



SHEAR WAVE ELASTOGRAPHY IN CHRONIC KIDNEY DISEASE: A CASE SERIES

| | |
|---------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Dr. Akshay Satai | Senior Resident, Department Of Radio-diagnosis, Government Medical College And Hospital Akola. |
| Dr. Pankaj Badarkhe | Associate Professor, Department Of Radio-diagnosis, Government Medical College And Hospital Akola. |
| Dr. Payal Mahagaonkar-Badarkhe | Senior Resident, Department Of Biochemistry, Government Medical College And Hospital Akola. |
| Dr. Tauseef Manihar | Junior Resident, Department Of Radio-diagnosis, Government Medical College And Hospital Akola. |
| Dr. Meenakshi Gajbiye | Dean, Professor And Head Of Department Of Radio-diagnosis, Government Medical College And Hospital Akola. |

ABSTRACT

Introduction: B-mode ultrasound plays a crucial role in diagnosing chronic kidney disease (CKD) and determining its severity by assessing changes in renal cortex echogenicity. However, while it aids in grading CKD based on increasing renal cortical echogenicity, it lacks accuracy in detecting renal cortical fibrosis or stiffening. To address this limitation, our study aims to establish a correlation between renal cortical stiffness, measured in terms of elasticity values, and B-mode grades of CKD. This correlation is explored using shear wave elastography, a non-invasive technique for assessing tissue stiffness. The study objectives include evaluating the relationship between B-mode sonographic grading of renal parenchymal changes, the severity of renal disease, and the estimated glomerular filtration rate (eGFR) calculated based on patient age, gender, and serum creatinine levels. **Material and Methods:** This observational study was performed in a tertiary level medical college, based in the periphery of Maharashtra, India. In this study 20 patients with sonographically evident chronic kidney disease were studied. The shear wave elastography was performed in these individuals with help of Samsung RS80 EVO ultrasound equipment. The elastography values (measured in kPa) were taken at upper, middle and lower pole of diseased kidney. In bilateral chronic kidney disease, the elastography was performed in kidney with higher grade of chronic kidney disease. The ultrasound was performed by single observer to avoid inter-observer variability. **Results:** Using elastography, the renal cortical elasticity of patients with B-mode ultrasonographically diagnosed chronic kidney disease was shown to be considerably reduced. There was significant correlation between increasing sonographic grades of RPD and decreased elasticity of renal cortex (increasing kPa values). **Conclusions:** The correlation between renal tissue elasticity and B-mode ultrasound implies that shear wave elastography (SWE) has the potential to serve as an indicator of chronic kidney disease (CKD) severity. While biopsy remains the gold standard for grading renal cortex stiffness or fibrosis, SWE cannot entirely replace it; however, it can be utilized for staging renal parenchymal disease (RPD). Serving as a cost-effective measuring tool, SWE aids in grading renal cortical stiffness and consequently RPD. When used in conjunction with B-mode ultrasound and aligned with its findings, SWE emerges as a valuable, low-cost tool for more effectively staging RPD.

KEYWORDS : Chronic kidney disease, Chronic kidney disease, Elastography, shear wave elastography, eGFR.

INTRODUCTION

Chronic kidney disease (CKD) is a prevalent condition frequently encountered in clinical settings. Factors such as shifts in dietary patterns and a rise in sedentary lifestyles have contributed to the increasing prevalence of CKD, particularly in association with Type II diabetes^[1]. CKD, characterized by a decrease in estimated glomerular filtration rate (eGFR) or the presence of albuminuria, is linked to the progression to end-stage renal disease (ESRD), necessitating interventions like dialysis or kidney transplantation to sustain life^[2]. Moreover, individuals with CKD face heightened risks of premature mortality due to cardiovascular disease (CVD)^[1,2].

