Correlation between Sonoelastographic, Doppler and Histopathological Findings in Chronic Kidney Disease Patients in Tertiary Care Centre

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ABSTRACT

Background

Ultrasound (USG) with Doppler examination of intrarenal vessels is the imaging modality of choice employed in patients with renal failure and is commonly performed early in the clinical course. The pulsatility index (PI) and the resistive index (RI) of downstream renal artery have been found to correlate with renal vascular resistance, filtration fraction and effective renal plasma flow in chronic renal failure. Pathological process in any tissues alters their elastic properties which can be assessed non-invasively through newer technique like elastography.

Objective

To correlate the findings obtained by sonoelastographic, doppler and histopathological studies in chronic kidney disease patients.

Method

Study was done in 146 patients referred to Department of Radiodiagnosis and Imaging, TUTH for native renal biopsy. Renal sonographic morphology (length, echogenicity, cortical thickness), Sonoelastography (Young's modulus) and Doppler parameters (peak systolic velocity, resistive index) were assessed. The grading of estimated GFR (eGFR) was calculated based on chronic kidney disease (CKD) criteria.

Result

Among 146 patients, 63 (43.2%) were females and 83 (56.8%) were males. Maximum patients were in age group of 41-50 years (25.3%) followed by age group 51-60 years (24%). Mean age of patient was 42.06±14.70 for males and 39.57±12.54 females. Maximum mean Young's modulus was seen in eGFR stage G1 with 46.57±19.51 kPa followed by in stage G3a with 36.46±10.01 kPa and observed to be statistically non-significant (p=0.172). However, statistical significance difference was noted between the resistive index and elastographic measurement of Young's modulus (r=0.462, p=0.0001). Minimum mean cortical thickness was seen in eGFR stage G5 with 4.42±1.48 mm followed by stage G4 with 5.57±1.24 mm (p= 0.0001). Cortical thickness is decreasing as eGFR stage was increasing in our study (p=0.0001). Resistive index is increasing with decrease in renal size (r=-0.202, p=0.015).

Conclusion

Ultrasonography along with doppler study and elastography have limited role in diagnosing the pathology of chronic kidney disease, however, it has significant role in the disease progression.

KEY WORDS

Chronic kidney disease, Doppler, Elastography, Resistive index, Ultrasonography

INTRODUCTION

Ultrasounography (USG) with doppler examination of intrarenal vessels is the non invasive imaging modality of choice to be employed in patients with renal failure and is commonly performed early in the clinical course.[1] The pulsatility index (PI) and the resistive index (RI) are used as pulsed-wave Doppler measurements of downstream renal artery resistance. PI and RI have been found to correlate with renal vascular resistance, filtration fraction and effective renal plasma flow in chronic renal failure.[2]

Pathological process in any tissues alters their elastic properties which can be imaged through newer technique like elastography. Intra-renal fibrosis is a final common pathway for all chronic kidney disease (CKD), with fibrosis degree correlated with disease severity. Non-focal renal biopsy is the only method in current clinical use for the evaluation of intra-renal fibrosis.[3] With real-time ultrasound elastography, or conventional elastography, the physical properties of soft tissue are revealed through characterization of the differences in stiffness between the region of interest and the surrounding tissue on the basis of uniform, mechanically induced deformation (strain) of structures during B-mode scanning. The degree of deformation of the underlying soft tissue is calculated to estimate the tissue stiffness, not true elasticity, in kilopascals (kPa).[4] Shear wave elastography (SWE) uses focused acoustic energy pulses to produce microscopic tissue displacement, which induces perpendicular shear waves that are sonographically tracked as they progress through tissue. Stiffer tissues have been shown to have increased shear wave velocities. Estimates of tissue Young's modulus (YM), measured in kilopascals (kPa) can be derived from shear wave velocity, where higher values correlate with a higher degree of fibrosis.[3]

The opportunity was taken with ultrasound guided non-focal renal biopsy to correlate various sonographic parameters including elastography and doppler with histopathological findings in Chronic kidney disease patients.

