1. Introduction

Chronic kidney disease (CKD) is a public health problem worldwide, which is a gradual impairment of renal function.[1] Patients with CKD are at an increased risk of cardiovascular disease and other chronic conditions with their daily lives.[2] Clinically, CKD is characterized by a low estimated glomerular filtration rate (eGFR, <60 mL/min/1.73 m²), which may progress at varying rates depending on blood pressure management, history of decreased GFR, level of proteinuria.[3] CKD may result in abnormalities of multiple physiological processes including removal of waste products of metabolism, heterogeneous disorders on kidney structure and function, electrolyte balance that substantially increases mortality risk due to atherosclerotic cardiovascular disease (ASCVD).[4] Therefore, CKD patients require imaging monitoring to accurately predict the risk of declining renal function and guide therapeutic schedules.
CKD is generally diagnosed by imaging of the kidney using ultrasonography (US), contrast-enhanced ultrasound (CEUS), computed tomography (CT), or magnetic resonance imaging (MRI).\(^{[1]}\) Cardiovascular magnetic resonance (CMR) is a standard method for imaging impairment in kidney function, renal injury, and fibrosis.\(^{[2]}\) MRI technique in particular has the potential to present both structural and functional parameters in the kidney by using targeted magnetic nanoparticles.\(^{[2]}\) Gadolinium (GB)-based are an important aid in MRI diagnostics for improving the detection and characterization of pathologic processes.\(^{[3]}\) Gadolinium GB-based contrast agents are frequently used to enhance the diagnostic efficacy of MRI in patients with kidney diseases.\(^{[4]}\) In addition, GB is widely employed as a contrast agent for MRI and has generally been considered to be safe in patients with kidney disease.\(^{[5]}\) Furthermore, a potential alternative imaging modality for evaluating GFR and renal fibrosis is diffusion tensor imaging findings generated by Gadolinium-based MRI (DTI-GBMRI).\(^{[6]}\) Thus, DTI-GBMRI may be ideal for renal function assessment in patients with CKD.

The purpose of this study was to comprehensively assess renal histopathology and renal efficiency, renal fibrosis and damage, noninvasive quantification of renal blood flow (RBF) in patients with CKD using DTI-GBMRI. The sensitivity and accuracy between DTI-GBMRI and DTI-MRI method in assessing renal function and evaluating renal impairment was compared in CKD patients. The association between the RBF value and eGFR was analyzed in patients with CKD.

### 2. Materials and methods

#### 2.1. Patients

A total of 186 CKD patients were recruited in Hongqi Hospital Affiliated To Mudanjiang Medical University between January 2017 and May 2019. The inclusion criteria were as follows: age > 18 years; and Stage 2 of CKD (60ml/min/1.73 m² ≤ eGFR <90ml/min/1.73 m²); Stage 3a of CKD (30ml/L/min/1.73 m² ≤ eGFR <60ml/min/1.73 m²); The exclusion criteria were as follows: patients with HIV infection, polycystic kidney disease, cancer; transplant recipients; pregnant and breastfeeding women; and history of adverse reaction to gadolinium. The protocol was approved by the ethics committee of Hongqi Hospital Affiliated To Mudanjiang Medical University. CKD patients received DTI-GBMRI (n = 92) or DTI-MRI (n = 94) diagnosis. All participants signed written informed consent.

#### 2.2. Magnetic resonance imaging

MRI examinations were performed using a 3 T unit (Canon Medical Systems, Tustin, CA). Diffusion-weighted imaging/ diffusion tensor imaging scans were obtained by using the following parameters: 256 diffusion directions, TR: 8000 ms, TE: 60 ms, 8 diffusion-weighted b-values in steps of 200 s/mm² ranging from b: 0 to 14,000 s/mm², flip angle: 90°; bw: 1860 Hz/pix, transversal base resolution matrix: 128×128. For DTI-GBMRI, a bolus injection of 0.2mL/kg body weight gadolinium (Omniscan; Bracco, Daichi-San-kyo Co., Ltd, Tokyo, Japan) was intravenously administered, followed by a 20-mL saline flush at 2 mL/s. The location of impairment of renal structure was intravenously administered, followed by a 20-mL saline flush at 2 mL/s. The location of impairment of renal structure can be observed in MRI images, where exposure to GB-based contrast agent in CKD patients. MR renography was obtained from all CKD patients to analyze renal histopathology and renal efficiency, renal fibrosis and damage, and noninvasive quantification of RBF.

