminary clinical study

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ABSTRACT

Objective: To investigate the clinical potential of diffusion-weighted imaging (DWI) in assessing renal pathology of chronic kidney disease (CKD).
Methods: Seventy-one CKD patients and twelve healthy volunteers were examined using DWI with prospective acquisition correction. Renal biopsy specimens from the CKD patients were scored based on the severity of renal pathology and to confirm pathology type. CKD patients were divided into three groups according to pathology scores: mild, moderate, or severe. The association between renal apparent diffusion coefficient (ADC) values and pathology scores was investigated using Pearson's correlation and single factor analysis of variance. Multiple linear regression analysis was performed to explore associations between renal ADC values and pathology score, glomerular filtration rate, serum creatinine, and age. The Kruskal–Wallis *H* test was conducted to compare ADC values and pathology type.
Results: Renal ADC values correlated negatively with pathology scores ($r = -0.633$, $P < 0.001$). The ADC values among the four groups (mild, moderate, severe impairment, and controls) were significantly different ($F = 19.512$, $P < 0.001$). However, when patients were stratified by pathology type, no significant differences were found in ADC values among these groups ($\chi^2 = 9.929$, $P = 0.270$). Further multiple linear regression analysis showed that only the pathology score and ADC values were related ($t = -4.586$, $P = 0.000$).
Conclusions: DWI has clinical potential in assessing the severity of renal pathology in CKD and shows promise as a non-invasive and effective technique to guide therapy and follow-up.

1. Introduction

The incidence of chronic kidney disease (CKD) increases annually. If not well controlled, CKD can lead to renal tissue destruction, gradual decline in renal function, and eventual uremia [1]. Hence, the evaluation of renal pathology (type and severity) in CKD patients is required for planning treatment and follow-up. Renal biopsy is the most common technique to identify the type and severity of renal pathology in CKD and is vital in guiding treatment and assessing outcome and prognosis [2]. However, renal biopsy also carries risks such as hematuria, perirenal hematoma, arteriovenous fistula, infection, and even death, and should not be repeated exclusively for follow-up [3]. In addition, results from biopsies are susceptible to sampling errors and observer bias.

Diffusion weighted imaging (DWI) is a non-invasive magnetic resonance imaging (MRI) technology that reflects the apparent diffuse movement of water molecules and is quantitated by the apparent diffusion coefficient (ADC) [4,5]. Previous studies of renal DWI have focused on the clinical importance of the ADC in the assessment of renal function [6–8]. However, renal pathology is more important than renal function in guiding therapy and follow-up. Recently Inoue et al. [9] studied ureteral obstruction-induced renal fibrosis in rats and found that the ADC value decreased with increasing proliferation of fibroblasts in the renal tissues. This suggests that the ADC value might be useful as a non-invasive and accurate index of renal fibrosis. However, renal fibrosis is only one manifestation of the renal pathology, and is only one determinant of patient treatment and prognosis; other components in CKD include the presence of impairments of the renal glomeruli, tubules, and blood vessels, as well as the pathology type.

In the present study, we conducted a preliminary investigation of the clinical potential of DWI, with navigator-triggered

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prospective acquisition correction (PACE), in the evaluation of renal pathology associated with CKD.

2. Patients and methods

2.1. Patients

The Ethics Committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University approved this study. Each subject provided written informed consent prior to enrollment in the study.

Inclusion criteria for this group of CKD patients were: (1) meet diagnostic criteria for clinical CKD, which encompasses various degrees of chronic renal structural and functional abnormalities (kidney damage history for more than three months), including glomerular filtration rate (GFR), normal or abnormal pathological damage, blood or urine composition abnormalities, radiographic abnormalities, and unexplained decline in GFR (GFR < 60 mL/min) for more than three months; (2) fulfilled intervention measures undertaken prior to the MR examination and renogram, consisting of a vegetarian diet for three days, avoidance of strenuous exercise, and avoidance of drugs affecting renal blood flow and urine formation (e.g., angiotensin II receptor antagonists, dopamine agonists, and diuretics); (3) with renal pathology confirmed by renal biopsy; (4) no medical history that may affect renal function, such as gout, diabetes, hypertension, or others; (5) MRI examination completed 2–10 days prior to renal biopsy with image quality that meets the analytical requirements of the study; and (6) with no other organ or systemic severe disease.

Exclusion criteria for this group of CKD patients were: (1) could not tolerate MRI examination; (2) the image quality did not meet requirements of the study; (3) presence of malignant kidney or liver lesions; (4) multiple benign renal masses (such as angioleiomyolipoma, cysts, and others) that affect analysis of the data; (5) presence of other kidney lesions, such as kidney stones, hydronephrosis, congenital variation, or urinary tract tumors; (6) an inadequate biopsy specimen that therefore prevented pathology scoring; or (7) existence of MRI contraindications.