METHODS

The study was done in 146 patients referred to Department of Radiodiagnosis and Imaging, Tribhuvan University Teaching Hospital (TUTH), Maharajgunj, Nepal for native renal biopsy from July 2017 to July 2018. Clinical and lab parameters were taken. eGFR was calculated from patient age, weight and serum creatinine value using Cock Croft Gault's formula and CKD staging was based on eGFR values. Renal sonographic morphology (length, echogenicity, cortical thickness), Sonoelastography (Young's modulus) and Doppler parameters (peak systolic velocity, resistive index) were assessed. Histopathological diagnosis was obtained from the department of pathology. Study was done after ethical clearance from the Institutional Review Board IRC number 462, TUTH. The Patients with post-transplant kidney biopsy (Graft Kidney does not show the native CKD pathology), with gross ascites, under dialysis (Dialysis changes the echogenicity of Kidney) were excluded from the study.

USG Doppler and Elastography process

The 5-MHz curved probe and a 7.5 - 10 MHz linear probe was used for evaluating kidney in patients. First step was to evaluate through gray scale ultrasound. Assessment included size of kidney, cortical thickness, echogenicity, corticomedullary differentiation. For Doppler evaluation of kidney, following optimization on machine settings was done: Pulse repetition frequency (PRF) between 700-1000 MHz, wall filter as low as possible (50 to 100Hz max). The color gain was initially increased to a level which shows color noise, and then decreased to the level where the noise just disappears and at the same time avoiding artifactual color noise. The sample volume of 1.5 mm was centered in the vessel, and the angle of insonation was kept at 60 degree or less in all examinations. The Peak systolic velocity (PSV) and Resistivity Index (RI) parameters were assessed by color and spectral Doppler.

Elastography was performed during quiet respiration. Excessive transmission gel was used to eliminate any compression artifact of the probe. Elastogram images and gray-scale images were simultaneously displayed. A rectangular electronic box was used for shear wave elastography examinations which were kept in relatively homogenous parts of kidney. Three elastograms were captured from upper, middle and lower pole cortex of kidney. Young's modulus data was automatically displayed for ROI. The measured data for each ROI were used for statistical analysis. Values less than 1 kPa were rejected.

Biopsy process

Single 18G core biopsy needle with automated biopsy gun is used to obtain two 20 mm cores of tissue samples, one preserved in normal saline (0.9%) and another preserved in formalin, and are sent to the Department of Pathology for histopathological processing in automated histology analyzer, and tissue diagnosis is obtained.

The data was collected in predesigned proforma and was entered in Statistical Package for social service (SPSS) version 16. The data were expressed in frequency (%), Mean ± SD and compared using Analysis of Variance (ANOVA) and Pearson's correlation. P value< 0.05 was considered to be statistically significant.

RESULTS

Among 146 patients, maximum patients were in age group of 41-50 years (25.3%) followed by age group 51-60 years (fig. 1). 63 (43.2%) were females and 83 (56.8%) were males (fig.2). Mean age of patient was 42.06±14.70 for males and 39.57±12.54 females.

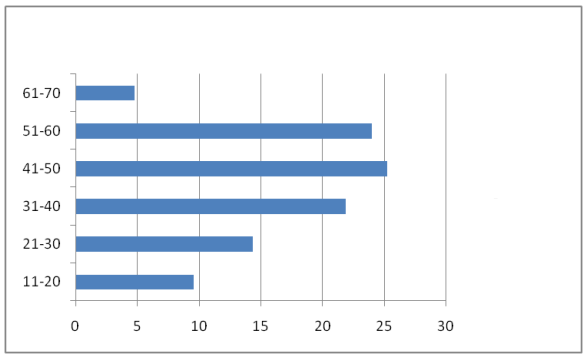

Figure 1. Age wise distribution of study subjects

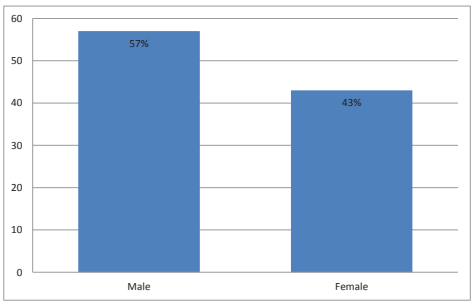

Figure 2. Gender wise distribution of study subjects

Table 1 shows mean Young's modulus (kPa) based on eGFR stage where the maximum mean Young's modulus was seen in eGFR stage G1 with 46.57±19.51 kPa followed by stage G3a with 36.46±10.01 kPa. No significant statistical correlation was seen between the eGFR staging with elastographic measurement of Young's modulus (p value 0.172).