#### 2.3. Outcomes

Kidney volume, the number, diameter, and volume of glomeruli in CKD patients were automatically analyzed using MRI image data. The eGFR was calculated using the estimation equation for CKD patients determined by MRI image data. The GFR was calculated for each kidney by 3 radiologists by using Mirage software.\(^{[7]}\) The mean transit time (MTT) was used to evaluate function of kidney in CKD patients as described previously.\(^{[8]}\) RBF was determined by MRI image data.\(^{[9]}\) The procedure includes preprocessing of image data, segmentation of the kidney region, segmentation of the glomeruli, and quantification of the segmented regions as described previously.\(^{[10]}\) All parameters were automatically analyzed by Syngo software (Siemens, Erlangen, Germany).

### 2.4. Statistical analyses

Data are expressed means ± SD. All statistical analyses were performed using SAS software (version 9.4; SAS Institute, Inc., Tokyo, Japan). The P values were calculated via independent sample t test for continuous variables and chi-square test for categorical variables. Receiver operating characteristic (ROC) analyses were used to analyze the diagnostic performance of the DTI-GBMRI diagnosis. The cutoff was determined according to the ROC curve, and then the specificity and sensitivity of various scoring systems were calculated separately. Statistical significance was defined as a P value <.05.

### 3. Results

#### 3.1. Characteristic of patients with CKD

A total of 186 CKD patients were enrolled in this study. All CKD patients in stage 1 or 2 were enrolled between May 2017 and June 2019. A flowchart of CKD patient recruitment is shown in Figure 1. The age of CKD patients was 46.5 years old (range, 30–65 years). CKD patients received diagnosis of DTI-GBMRI (n = 92) or DTI-MRI (n = 94) to identify the pathological characteristics and depict renal efficiency. Table 1 showed the demographics and characteristics of patients with CKD. There were no significant differences in BMI, age, sex, blood pressure, cerebrovascular disease, and intraocular pressure between 2 groups. Signalement and renal biomarkers in 2 groups were not significant difference.

#### 3.2. The pathological characteristics and depict renal efficiency diagnosed by DTI-GBMRI

We compared the pathological characteristics and depict renal efficiency in CKD patients diagnosed by DTI-GBMRI or DTI-MRI. CKD patients diagnosed by DTI-GBMRI showed more renal vascular lesions and bigger diameters of lesions than those patients in DTI-MRI group. The average diameter diagnosed by DTI-GBMRI was 3.28 cm, while was in 3.02 cm in CKD patients diagnosed by DTI-MRI. DTI-GBMRI had significantly better performance than DTI-MRI in measuring lumen depiction scores (4.8 ± 0.2 vs 3.2 ± 0.2 for arterial inflow, 4.2 ± 0.1 vs 3.0 ± 0.2 for venous outflow).

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Figure 1. Flow diagram showing CKD patients in this study. CKD = chronic kidney disease.
Table 1  
Characteristic of CKD patients.

|                  | DTI-MRI | DTI-GBMRI |
|------------------|---------|-----------|
| Number           | 94      | 92        |
| Male/female      | 54/40   | 53/39     |
| Age (y)          | 52 ± 10 | 52 ± 10   |
| BMI (kg/m²)      | 25.2 ± 2.6 | 25.8 ± 3.1 |
| Blood pressure (mm Hg) | 132.3 ± 5.8 | 130.8 ± 9.0 |
| Systolic         | 82.6 ± 5.8 | 84.2 ± 6.5 |
| Diastolic        | 10 (10.6%) | 10 (10.9%) |
| Cognitive disorder | 10 (10.6%) | 9 (9.8%) |
| Intraocular pressure (mm Hg) | 14.5 ± 2.6 | 14.8 ± 3.1 |
| Smoking, n (%)   | 10 (10.6%) | 10 (10.9%) |
| CKD stages       | 2 (mild) | 50 (53.2%) |
|                  | 3a (mild to moderate) | 50 (54.3%) |

Data are expressed as mean ± or n (%). The P values were calculated via independent sample t test for continuous variables and chi-square test for categorical variables.

