Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–8, 2017

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2017.04.019

● *Original Contribution*

ULTRASOUND-BASED SHEAR WAVE ELASTOGRAPHY IN THE ASSESSMENT OF PATIENTS WITH DIABETIC KIDNEY DISEASE

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(*Received* 13 *November* 2016; *revised* 18 *April* 2017; *in final form* 20 *April* 2017)

Abstract—In previous studies of acoustic radiation force impulse (ARFI) elastography, using Virtual Touch tissue quantification (VTQ) (Siemens Acuson S2000), it was reported that the measurement of renal shear wave speed in patients with chronic kidney disease (CKD) is not influenced exclusively by renal fibrosis. The purpose of the present study was to analyze the role of VTQ in patients with diabetic kidney disease, considered the main cause of CKD. The study group included 164 patients: 80 patients with diabetic kidney disease (DKD) and 84 without renal disease or diabetes mellitus. In each subject in lateral decubitus, five valid VTQ measurements were performed in each kidney and a median value was calculated, the result being expressed in meters/second. The following means of the median values were obtained In DKD patients, the means of the median values were for VTQ right kidney, 2.21 ± 0.71 m/s, and for VTQ left kidney, 2.13 ± 0.72 m/s, whereas in the normal controls statistically significant higher values were obtained: 2.58 ± 0.78 m/s for VTQ right kidney ($p = 0.0017$) and 2.46 ± 0.81 m/s for VTQ left kidney ($p = 0.006$). Patients with an estimated glomerular filtration rate (eGFR) >60 mL/min (DKD stages 1 and 2 together with normal controls) had a significantly higher kidney shear wave speed compared with patients with an eGFR <60 mL/min (2.53 m/s vs. 2.09 m/s, $p < 0.05$). In the DKD group, there was a significant correlation between eGFR and VTQ levels for the right kidney ($r = 0.28$, $p = 0.04$). There was no correlation of VTQ values with proteinuria level, stage of diabetic retinopathy or glycated hemoglobin. Our study indicates that shear wave speed values in patients with diabetic kidney disease and eGFRs <60 mL/min are significantly lower compared with those of patients with eGFRs >60 mL/min (either normal controls or diabetic patients with DKD stages 1 and 2), and values decrease with the decrease in eGFR. However, proteinuria, diabetic retinopathy and glycated hemoglobin have no influence on VTQ. (E-mail: iuliag_13@yahoo.com) © **2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Virtual Touch quantification (VTQ), Diabetic kidney disease, Kidney shear wave speed.**

INTRODUCTION

In the assessment of chronic kidney disease (CKD), there is a constant search for reliable markers, histologic or biochemical. In addition to these markers, reliable and reproducible imaging assessment methods are important. There are data on the use of contrast-enhanced ultrasound (CEUS), ultrasensitive Doppler techniques, magnetic resonance imaging and computed tomography for quantification of renal perfusion (Correas et al. 2016; Grenier et al. 2013b; Ma et al. 2012). Another imaging method that can be used to assess the properties of renal tissue is elastography.

Elastography is an ultrasound-based method used to assess tissue elasticity by measurement of the speed of shear waves generated into the tissue by an external stimulus, and is used mainly for the non-invasive assessment of liver fibrosis (Bota et al. 2013; Nierhoff et al. 2013), spleen stiffness for predicting portal hypertension (Bota et al. 2012; Takuma et al. 2013), for thyroid nodules (Hou et al. 2013; Zhang et al. 2013), prostate lesions (Zhai et al. 2010) or focal liver lesions (Ying et al. 2012). Among the different elastographic methods, those

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based on point shear wave elastography using the ARFI (acoustic radiation force impulse) technique have been reported in previous studies to be useful for the kidney as well. Despite the difficulties related to the high anisotropy of renal tissue, the method has been proven to have strong inter-observer reproducibility (Bob et al. 2014).

In previous ARFI elastography studies, it was reported that the measurement of kidney shear wave speed (KSWS) in patients with chronic kidney disease is not influenced exclusively by fibrosis. KSWS decreases with the progression of renal disease, with a pattern opposite that of the liver, the stiffness of which increases as liver disease progresses (Alan et al. 2017; Bob et al. 2015; Hu et al. 2014).