In India, diabetes stands out as the leading contributor to the burden of CKD/ESKD, constituting approximately one-third of CKD cases, followed by other causes such as hypertension, glomerulonephritis, and undetermined factors^[3,4]. The global impact of CKD on mortality and morbidity is significant. However, accurate assessment of CKD in India has been hindered by the absence of a comprehensive renal registry. Nonetheless, it is estimated that CKD affects around 800 per million population in India, with ESRD incidence ranging from 150 to 200 per million population^[6].

Population-based studies have identified diabetic nephropathy as the most prevalent cause of CKD, affecting 30-40% of individuals with diabetes and contributing to half of all cases of kidney failure^[7]. Advanced stages of CKD are associated with heightened mortality and morbidity rates. Currently, CKD staging relies on estimated glomerular filtration rate (eGFR) calculated from serum creatinine levels^[8]. Timely detection of CKD and initiation of both non-pharmacological and pharmacological interventions have been shown to mitigate its progression to ESRD^[9-17].

Despite the plethora of risk factors and complications associated with CKD, it often goes unnoticed, frequently being incidentally detected via ultrasonography. This is primarily due to the asymptomatic nature of early-stage CKD. Enhancing awareness and encouraging proactive health-seeking behavior through screening efforts can be instrumental in identifying CKD in its early stages^[18]. Studies have demonstrated the cost-effectiveness of screening and treating CKD, particularly in individuals with diabetes^[19].

In advanced stages, chronic kidney disease (CKD) is associated with increased mortality and morbidity^[20].

Currently, the estimated glomerular filtration rate (eGFR) derived from serum creatinine values is used to stage CKD^[20]. However, this technique has limitations, including confounding by race, gender, and muscle mass. Intra-renal fibrosis is a final common pathway and pathological end-stage for all CKD patients, and the degree of fibrosis can be correlated with disease severity^[21].

Elastography, a non-invasive technique that measures tissue elasticity, has emerged as a promising approach. Most elastography techniques, such as shear wave elastography (SWE) utilizing Acoustic Radiation Force Impulse (ARFI) quantification, are ultrasound-based. Shear wave elastography involves applying a low-frequency focused impulse to induce a shear wave in the tissue, perpendicular to the direction of the applied impulse. The speed of the shear wave, referred to as shear wave velocity, is proportional to tissue stiffness. Elastography quantification of shear wave velocity has shown promise as an alternative technique for assessing liver fibrosis^[22,23].

Until now, renal biopsy has been the only known method for the detection of intra-renal fibrosis, serving as the gold standard for diagnosis^[21]. However, it presents significant disadvantages, including invasiveness, expense, and an increased risk of complications. Moreover, insufficient biopsy samples often lead to challenges in proper histopathological diagnosis of the disease.

MATERIALS AND METHODS

Patient Selection

The inclusion criteria of the cases were as follows:

1. Subjects with an eGFR less than 90 (ml/min-1/1.73 m²).
2. Participants with serum creatinine levels exceeding 1.2 mg %.

Exclusions were applied under specific circumstances:

1. Subjects displaying normal kidneys with normal cortical echogenicity.
2. Individuals who declined participation in the study.
3. Participants unable to adhere to the sonographer's breathing instructions during the Shear Wave Elastography (SWE) procedure.

The cohort under investigation consisted of 20 patients (12 males, 08 females) undergoing treatment at Government Medical College, Akola. Comprehensive patient data including age, gender, and kidney function test results were documented, along with corresponding ultrasound shear wave elastography images.

METHODS

Written consent, duly informed, was acquired from all study participants. The data encompassed 20 adults (12 males, 8 females, mean age 55), referred to the Department of Radiology, Government Medical College, Akola, for routine abdominal ultrasound between September 1, 2023, and November 30, 2023. The staging of chronic kidney disease (CKD) relied on eGFR values, with radiological classification based on parenchymal thickness, delineated as Grade I, II, or III renal parenchymal disease (RPD). eGFR computations were executed via the CKD-EPI creatinine equation (2021) utilizing the online eGFR calculator provided by the National Kidney Foundation^[27].

