ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 3, May – 2023 , Page No. : 322 – 328

Correlation of Renal Elasticity with Biochemical and Ultrasound Parameters used to Assess Renal Function in Patients with Diabetic Kidney Disease.

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Citation this Article: Abhishek Garg, Kirti Chaturvedy, Manish Chaturvedy, Divyangi Mishra, Sonali Barad, Hema Ram, Sarthak Batra, Mohammad Arshad, " Correlation of Renal Elasticity with Biochemical and Ultrasound Parameters used to Assess Renal Function in Patients with Diabetic Kidney Disease ", IJMSIR- May - 2023, Vol – 8, Issue - 3, P. No. 322 – 328.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Current methods for the evaluation of structural renal changes as a result of chronic kidney disease in patients with diabetes are his to patho logy as a gold standard, CT, MRI and conventional ultrasound. These methods have their own limitations and high cost; therefore, a new noninvasive and cost-effective method needs to be developed. Shear wave elastography can therefore serve as an effective technique.

Aim: To evaluate the correlation of renal tissue elasticity by Shear wave elastography (SWE) with eGFR and con ventional ultrasound parameters.

Methodology: The study included 50 patients with diabetic nephropathy. The kidney elasticity was assessed quantitatively by measuring the shear-wave velocity and young's modulus using acoustic radiation force impulse imaging. The changes in the renal elasticity were compa red between the different stages of diabetic nephropathy.

Statistical analysis: Continuous data was expressed in mean +/- standard deviation and ANOVA test was used for analysis. To calculate correlation coefficient 'r', person's correlation coefficient was used. P value of less than 0.05 is taken as statistically significant.

Results and Conclusion: Renal stiffness was signi ficantly correlated with eGFR (r=-0.317, p=0.024), serum creatinine (r=0.322, p= 0.022) and blood urea (r=0.299, p =0.034). No statistically significant correlation was found with renal length, renal width and renal cortical thick ness. As renal dimensions often do not change signific antly in diabetic CKD, SWE has advantage over the con

ventional ultrasound. Shear wave velocities were 1.81 ± 0.87, 2.34 ± 0.57, 2.59 ± 0.57, 2.49 ± 8.81, 2.81 ± 0.77 & 2.66 ± 0.98 in m/sec for diabetic nephropathy stages I, II, IIIa, IIIb, IV and V respectively.

Keywords: CKD, CT, MRI.

Introduction

Chronic kidney disease (CKD) is structural or functional damage to kidneys resulting in progressive loss of kidney function. Major causes are hypertension, diabetes, and primary kidney disease. "Diabetes mellitus is the most common cause of CKD worldwide" [1, 2]."Diabetic nephro pathy is one of the major complications of diabetes and is directly related to disease progression" [1]. Early diag nosis of nephropathy is important for the prognosis of patients with diabetes. Diabetic CKD is classified into five stages according to "KDIGO guidelines and eGFR is calculated using the equation CKD-EPI" [3, 4]. (TABLE 1)

Table 1: According to "Kidney Disease Improving Global Outcomes (KDIGO) classification currently CKD is classified into five severity-based stages based on the estimated glomerular filtration rate (eGFR), which is calculated from serum creatinine values using chronic kidney disease epidemiology collaboration (CKD-EPI) equation" [3, 4]

Classification of CKD based on eGFR		
Stage	Description	eGFR (ml min–1/1.73 m²)
1	Hyperfiltration	≥90
2	Microalbuminuria	60–89
3a	Overt proteinuria (mild to moderate reduction)	45–59
3b	Overt proteinuria (moderate to severe reduction)	30–44
4	Progressive nephropathy	15–29
5	End stage renal disease	<15

Staging according to urine albuminuria	Urinary albumin excretion (mg/dl)
A1	<30
A2	30-300
A3	>300

"CKD-EPI equation" expressed as a single equation [3]:

"eGFR = 141 × min (Scr /κ, 1) α × max (Scr /κ, 1)-1.209 × 0.993Age × 1.018 [if female] × 1.159 [if black]"

where: Scr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr /κ or 1, and max indicates the maximum of Scr /κ or 1.