Table 1. Mean ± SD Young's modulus based on eGFR stage of CKD patients

	Frequency (N=146)	Mean Young's modulus (kPa)		p value
		Mean	SD	
G1	5	46.57	19.52	0.172
G2	9	27.58	10.61	
G3a	14	36.46	10.01	
G3b	44	35.08	12.47	
G4	47	34.12	12.84	
G5	27	34.05	12.49	

Table 2 shows mean cortical thickness (mm) based on eGFR stage where the minimum mean cortical thickness was seen in eGFR stage G5 with 4.42±1.48 mm followed by stage G4 with 5.57±1.24 mm. Significant statistical correlation was seen between the eGFR staging and mean cortical thickness (p value 0.0001). Cortical thickness is decreasing as eGFR stage was increasing.

Table 3 shows the histopathological diagnosis with most common histological diagnosis of Focal Segmental Glomerulosclerosis seen in 13% of cases followed by PLA2R associated Membranous Glomerulopathy in 9% cases and IgA nephropathy and Membranous Glomerulopathy in 8.2% of cases each.

Table 2. Mean ± SD Cortical thickness based on eGFR stage of CKD patients

	Frequency (N=146)	Mean Cortical thickness (mm)		p value
		Mean	SD	
G1	5	7.10	1.08	0.0001
G2	9	6.50	0.98	
G3a	14	6.69	0.62	
G3b	44	6.24	1.50	
G4	47	5.57	1.24	
G5	27	4.42	1.48	

Table 3. Distribution of sample by histological diagnosis of CKD patients

Histological diagnosis	Frequency	Percentage
Acute Tubular Injury	2	1.4
Acute Tubulointerstitial Nephritis	2	1.4
Chronic Glomerulonephritis	2	1.4
Chronic sclerosing IgA nephropathy	8	5.5
Chronic tubulointerstitial nephritis	4	2.7
Crescentic Glomerulonephritis	4	2.7
Diabetic nephropathy	7	4.8
Diffuse Proliferative Glomerulonephritis	2	1.4
Diffuse proliferative IgA nephropathy	6	4.1
Focal Mesangioproliferative Lupus Nephritis	2	1.4
Focal Proliferative Glomerulonephritis	4	2.7
Focal proliferative IgA nephropathy	7	4.8
Focal Proliferative Immune-complex	2	1.4
Focal proliferative lupus nephritis	4	2.7
Focal Segmental Glomerulosclerosis	19	13
Heavy Chain Deposition Disease	2	1.4
Hypertensive nephrosclerosis	9	6.2
Hypertensive nephrosclerosis leading to secondary FSGS	7	4.8
IgA nephropathy	12	8.2
IgA nephropathy with FSGS like morphology	5	3.4
Membranous Glomerulopathy	12	8.2
Mesangioproliferative lupus nephritis	3	2.1
Mild mesangioproliferative glomerulonephritis	1	0.7
Minimal change disease	4	2.7
Normal	2	1.4
PLA2R associated Membranous Glomerulopathy	14	9.6

Pearson correlation between mean Young's modulus and mean RI was observed to be r = 0.462 with p value 0.0001. Statistical significance was noted between the resistive index and elastographic measurement of Young's modulus. Pearson correlation between mean Young's modulus and mean Renal size was observed to be r = -0.053 with p

Table 4. Pearson's Correlation between mean Young's modulus (MYM), mean RI (MRI), mean renal size (MRS) and mean cortical thickness (MCT)

	Variables	MRI	MRS (cm)	MCT (mm)
MYM	**r**	**0.462****	-0.053	-0.059
	Sig. (2-tailed)	**0.0001**	0.527	0.477
MRI	**r**	1	**-.202***	-0.066
	Sig. (2-tailed)	NA	**0.015**	0.425
MRS	**r**	**-0.202***	1	**.424****
	Sig. (2-tailed)	**0.015**	NA	**0.0001**

**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)

value 0.527. High Young's modulus value was noted with decreasing renal size, however, statistical significance was not noted. Pearson correlation between mean Young's modulus and mean Cortical thickness was observed to be r = -0.059 with p value 0.477. High Young's modulus value was noted with decreasing renal size, however, statistical significance was not noted. Pearson correlation between mean RI and mean Renal size was observed to be r = -0.202 with p value 0.015. Resistive index is increasing with decrease in renal size.