Table 2  
The pathological characteristics and depict renal efficiency diagnosed by DTI-GBMRI.

|                  | DTI-MRI | DTI-GBMRI |
|------------------|---------|-----------|
| Diameters of lesions (cm) | 3.02 ± 0.32 | 3.28 ± 0.24 |
| Depiction scores  | 3.2 ± 0.2 | 4.8 ± 0.2 |
| Arterial inflow   | 1.8 ± 0.2 | 4.2 ± 0.1 |
| Arterial outflow  | 2.0 ± 0.3 | 3.8 ± 0.3 |
| Venous outflow    | 2.2 ± 0.2 | 4.2 ± 0.2 |
| Intraluminal signal homogeneity | 0.40 ± 0.05 | 0.24 ± 0.03 |
| CNR efficiency    | 2.6 ± 0.3 | 5.2 ± 0.3 |

Data are reported as mean ± SD. The P values were calculated via independent sample t test. CNR = contrast-to-noise ratio, DTI-GBMRI = diffusion tensor imaging findings generated by gadolinium-based MRI, DTI-MRI = diffusion tensor imaging findings generated by MRI.

Table 3  
Kidney volume and functional parameters estimates diagnosed by DTI-GBMRI.

|                  | DTI-MRI | DTI-GBMRI |
|------------------|---------|-----------|
| Kidney volumes (mL) | 1868 ± 224 | 2046 ± 214 |
| Creatinine (mg/dL) | 1.68 ± 0.32 | 1.75 ± 0.40 |
| MT1r             | 186.2 ± 40.5 | 137.6 ± 30.6 |
| Impairment of renal perfusion (mL/min) | 293 ± 45.7 | 156 ± 7.5 |
| T2 pronounce (ms) | 45.7 ± 1.2 | 60.1 ± 2.0 |
| T1 relaxation times (ms) | 1938 ± 53 | 1350 ± 27.3 |
| CNR efficiency (mm²/s) | 1.83 ± 0.05 × 10⁻³ | 1.39 ± 0.14 × 10⁻³ |

Data are reported as mean ± SD. The P values were calculated via independent sample t test. CNR = contrast-to-noise ratio, DTI-GBMRI = diffusion tensor imaging findings generated by gadolinium-based MRI, DTI-MRI = diffusion tensor imaging findings generated by MRI.

Table 4  
Analysis of Cortical RBFs and eGFR in CKD patients.

|                  | DTI-MRI | DTI-GBMRI |
|------------------|---------|-----------|
| Serum creatinine (mg/dL) | 1.68 ± 0.32 | 1.75 ± 0.40 |
| eGFR (mL/min/1.73 m²) | 36.4 ± 20.8 | 44.7 ± 16.5 |
| BFR (mL/min) | 503.5 ± 32.4 | 315.8 ± 23.6 |

Data are reported as mean ± SD. The P values were calculated via independent sample t test. BFR = renal blood flow.

RBF values of CKD patients in the DTI-GBMRI group were lower than patients in DTI-MRI group (315.8 ± 23.6 vs 503.5 ± 32.4, P < .01). The ROC curve was used to determine the diagnostic efficacy of DTI-GBMRI compared to DTI-MRI. The AUC value of DTI-GBMRI was significantly higher than that of DTI-MRI (0.92 vs 0.85, respectively).