The main cause of chronic kidney disease is diabetes mellitus, according to the U.S. Renal Data System (USRDS) (40% of patients with CKD having also diabetes) (USRDS 2016). Diabetic kidney disease is a clinical diagnosis, based on the presence of albuminuria, of a decline in glomerular filtration rate (GFR) and, from the morphological point of view, of the presence of fibrosis in advanced stages.

The aim of the present study was to analyze the role of point shear wave elastography (Virtual Touch tissue quantification using ARFI technology) in patients with diabetic kidney disease (DKD) and to determine what factors are influencing kidney shear wave speed in these patients.

METHODS

Patients

Our prospective study included 80 consecutive patients with diabetic kidney disease and 84 normal controls (without chronic kidney disease and without diabetes mellitus). In all patients, kidney shear wave speed was evaluated using the Virtual Touch Tissue Quantification (VTQ) ARFI elastography method. The normal patients were selected from patients hospitalized in various departments of our hospital who did not have a history of diabetes mellitus or chronic kidney disease and who had normal serum biological tests (fasting glycemia, serum creatinine and blood urea nitrogen) and normal urinary tests (defined as absence of proteinuria and hematuria). Renal ultrasonography was normal in these patients (with the kidney being 10 cm in the long axis) and the difference in length between the right and left kidneys was $<$15 mm.

The patients with diabetic kidney disease were patients previously diagnosed in the Nephrology Department and in the Department of Diabetes and Metabolic Diseases using the KDIGO (Kidney Disease International Global Outcomes) definition (estimated glomerular filtration rate [eGFR] $<$60 mL/min and/or the presence of markers of kidney damage such as a urinary albumin/creatinine ratio $>$30 mg/g for more than 3 months) (KDIGO 2013). Patients undergoing hemodialysis or peritoneal dialysis, renal transplant recipients and patients with unilateral or bilateral hydronephrosis, kidney stones or renal tumors were excluded from the present study.

All patients included in our study signed an informed consent; the study was approved by the local ethics committee and was in accordance with the Helsinki Declaration of 1975.

Patients' assessments

In all patients included in the study serum biological tests (serum creatinine, blood urea nitrogen and glycated hemoglobin) were performed on the same day as kidney shear wave speed measurements. The serum creatinine results were used for estimation of the GFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) formula (Levey et al. 2009). Diabetic kidney disease was classified into five stages on the basis of eGFR using KDIGO criteria: stage G1 = eGFR $>$90 mL/min, stage G2 eGFR = 60–89 mL/min, stage G3 = 30–59 mL/min, stage G4 = 15–29 mL/min, stage G5 $\leq$15 mL/min. For stages G1 and G2 (eGFR $>$60 mL/min), the presence of markers of kidney damage (urinary albumin/creatinine ratio $>$30 mg/g) is necessary to diagnose DKD (KDIGO 2013) In 66 of the 80 patients with diabetic kidney disease, urine tests (24-h proteinuria and spot urinary albumin/creatinine ratio) were performed, within 7 d of inclusion. The statistical analysis included only laboratory results obtained after inclusion in the study (eGFR, urinary albumin/creatinine ratio); no previous data were used.

In 34 patients with diabetic kidney disease, fundoscopy was performed within 7 d of the inclusion, to assess the presence or absence of diabetic retinopathy.

Ultrasound examination

For all patients an ultrasound examination was available before the invitation to participate in the present study, but a new ultrasound examination was performed in each subject on the same day as kidney shear wave speed measurements.

Kidney length and the renal parenchyma thickness were recorded. None of the patients had hydronephrosis, kidney stones, renal tumors or a discrepancy in renal size $>$15 mm between the kidneys. Only patients with a renal parenchymal thickness $>$10 mm were included, to permit elastography measurements (fixed dimension of the region of interest: 10 mm).

Shear wave elastography measurements

Kidney ultrasound-based shear wave elastography was performed in all patients with a Siemens Acuson