One of the common investigations for early diagnosis of diabetic nephropathy is determination of microalbumin levels in urine samples. According to previous studies, micro albuminuria is a strong predictor of diabetic nephro pathy [1]. However, urinary micro albuminuria is also influenced by blood pressure, exercise, and blood glucose levels. "Some studies suggest that daily urinary albumin deposition can vary by as much as 40-50%" [5], but others found that urinary albumin deposition can occur even without the development of diabetic nephro pathy. According to Mogensen [6], "micro albuminuria is a symptom of stage 3 diabetic nephropathy". Micro albuminuria should not be regarded as a sensitive and specific sign for the early detection of diabetic nephro pathy as a result.

eGFR is another reliable indicator of diabetic nephro pathy. However, in situations like abrupt changes in renal function, excessive dietary protein intake, extreme body size, and acute liver illness, eGFR readings frequently give false information [7].

Because it is safe, non-invasive, and affordable, con ventional renal ultrasonography is frequently utilised for preliminary evaluation. It is simple and easy to evaluate renal ultra sono graphy characteristics such increased par

en chymal echogenicity, reduced renal size, and par en chymal thickness [8]. However, parenchymal echogenicity is a subjective marker and often does not allow quanti fication of renal abnormalities. CKD due to diabetes differs from other causes in that renal size does not change significantly in diabetes, which is an infiltrative process. Therefore, conventional ultrasound parameters often provide different results, and the patient cannot be treated based on conventional ultrasound parameters. Renal biopsy is the gold standard for the diagnosis of diabetic kidney disease with the classic Histo patho logical findings of Kimmelstiel-Wilson nodules and Armanni-Ebstein lesions. However, renal biopsy is associated with complications such as bleeding, shock, infection, and Hospitalisation (8).

Other modalities such as CT and MRI have their limitations in terms of high cost and IV contrast administration. High radiation exposure is a risk factor in CT examination.

Therefore, the develop ment of another diagnostic tool is urgently needed. In our study, we used shear wave elastography (SWE) to measure changes in renal parenchy mal elasticity in patients at different stages of diabetic nephropathy. By comparing these results with creatinine clearance measure ments (eGFR, serum creati nine) and conventional ultra sound parameters, we aimed to assess this method's validity as a diagnostic and screening tool for diabetic nephropathy. Shear wave elas to graphy (SWE) is a growing ultrasound technique that measures tissue stiffness in various organs like thyroid, breast, liver, kidneys etc. Shear waves that travel per pendicular to the main ultrasound beam are created using a short-duration acoustic push pulse that is generated in real-time by the ultrasound transducer. The waves push the targeted tissue in the direction of propagation when they strike it, thus temporarily shifting the targeted tissue. This tissue displacement is then monitored by the ultra sonic scanner, which can also measure when the tissue is most displaced and when it returns to its normal position [9].

Shear wave velocity and the young's modulus increases in diseased tissues, which are significantly stiffer than normal ones. The parameters are expressed in pressure units of kilopascals (kPa) and velocity (m s−1).

Materials and Methodology

The study is an observational, cross-sectional study con ducted over a period of 1 year and includes 50 Patients with clinically diagnosed diabetic kidney disease after obtaining a written informed consent. For statistical analysis, all continuous data was expressed in mean +/- standard deviation and ANOVA test was used. To calculate correlation coefficient 'r', person's correlation coefficient was used. P value of less than 0.05 was taken as statistically significant.

Selection of Cases

Inclusion criteria: Patients with clinically diagnosed diabetic kidney disease of age >/= 18 years and giving consent to participate in the study.

Exclusion criteria

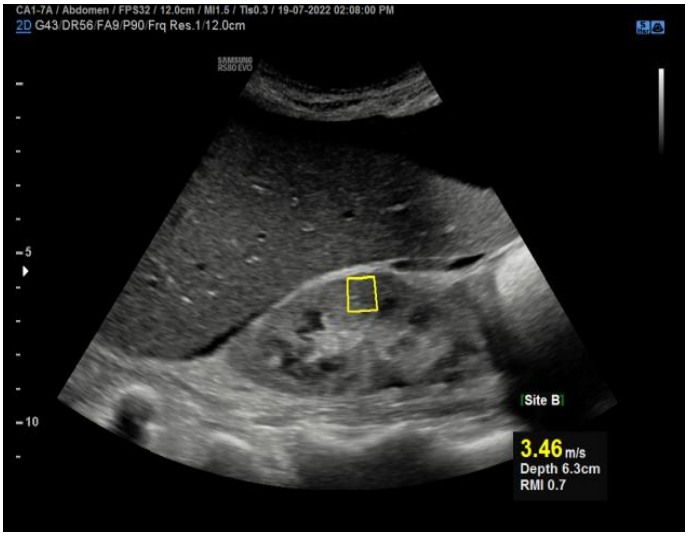
1. Patients with evidence of hydronephrosis, renal stones, renal mass/ tumor.
2. Obese patients in which depth of renal parenchyma is > 8 cm.
3. Patients who were unable to breath hold.
4. Patients with known systemic disease affecting renal outcome.