DISCUSSION

Use of ultrasonography with doppler study is a common modality in evaluation of chronic kidney disease. Recently, elastography has emerged as an option in several commercial ultrasound systems, and is starting to prove clinically valuable in many areas. It is a newly developed dynamic technique that uses US to provide an estimation of tissue stiffness by measuring the degree of distortion under the application of an external force.[5]

SWE-derived estimates of renal stiffness and intra-subject estimated stiffness variability are higher in patients with CKD than in healthy controls. Renal fibrosis is a plausible explanation for the observed difference in YM. The study done by Sook Sam Leong et al in 106 CKD patients and 203 control subjects revealed negative correlation between YM measurements and eGFR ($r = -0.576$, $p < 0.0001$), and Positive correlations between YM measurements and age ($r = 0.321$, $p < 0.05$), serum creatinine ($r = 0.375$, $p < 0.0001$) and urea ($r = 0.287$, $p < 0.0001$).[6]

In our study, maximum mean Young's modulus was seen in eGFR stage G1 with value of 46.57±19.51 kPa followed by in stage G3a with value of 36.46±10.01 kPa (p value = 0.172). No significant statistical correlation was seen between the eGFR staging with elastographic measurement of Young's modulus in our study.

Radermacher et al. in 137 patients with proteinuric chronic renal disease reported that renal RI more than 0.80 was associated with faster decline of renal function over a 5 year median follow-up period.[7] Parolini et al. found a strong correlation between initial RI and final renal function in a study done in 177 patients.[8]

Study done by Ghonge et al. in 60 allograft renal transplant patient found the inverse correlation of parenchymal stiffness with eGFR and positive correlation with RI and serum creatinine level show that shear-wave sonoelastography may reflect functional status of the renal allograft.[9] Mean parenchymal stiffness values in stable allograft, acute allograft dysfunction, and chronic allograft dysfunction were 8.51 kPa 6 2.44, 11.06 kPa 6 2.91, and 24.50 kPa 6 4.49, respectively.[9]

Study done by Yang et al. revealed that elastography may reflect renal function and can be a non-invasive method for the evaluation of renal function after kidney transplantation.[10]

In our study, Pearson correlation between Mean Young's modulus and Mean RI was observed to be r = 0.462 with p value of 0.0001. Statistical significance was noted between the resistive index and elastographic measurement of Young's modulus.

Study done by Michael D. Beland in 25 patients revealed that cortical thickness measured on ultrasound appears to be more closely related to eGFR than renal length. According to Korkmaz et al. ultrasonographic cortical thickness measurements may be an important imaging technique in the follow-up care of patients with CKD.[11]

In our study, minimum mean cortical thickness was seen in eGFR stage G5 with value of 4.42±1.48 mm followed by in stage G4 with value of 5.57±1.24 mm (p value = 0.0001). Significant statistical correlation was seen between the eGFR staging and mean cortical thickness. Cortical thickness is decreasing as eGFR stage was increasing in our study. According to Sanusi et al. kidney length is not an accurate predictor of kidney abnormality as compared to kidney volume.[12] Study done by Jovanovic et al. in 49 patients revealed kidney size of patients with CKD correlated significantly with kidney function, while correlation with anthropometric parameters, which is otherwise present in healthy subjects, was lost in patients with CKD.[13]

In our study, Pearson correlation between Mean RI and Mean Renal size was observed to be r = -0.202 with p value of 0.015. Statistical significance was noted between the mean resistive index and mean renal size. Resistive index is increasing with decrease in renal size.

Histopathologic analysis of the biopsy specimen is indispensable for the initial diagnosis of medical renal disease. Study done by Hricak et al. in 109 patients revealed the lack of specificity of the sonograms and the limited responses of the kidney to various pathological insults may well remain a limitation to specific sonographic diagnosis, even when accurate quantitative measurements by ultrasound become available.[14]

Study done by Rosenfield et al. in 25 patients concluded that there is no correlation between the nature or severity of the gbomerular lesion and the sonognaphic findings; there is no correlation between the degree of medullary definition and the sonographic findings; and there is a definite correlation between the degree and severity of the interstitial changes and the sonognaphic findings.[15]

CONCLUSION

Ultrasonography along with doppler study and elastography have limited role in diagnosing the pathology of chronic kidney disease, however, it has significant role in following up the disease progression. However, additional studies are required to further evaluate its usefulness in accurately depicting the pathology of chronic kidney.

