ORIGINAL RESEARCH

Application Value of Conventional Ultrasound Combined with Shear Wave Elastography in Diagnosing Renal Fibrosis in Diabetic Nephropathy

Min Sun, PhD; Yiwei Wang, PhD; Guixia Zheng, PhD; Binhong Duan, PhD; Lutong Zhang, PhD; Shifang Yu, PhD; Xiaodan Zhao, PhD; Jie Fan, PhD

ABSTRACT

Background • Diabetic nephropathy is a common acute complication of diabetes mellitus and is the leading cause of chronic kidney disease (CKD) worldwide. Renal fibrosis is a major pathological change in diabetic nephropathy.

Objective • To explore the diagnostic value of shear wave elastography (SWE) for renal fibrosis in patients with advanced diabetic nephropathy.

Design • This was a retrospective study.

Setting • This study was conducted in Heilongjiang Provincial Hospital.

Participants • Sixty patients with diabetic nephropathy renal fibrosis who accepted therapy in our hospital from January 2021 to December 2022 (observation group, OG) and 60 healthy physical examination patients (control group, CG) in the same period were selected for the study.

Interventions • All subjects were examined by conventional ultrasound and SWE.

Primary Outcome Measures • (1) conventional ultrasonic parameters and SWE parameters and (2) clinical biochemical indicators.

Results • Compared to CG, SCr and BUN in OG were higher, while eGFR in OG was lower ($P < .05$). Compared to CG, the cortical thickness of OG was less, and the cortical hardness of OG was more ($P < .05$). Compared to CKD4 patients, eGFR in CKD3 patients was higher, while SCr and BUN in CKD3 patients were lower ($P < .05$). Compared to CKD4 patients, the cortical thickness in CKD3 patients was higher, and cortical hardness in CKD3 patients was lower ($P < .05$).

Conclusion • The cortical thickness and cortical hardness parameters in SWE imaging of patients with advanced diabetic nephropathy renal fibrosis are different from those of healthy people. The parameters are also significantly different in patients with different CKD stages and are significantly correlated with SCr, BUN, and eGFR, which can be used for the diagnosis of diabetic nephropathy renal fibrosis. (*Altern Ther Health Med.* [E-pub ahead of print.])

Min Sun, PhD, Department of Nephrology; Heilongjiang Provincial Hospital; Harbin; Heilongjiang; China. **Yiwei Wang**, PhD, Department of Science and Education; Heilongjiang Provincial Hospital; Harbin; Heilongjiang; China. **Guixia Zheng**, PhD; **Lutong Zhang**, PhD; **Shifang Yu**, PhD; **Xiaodan Zhao**, PhD; **Jie Fan**, PhD, Department of Ultrasound; Heilongjiang Provincial Hospital; Harbin; Heilongjiang; China. **Binhong Duan**, PhD, Department of Endocrine; Heilongjiang Provincial Hospital; Harbin; Heilongjiang; China.

Corresponding author: Jie Fan, PhD
E-mail: shengyiyuanfanjie@163.com

INTRODUCTION

Diabetic nephropathy is one of the most serious complications of diabetes. The major clinical manifestations are proteinuria, reduced estimated glomerular filtration rate (eGFR), enhanced blood pressure, as well as renal failure.[1] Advanced diabetic nephropathy can cause morphological changes such as renal fibrosis, which is the major cause of end-stage renal disease (ESRD).[2] The pathogenesis of diabetic nephropathy is still not clear, and it is believed that the disease is caused by multiple factors including genetic factors and other risk factors such as abnormal glucose metabolism, renal hemodynamic changes, oxidative stress, and immunoinflammatory factors.[3] Although diabetic nephropathy can be assessed through routine biochemical tests, such as urinary protein together with serum creatinine levels, the measurement of the degree of renal fibrosis still requires kidney biopsy, which is associated with large puncture trauma, a small sampling range, and high cost, and multiple complications may occur after renal biopsy, which may lead to renal insufficiency in severe cases.[4] Hence, it is urgent to explore a non-invasive method for testing the severity of renal fibrosis in patients with diabetic nephropathy. Patients with single-kidney diabetic nephropathy or those receiving anticoagulant therapy should generally avoid renal biopsy.