Procedure

Ultra sound examination of both kidneys was performed on Samsung RS 80 Evo machine using convex C5-1 probe by single person. Examinations were performed post micturition. Renal length and width were measured on coronal plane in lateral decubitus position. Renal

length was measured from upper to lower pole and width was measured from renal capsule to hilum. Cortical thickness was measured at mid pole from renal capsule up to renal pyramid. Maximal cortical depth was measu red from skin surface to renal cortex at mid pole. Shear wave elastography was then performed using the same convex C5-1 probe in lateral decubitus position. Care was taken to avoid any compression by the probe. Patients were asked to hold breath for few seconds to minimise motion artefacts. ROI box with dimensions 1x0.5cm was positioned in the renal cortex at mid pole, excluding the medulla (Figure 1). By pressing the Update button, elasticity measurements, both as SWV (m/s) and young's modulus (kPa), were taken in single kidney. Total 5 valid measurements were taken during separate breath holds. Then the mean value for particular kidney was calculated. Procedure was then repeated for the contralateral kidney.

Figure1:



USG image shows right kidney from the coronal view by placing the probe on right flank region. Image shows the correct placement of ROI box in the renal cortex at mid pole. Shear wave velocity calculated is 3.46 m/s with depth of ROI box 6.3cm. Note that there is no evidence of hydronephrosis, renal calculus or renal mass in the image's kidney.

Results

1. There was significant negative correlation found between young's modulus and eGFR (r=-0.317, p = 0.0 24). This implies that as the eGFR decreases, renal stiffness increases (given by young's modulus in kPa) and the shear wave velocity increases (m/sec) indicating stiffer and diseased kidneys.

2. There was no statistically significant correlation of eGFR between renal length (r=0.272, p=0.055), renal width (r=0.034, p=0.814) and renal cortical thickness (r=0.127, p=0.378) in patients with diabetic kidney disease. This implies that as the eGFR decreases in patients with diabetic kidney disease, there was no significant change in renal dimensions.

3. Mean values of renal stiffness & SWV were 12. 28 ± 10.65, 17.65±8.58, 21.72±8.15, 19.82±12.2, 24.85±10.7 & 24.02 ± 16.83 in kPa and 1.81±0.87, 2.34±0.57, 2.59 ± 0.57, 2.49±8.81, 2.81±0.77 & 2.66±0.98 in m/sec for diabetic nephropathy stages I, II, IIIa, IIIb, IV and V respectively. TABLE 2A and 2B

4. There was no statistically significant correlation of renal stiffness with renal length (r=-0.104, p=0.474), renal width (r=-0.205, p=0.151) and renal cortical thick ness (r=-0.252, p=0.076) in patients with diabetic kidney disease.

5. There was statistically significant correlation of renal stiffness with serum creatinine (r=0.322, p= 0.022) and blood urea (r=0.299, p=0.034). However there was no statistical significant correlation of renal stiffness found with HbA1c (r=0.227, p=0.112) and RBS (r=0.204, p=0.155).

Table 2 A: Renal stiffness values (kPa) for kidneys by diabetic nephropathy (CKD) stages

CKD stages	No. of patients	Renal stiffness (kPa)			f value	p value
		Mean	SD	Range		
I	4 (8%)	12.28	10.65	2.15-27.25	1.082	0.383
II	10 (20%)	17.65	8.58	6.50-32.55		
3a	6 (12%)	21.72	8.15	11.30-35.30		
3b	9 (18%)	19.82	12.2	5.35-39.50		
4	14 (28%)	24.85	10.7	2.20-46.75		
5	7 (14%)	24.02	16.83	3.30-53.75		

Table 2B: Shear wave velocity values (m/sec) for kidneys by diabetic nephropathy (CKD) stages

CKD stages	No. of patients	SWV (m/sec)			f value	p value
		Mean	SD	Range		
I	4	1.81	0.87	0.83-2.97	1.25	0.302
II	10	2.34	0.57	1.55-3.320		
3a	6	2.59	0.57	1.865-3.495		
3b	9	2.49	0.81	1.340-3.670		
4	14	2.81	0.77	0.855-4.165		
5	7	2.66	0.98	1.310-4.240		

Discussion

Ultrasonography is the most common modality used for the evaluation of renal morphology in patients with chronic kidney disease and diabetes is no exception. Shear wave elastography is emerging as a new tool for the evaluation of these structural changes and can complement the conventional ultrasound and biochemical parameters for the evaluation of diabetic kidney disease.