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REFERENCES

1. Fauci AS, Hauser SL, Jameson JL, Kasper DL, Longo DL, Loscalzo J, editors. Harrison's Manual of Medicine, 19e. McGraw-Hill Education LLC.; 2016.
2. Degrassi F, Quaia E, Martingano P, Cavallaro M, Cova MA. Imaging of haemodialysis: renal and extrarenal findings. *Insights Imaging* [Internet]. 2015 Jun 14 [cited 2018 Jul 15];6(3):309-21. Available from: http://link.springer.com/10.1007/s13244-015-0383-3
3. Petersen LJ, Petersen JR, Talleruphuus U, Ladefoged SD, Mehlsen J, Jensen H. The pulsatility index and the resistive index in renal arteries. Associations with long-term progression in chronic renal failure. *Nephrol Dial Transplant*. 1997;12(7):1376-80.
4. Samir AE, Allegretti AS, Zhu Q, Dhyani M, Anvari A, Sullivan DA, et al. Shear wave elastography in chronic kidney disease: A pilot experience in native kidneys. *BMC Nephrol* [Internet]. 2015;16(1). Available from: http://dx.doi.org/10.1186/s12882-015-0120-7.
5. Bhargava S, Bhargava SK, Sharma S, Prakash M. Elastography: a new imaging technique and its application. *JIMSA*. 2013;26(1):25-30.
6. Leong SS, Wong JHD, Md Shah MN, Vijayananthan A, Jalalonmuhali M, Ng KH. Shear wave elastography in the evaluation of renal parenchymal stiffness in patients with chronic kidney disease. *Br J Radiol*. 2018 Sep;91(1089):20180235. doi: 10.1259/bjr.20180235.
7. Radermacher J, Ellis S, Haller H. Renal resistance index and progression of renal disease. *Hypertens* (Dallas, Tex 1979) [Internet]. 2002 Feb [cited 2018 Nov 1];39(2 Pt 2):699–703. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11882634
8. Parolini C, Noce A, Staffolani E, Giarrizzo GF, Costanzi S, Splendiani G. Renal resistive index and long-term outcome in chronic nephropathies. *Radiology.* 2009 Sep;252(3):888-96.
9. Ghonge NP, Mohan M, Kashyap V, Jasuja S. Renal Allograft Dysfunction: Evaluation with Shear-wave Sonoelastography. *Radiology* [Internet]. 2018;288(1):1460-52. Available from: http://pubs.rsna.org/doi/10.1148/radiol.2018170577
10. Yang J, Wang F, Pan W, Ruan L, Ai H. Correlation between ultrasound elastography parameters and renal function after kidney transplantation. *Int J Clin Exp Med*. 2017;10(2):3211-7.
11. Korkmaz M, Aras B, Güneyli S, Yılmaz M. Clinical significance of renal cortical thickness in patients with chronic kidney disease. *Ultrason* (Seoul, Korea) [Internet]. 2018;37(1):50-4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28618770%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5769950
12. Sanusi AA, Arogundade FA, Famurewa OC, Akintomide AO, Soyinka FO, Ojo OE, et al. Relationship of ultrasonographically determined kidney volume with measured GFR, calculated creatinine clearance and other parameters in chronic kidney disease (CKD). *Nephrol Dial Transplant*. 2009;24(5):1690-4.
13. Jovanović D, Gasic B, Pavlovic S, Naumovic R. Correlation of kidney size with kidney function and anthropometric parameters in healthy subjects and patients with chronic kidney diseases. *Ren Fail*. 2013;35(6):896-900.
14. Hricak H, Cruz C, Romanski R, Uniewski M, Levin NW, Madrazo BL, et al. Parenchymal Disease. *Radiology*. 1982;144:141-7.
15. Rosenfield AT, Siegel NJ. Renal parenchymal disease: histopathologic-sonographic correlation. *Am J Roentgenol.* 1981 Oct;137(4):793-8. doi: 10.2214/ajr.137.4.793. PMID: 6974977.