Traditional 2D and color Doppler ultrasound can only reflect parameters such as renal blood flow, cortical thickness,

and echo intensity, and can effectively diagnose renal cysts and calculi. However, its diagnostic value for renal fibrosis is still limited,[5] and the emergence of shear wave elastography (SWE) technology makes up for the shortcomings of traditional ultrasound.[6]

Due to the deposition of pathological fiber matrix in the renal tubules and peritubular capillary space during the process of renal fibrosis, changes in parenchymal elasticity of the kidney can be caused, which provides a pathological basis for the diagnosis of renal fibrosis by SWE.[7] Although SWE has been reported in recent years for the diagnosis of renal fibrosis, there are few studies on the diagnostic value of renal fibrosis in diabetic nephropathy patients.[8] In our study, we aimed to explore the value of SWE in the diagnosis of renal fibrosis in diabetic nephropathy patients.

DATA AND METHODS

General data

Sixty patients with diabetic nephropathy renal fibrosis who accepted therapy in our hospital from January 2021 to December 2022 (observation group, OG) and 60 healthy physical examination patients (control group, CG) during the same period were selected for the study. There were 32 patients in the stage 3 chronic kidney disease (CKD) and 28 patients in the stage 4 CKD in the OG.

Inclusion criteria: (1) Patients in the OG met the relevant diagnosis of diabetic nephropathy,[9] the stage of CKD was determined to be 3~4, and renal fibrosis was confirmed by biopsy pathology; (2) Patients could clearly express and communicate with medical staff without barriers; (3) Patients signed the informed consent.

Exclusion criteria: (1) Patients with hepatitis B-related nephropathy; (2) Patients with hypertensive nephropathy; (3) Patients with primary glomerulonephritis; (4) Patients with acute nephritis syndrome.

Methods

All subjects were examined by Philips iU22 xMATRIX ultrasound system (Philips, Netherlands) together with acoustic radiation force impulse technology. Conventional ultrasound imaging with a C5-1 convex probe (frequency 5 MHz) was used for routine renal scanning and SWE. Immediately after the image was captured, the screen displayed the image and measurement results, containing the mean and median and the deviation expressed as pressure. Imaging examinations, including routine ultrasound and SWE, were performed by the same experienced sonographer. The patient was examined in supine, right-side, and left-side positions. The patient was instructed to hold his breath during the examination for 20 to 30 minutes. Before performing kidney SWE, the kidneys were examined using routine ultrasound to detect underlying renal lesions; the length and width of each right and left kidney were recorded. Cortical thickness was examined at 10 locations between the renal poles of the two kidneys, and the average of the 10 measurements was considered the final measurement (mm). Elastic measurements of cortical hardness were performed at 10 locations between the renal poles of the two kidneys, and the average of the 10 measurements was considered the final measurement result (kPa). A region of interest (ROI) could be placed anywhere for the measurement but required a depth of <8 cm.

Clinical data collection

Age, gender, and body mass index (BMI) were recorded in detail. All subjects had their peripheral elbow venous blood drawn the next morning after an 8-hour fasting period. Serum creatinine (SCr), blood urea nitrogen (BUN), and glomerular filtration rate (GFR) were measured according to the estimated glomerular filtration rate (eGFR). e-GFR was estimated using the modified and simplified Modification of Diet in Renal Disease (MDRD) equation.

Statistical analysis

SPSS 22.0 statistical software (International Business Machines Corporation, USA) was implemented for data analysis. Counting data were exhibited as n (%) and compared with the help of the χ^2 test. Measurement data were exhibited as ($\bar{x} \pm s$), and compared with the help of the t test. $P < .05$ was considered statistically significant.

RESULTS

General data of patients in both groups

No significant difference was observed in age, gender, and BMI of patients in both groups ($P > .05$), as displayed in Table 1.

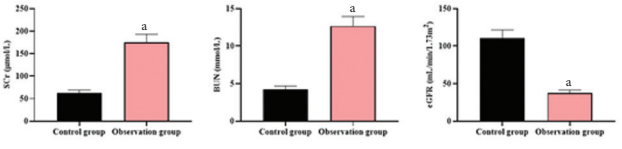
Clinical biochemical indicators in different groups

Figure 1 revealed that the SCr and BUN of patients in the OG were 175.43 μmol/L and 12.67 mmol/L, respectively, and the values were higher when compared to those of CG (62.68 μmol/L and 4.26 mmol/L, respectively). Meanwhile, the eGFR of patients in the OG was 37.56 mL/min/1.73m^2, which was found to be lower compared to that of CG (110.62 mL/min/1.73m^2), with statistical significance ($P < .05$)