DWI was performed on 83 CKD patients and 12 healthy volunteers. Finally, 71 patients and 12 healthy volunteers were enrolled in the study. Procedures used in patient enrollment are illustrated in Fig. 1.

2.2. MRI and analysis

Images were taken using a 1.5-T MRI system (Avanto, Siemens Medical Solutions; Erlangen, Germany) and abdominal phased-array surface coil. There was no requirement for the patients to fast, and they remained hydrated on the day of the examination. Each underwent positioning acquisition in the supine position. After the scout view was completed, the following was performed: half-Fourier acquisition single-shot turbo spin-echo (HASTE) T2-weighted imaging (TR: 1000 ms, TE: 83 ms, section thickness: 7.0 mm, FOV: 360 mm × 270 mm, matrix: 256 × 194, bandwidth: 391 Hz, single breath-hold), and coronal two-dimensional fast low-angle shot gradient-echo (2D FLASH) T1-weighted imaging (TR: 233 ms, TE: 2.52 ms, section thickness: 7.0 mm, FOV: 360 mm × 270 mm, matrix: 256 × 179, bandwidth: 260 Hz, frequency-selective fat suppression, single breath-hold).

Spin echo–echo planar imaging sequence with PACE technology was used for DWI. Generalized auto-calibrating partially parallel acquisition, with an acceleration factor of 2, was applied to the coronal scan. The navigation bar was located on the right side of the diaphragm (coronal, section thickness: 10 mm, FOV: 32 mm × 30 mm, acquisition window width ±2 mm). TR/TE was 1300/82 ms, section thickness 5 mm, slice spacing 1.5 mm, matrix size 192 × 192, FOV 360 mm × 360 mm, partial Fourier factor 6/8, and bandwidth 1736 Hz. Frequency-selective fat suppression was applied. In addition, two pre-saturated bands were added to the upper and lower scanning fields (twice stimulating and twice sampling) with 17% over-sampling. The selected b value was 800 s/mm^2, which was added to the three orthogonal directions to reduce the influence of diffusion anisotropy. All subjects were instructed to breathe freely during scanning. The scan covered the entire kidney.

An MRI workstation (1.5-T Avanto with Leonardo Syngo; Siemens Healthcare) was used to analyze the images. Two abdominal radiologists with expertise in abdominal MRI, and blinded to the clinical details of patients in the present study, evaluated the DWI images. When they had different opinions, consensus was reached through discussion.

The ADC value was calculated using the following equation:

$$\mathrm{ADC} = \frac{\ln(S_1/S_0)}{b_0 - b_1}$$

where S_1 is the signal intensity when $b_1 = 800$ s/mm^2, S_0 is the signal intensity when $b_0 = 0$ s/mm^2, and ln is the natural logarithm. The ADC values were measured from the fitted ADC map. The free-hand regions of interest (ROI) were positioned in the parenchyma of the renal mesorenal area, as recommended by Xu et al. [7], who suggested that evaluation of ADC values in the central portion of the kidneys is reliable and suitable for use in longitudinal studies.

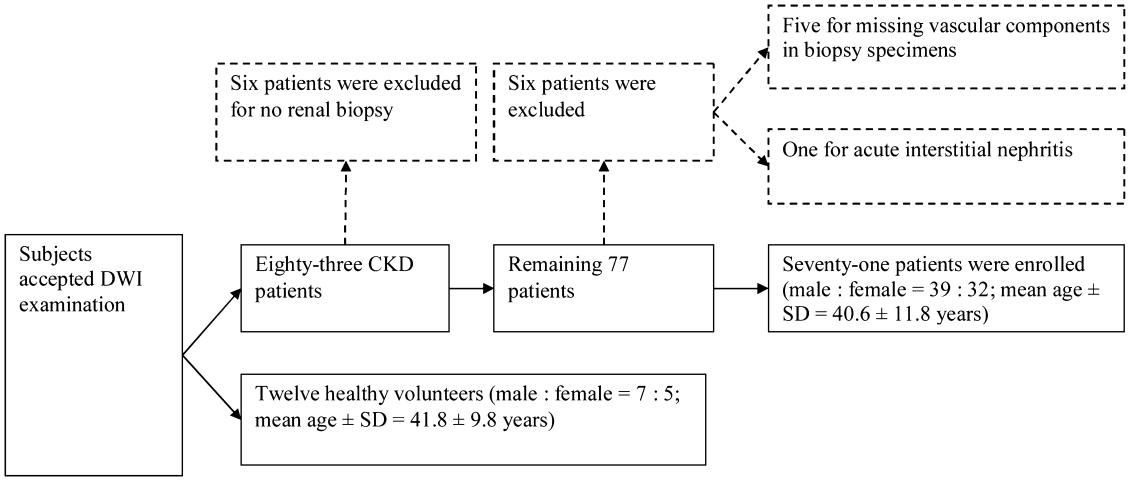

Fig. 1. Flow diagram describing procedures used in patient enrollment.