In a study by Guo et al [10], no significant correlation found between SWV and renal dimensions which are consistent with our study results. SWV correlated significantly to eGFR, blood urea and serum creatinine in their study which is consistent with our results. In their study, "the mean SWV was 1.81±0.43 m/s, 1.79±0.29 m/s, 1.81±0.44 m/s, 1.64±0.55 m/s, and 1.36±0.17 m/s for stage 1, 2, 3, 4 and 5 in CKD patients respectively". These values significantly differ from our study results. In their study, mean SWV decreases as the CKD stage increases thus having reciprocal relationship. However in our study the overall trend of SWV from stage 1 to stage 5 is increasing, but there is interstage variability in this trend which can be possibly removed by taking a larger sample size in future studies.

In a study by Goya et al [1], serum creatinine and blood urea nitrogen were statistically significantly correlated with shear wave velocity (positive correlation) which is consistent with our study. "Shear-wave velocity values for the kidneys were 2.87, 3.14, 2.95, 2.68, and 2.55 m/s in patients with stage 1, 2, 3, 4 and 5 diabetic nephro pathies respectively".

Mean values for young's modulus (kPa) and shear wave velocity (SWV) for different stages of diabetic kidney disease in our study are 12.28±10.65, 17.65±8.58, 21.72 ± 8.15, 19.82 ± 12.2, 24.85 ± 10.7 & 24.02 ± 16.83 in kPa and 1.81 ± 0.87, 2.34 ± 0.57, 2.59 ± 0.57, 2.49 ± 8.81, 2.81 ± 0.77 & 2.66 ± 0.98 in m/sec for diabetic nephropathy stages I, II, IIIa, IIIb, IV and V respectively. Although these values of renal tissue stiffness can be used to predict the diabetic nephropathy stage, but because of the high standard deviation and wide range as described in table no. 4a and 4b, there was no statistically significant difference between the mean SWE of different

stages of the diabetic kidney disease. This limitation can be possibly removed by taking a larger sample size in future studies so as to get a standard reference value for each stage of DKD.

As correlated with conventional ultrasound parameters, we found that there is no statistically significant correlation of renal elasticity with renal length (r=-0.104, p=0.474), renal width (r=-0.205, p=0.151) and renal cortical thickness (r=-0.252, p=0.076). This implies that as the disease progresses no significant changes occur in renal dimensions which is consistent with pathogenesis of the disease [(11)]. Thus, a patient of stage 4 or 5 diabetic kidney disease may have normal ultrasound parameters but will have increased renal stiffness, and therefore will not be misinterpreted as having normal kidneys.

There are certain limiting factors in our study which may be possible for the variation in SWV and renal stiffness with the previous studies.

- The most important one is the inability to hold the breath by the patient which leads to motion artefacts and spurious values of renal stiffness.
- The other factor that may be responsible is the renal blood flow as this factor is not considered in our study.
- Other limitation of our study was the absence of any histopathological diagnosis of diabetic kidney disease. Patient may have other causes of CKD but misinterpreted as diabetic CKD by the physician.
- Also as the ROI was fixed in dimension, renal parenchyma with thickness less than 0.5cm could not be evaluated.
- There was no interobserver variability assessment in our study as the study is performed by a single radiologist.
- Also, there is significant intra observer variability noted in the renal stiffness values at the same region of placement of ROI box, which may be due to motion artefacts or due to limitations of shear wave elastography itself.
- Further our study has a small sample size of 50, which is not sufficient to describe the results for a large scale of population.

This indicates need for more studies on renal elas to graphy with larger sample size so as to obtain standar dised data for values of SWV in different stages of diabetic kidney disease. Follow-up studies are needed as to know the progress of kidney disease on the basis of renal elasticity changes.

Conclusion

- Shear wave elastography (SWE) can be useful in early stages of DKD in which serum creatinine values can be normal and thus can be used for early screening of diabetic kidney disease.
- Increase in renal stiffness and shear wave velocity can be used as a useful adjunct to the common biochemical parameters like serum creatinine and blood urea in evaluation of the chronic kidney disease.
- Mean values for young's modulus (kPa) and shear wave velocity (SWV) can be used to predict the diabetic nephropathy stage.
- Patient can be followed upon for the progression of CKD by evaluating the renal stiffness changes.
- Shear wave elastography has an advantage over the conventional ultrasound findings in which there may be no significant changes detected in renal dimensions in patients of diabetic kidney disease.

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