Table 1. General Data of Patients in Both Groups [n (%)]/($\bar{x} \pm s$)

Groups	Cases	Gender (male/female)	Age (years)	BMI (kg/m^2)
Control group	60	32/28	60.73 ± 9.55	22.95 ± 2.97
Observation group	60	30/30	60.56 ± 9.62	23.04 ± 3.01
χ^2/t		0.13	0.10	0.16
P value		>.05	>.05	>.05

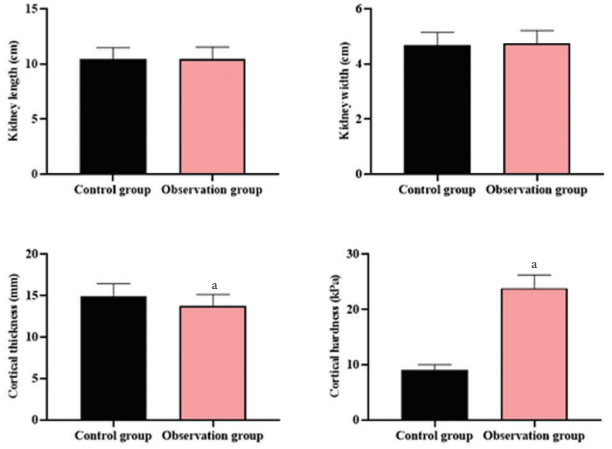
Figure 1. Clinical Biochemical Indicators in Different Groups



[a]$P < .05$.

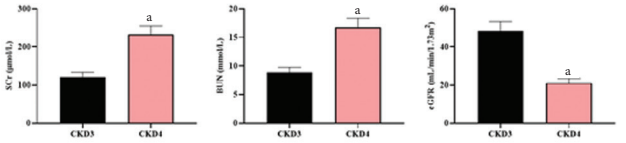
Abbreviations: SCr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate.

Figure 2. Conventional Ultrasonic Parameters and SWE Parameters in Both Groups



[a]$P < .05$

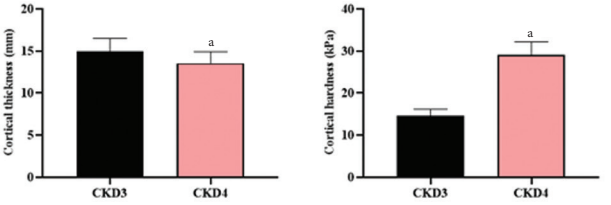
Figure 3. Clinical Biochemical Indicators in Patients with Different CKD Stages



[a]$P < .05$

Abbreviations: SCr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate.

Figure 4. Conventional Ultrasonic Parameters and SWE Parameters in Patients with Different CKD Stages



[a]$P < .05$

Conventional ultrasonic parameters and SWE parameters in both groups

Figure 2 revealed no significant difference in the length and width of the kidney between 2 groups ($P > .05$). The cortical thickness of the OG was 13.78 mm, which was lower than that of the CG (14.93 mm), and the cortical hardness of the OG was 23.83 kPa, which was higher than that of the CG (9.08 kPa), with statistical significance ($P < .05$).

Clinical biochemical indicators in patients with different CKD stages

Figure 3 revealed that eGFR in CKD3 patients was 48.46 mL/min/1.73m^2, which was higher compared to that of CKD4 patients (21.15 mL/min/1.73m^2). The SCr and BUN levels were 231.76 µmol/L and 16.69 mmol/L, respectively in CKD4 patients, and the values were higher than those found in CKD3 patients (121.34 µmol/L and 8.87 mmol/L, respectively), with statistical significance ($P < .05$).

Conventional ultrasonic parameters and SWE parameters in patients with different CKD stages

Figure 4 revealed that cortical thickness in CKD3 patients was 14.98 mm, which was higher than that in CKD4 patients (13.56 mm). The cortical hardness in CKD3 patients was 14.69 kPa, which was lower than that in CKD4 patients (29.18 kPa), with statistical significance ($P < .05$).