3.3. Kidney volume and functional parameters estimates
Kidney volumes and functional parameters estimates were compared in CKD patients between DTI-GBMRI and DTI-MRI groups (Table 3). The mean kidney volumes of CKD patients in DTI-GBMRI and DTI-MRI were 2046 ± 224 and 1868 ± 214 mL, respectively (P < .01). Creatinine levels were not significantly different between DTI-GBMRI and DTI-MRI groups. The total glomerular count in CKD patients diagnosed by DTI-GBMRI and DTI-MRI was around 16,320 ± 12,350 and 14,560 ± 10,180, respectively (P < .01). MTT was significantly higher in the DTI-MRI group (186.2 ± 40.5 seconds) than in the DTI-GBMRI group (137.6 ± 30.6 seconds). DTI-GBMRI revealed stronger impairment of renal perfusion (156 ± 7 vs 293 ± 44 mL/min × 100 g; P < .01) and more pronounced increases in T2 (60.1 ± 20.8 vs 45.7 ± 1.2 ms, P < .01) and T1 relaxation time (1938 ± 53 vs 1350 ± 27.3 ms, P < .01) than DTI-MRI. Apparent diffusion coefficient was 1.39 ± 0.14 × 10⁻³ and 1.83 ± 0.05 × 10⁻³ mm²/s in kidneys in the DTI-GBMRI and DTI-MRI group, respectively (P < .01).

3.4. Cortical RBFs and eGFR
The cortical RBFs and eGFR were compared in CKD patients undergone DTI-GBMRI (n = 92) or DTI-MRI (n = 94). The cortical

3.5. Diagnostic efficacy of DTI-GBMRI
The ROC curves were used to determine the diagnostic efficacy between DTI-MRI and DTI-GBMRI groups in CKD patients. The AUC value of DTI-GBMRI was significantly higher than that of DTI-MRI (0.92 vs 0.85, respectively).

4. Discussion
The assessment of early CKD damage is of crucial importance in preventing CKD-induced diseases.[15] In this study, we investigated the diagnostic efficacy of DTI-GBMRI in evaluating histological and renal efficiency in patients with CKD. Functional parameters associated with renal impairment in kidney function were analyzed in DTI-GBMRI-diagnosed CKD patients with CKD. Findings in this study demonstrated that DTI-GBMRI clearly demonstrated the pathological characteristics and depict renal efficiency compared to MRI in CKD patients. Thus, DTI-GBMRI may be a potential noninvasive method for measuring renal function for CKD patients. CKD has been associated with increased visual impairment and cardiovascular disease.[15] Inflammation and dysfunction of glomerular cells contributes to the cardiovascular disease burden associated with CKD, which is one of the most important
Table 5

|                  | DTI-MRI | DTI-GBMRI | P value |
|------------------|---------|-----------|---------|
| Sensitivity (%)  | 86.8    | 98.5      |  .0048  |
| Specificity (%)  | 88.3    | 98.2      |  .0070  |

Sensitivity and specificity differences between DTI-MRI and DTI-GBMRI were analyzed using Pearson nonparametric correlation analysis.

CKD = chronic kidney disease, DTI-GBMRI = diffusion tensor imaging findings generated by gadolinium-based MRI, DTI-MRI = diffusion tensor imaging findings generated by MRI.

Table 5
Diagnostic efficacy of DTI-GBMRI in CKD patients.

Figure 2. Receiver operating characteristic curve of DTI-GBMRI and DTI-MRI for the diagnosis of CKD patients. CKD = chronic kidney disease, DTI-GBMRI = diffusion tensor imaging findings generated by gadolinium-based MRI, DTI-MRI = diffusion tensor imaging findings generated by MRI.

In conclusion, this study demonstrates the benefits of DTI-GBMRI in measuring renal histopathology and renal efficiency, renal fibrosis and damage, and noninvasive quantification of RBF in CKD patients. Outcomes find that DTI-GBMRI improves testing methodologies for more accurate assessment of cortical RBFs, GFR, pathological characteristics, and depict renal efficiency than DTI-MRI, which further contributes to high sensitivity and specificity. These data suggest that DTI-GBMRI may be a reliable assessment of renal function combined with high-resolution morphological evaluation of the kidneys, as well as accurately identify stage CKD in certain clinical patients.

Author Contributions

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