DISCUSSION

Metabolic abnormalities including hyperglycemia and hyperlipidemia may produce glycated lipids together with reactive oxygen species, resulting in the production of inflammatory cytokines as well as pro-fibrotic factors, which may cause mesangial, endothelial, and epithelial damage and finally lead to the development of glomerular sclerosis and renal tubulointerstitial fibrosis resulting in diabetic nephropathy.[10,11]

Although the application of SWE in the kidney has been less studied, the method has emerged to be an effective method for evaluating other organs.[12] For instance, while liver biopsy has long been the gold standard for measuring the extent of chronic morphological changes in the liver, SWE has been implemented for diagnosing liver fibrosis.[13] In addition, SWE has been adopted to measure the pathological processes of breast, prostate, pancreatic, testicular, thyroid, and other diseases.[14] Since human kidneys are located lower than the liver, it is more difficult to assess kidney elasticity. Animal studies have shown a direct correlation between changes in renal cortical hardness and renal fibrosis, and between increased cortical hardness and decreased renal function.[15]

In our study, the results displayed no significant differences in age, gender, and BMI between the 2 groups, which was in line with the outcomes of Simona Bota et al.[16] Besides, our research revealed that the SCr and BUN of patients in the OG were higher compared to the CG, while the eGFR value of patients in the OG was lower compared to that of CG. More importantly, eGFR in CKD3 patients was higher than that in CKD4 patients, and SCr and BUN levels in CKD3 patients were lower compared to the levels in CKD4 patients. At the same time, the cortical thickness of the OG was less than that of the CG, while the cortical hardness of the OG was more than that of the CG. Furthermore, the cortical thickness in CKD3 patients was more than that of CKD4 patients, while the cortical hardness in CKD3 patients was less than that of CKD4 patients. Thus, SWE can quantify the levels of parameters such as eGFR, SCr, BUN, and cortical thickness and hardness in healthy individuals and diabetic nephropathy renal fibrosis patients and further help to distinguish between stage 3 and 4 CKD. These findings imply that SWE could be adopted as a non-invasive, simple, low-cost, and reliable imaging technique to quantitatively measure the extent of cortical fibrosis in advanced diabetic nephropathy.

Consistent with our findings, Selcan Koc et al. suggested that cortical stiffness value obtained by SWE was significantly

higher in type 2 diabetes mellitus patients with normal renal function compared to patients without diabetes mellitus.[17] Want et al. indicated that SWE is a better diagnostic tool for diabetic peripheral neuropathy than the conventional ultrasonic parameter, cross-sectional area.[18] Yuksekkaya et al. suggested that SWE may be used as a noninvasive, simple, and quantitative method to provide diagnostic information as a part of routine management of patients with type 2 diabetes mellitus, especially in the early stages of diabetic kidney disease.[6] Whereas, ultrasound together with other imaging methods, containing CT and MRI, are not quantitative in their measurement of the severity of chronic morphological alterations, and there is no correlation between these CKD stages.[19] The staging of CKD is based on the degree of eGFR reduction and the presence of markers of kidney injury, instead of direct measurement of kidney tissue, such markers contain abnormal urinary protein excretion, urine deposits, electrolytes, and pathological changes of kidney tissue acquired by biopsy, abnormal imaging, along with history of kidney transplantation.[20] Quantitative information acquired through SWE can more accurately evaluate chronic morphological alterations linked to diabetic nephropathy progression.[21] In addition, quantitative markers of kidney injury such as eGFR, SCr, and BUN can be used to distinguish CKD grade.[22] Some studies have evaluated renal elasticity in patients with CKD, and the results show that SWE can be utilized to evaluate renal morphological alterations in diabetic nephropathy patients,[23] which suggests that renal elastic changes in diabetic nephropathy can be distinguished using SWE. Consistently, the outcomes of this study also displayed that SWE can not only diagnose diabetic nephropathy with renal fibrosis but also distinguish between CKD stages in diabetic nephropathy.

This study also has certain limitations: First, the accuracy of the examination results is affected easily by the respiratory movement of patients during kidney examination by SWE technology. Excessive breathing amplitude and the presence of a thick fat layer will affect the accuracy of the examination results. Second, due to the short time and limited number of cases investigated, it is necessary to increase the sample size for further research in the future.

In summary, the parameters of cortical thickness and cortical hardness in SWE of patients with advanced diabetic nephropathy renal fibrosis are different from those of healthy people. These parameters significantly differ in patients with different CKD stages and are significantly correlated with SCr, BUN, and eGFR, and this can be used for the diagnosis of diabetic nephropathy renal fibrosis.

AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no competing interests.

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