Shear wave elastography, conducted utilizing "Samsung RS80" ultrasound equipment, entailed the measurement of elastography values (expressed in kPa) at the upper, middle, and lower poles of the affected kidney. In cases of bilateral CKD, elastography was performed on the kidney with the

higher grade of CKD. To mitigate inter-observer variability, the ultrasound procedure was carried out by a single observer.

Informed Consent

Regarding informed consent, explicit written consent was procured from each participant in the study, ensuring their anonymity. No form of incentive was provided to participants for their involvement in the research.

DISCUSSION

Sonographic shear wave elastography represents a novel non-invasive method for diagnosing renal parenchymal fibrosis and cortical stiffness. Our investigation revealed a correlation between escalating serum creatinine levels and advancing stages of chronic kidney disease (CKD), with a corresponding increase in the grade of renal parenchymal disease (RPD) observed on B-mode ultrasound. This finding is consistent with a study by Shakeel A. et al.^[26], which identified renal cortical echogenicity as the most reliable sonographic parameter correlating with serum creatinine levels in CKD patients. Additionally, our study found that the average kPa value of the renal cortex, measured at the upper, middle, and lower poles of affected kidneys, increased in tandem with the grades of RPD and stages of CKD. Kuttancheri T et al.^[24] similarly concluded in their original research that the correlation between renal tissue elastography values and estimated glomerular filtration rate (eGFR) suggests shear wave elastography (SWE) as an indicator of renal tissue injuries in CKD patients. A separate study by Samir et al.^[25] arrived at comparable results in a cross-sectional pilot study, indicating that Young's modulus obtained through SWE could effectively differentiate between renal tissue affected by CKD and normal renal tissue, even when renal size could not discern between the two conditions.

Kuttancheri T et al.^[24] established a cutoff value of 4.95 kPa for the median estimated tissue Young's modulus to distinguish CKD from normal kidneys with 2 standard deviations above the mean (2.7 ± 1.1 kPa). Our study observing a Young's modulus exceeding 5 kPa in all CKD cases, where the average eGFR was 30 ml/min/1.73 m², and the average value was 8.6 kPa. This led us to conclude that as eGFR values decrease, renal elasticity diminishes, and renal stiffness increases, indicating a positive correlation between CKD grades and renal parenchymal stiffness and fibrosis. Moreover, our study noted that with increasing grades of renal parenchymal disease on B-mode ultrasonography, the Young's modulus, indicative of renal stiffness/fibrosis, also rose. Statistical analysis was performed on the collected data, using Pearson correlation coefficient using Online software^[28,29]. Results of the Pearson correlation indicated that there is a significant large negative relationship between X and Y, ($r(18) = 0.931$, $p < 0.001$).

Utilizing shear wave elastography enables the grading of fibrosis based on Young's modulus values, akin to liver elastography. This approach facilitates early detection of renal fibrosis and holds the potential to reduce the necessity of renal biopsy and associated complications. Shear wave elastography offers ease of implementation, affordability, reduced time consumption, and fewer complications in detecting renal scarring/fibrosis.

Acknowledgements

We extend our sincere gratitude to Government Medical College, Akola, Maharashtra, for their encouragement and support throughout the study. We also express our appreciation to Dr. Meenakshi Gajbhiye, Dean, Professor and Head, Department of Radiology, GMC Akola, Maharashtra.

Conflict of Interest

The authors declare no conflicts of interest.

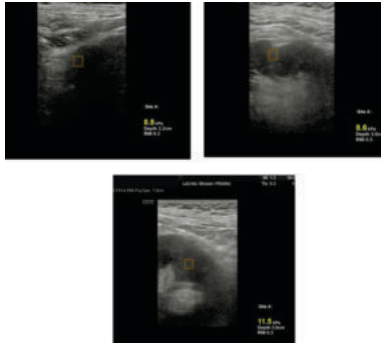


Image : 1 :- In a patient with Grade III renal parenchymal disease the Young's Modulus was calculated using Samsung RS80 EVO equipment. It was found to be increased (9.6 kPa) more than the normal reference value (i.e. approximately 5 kPa)^[24].

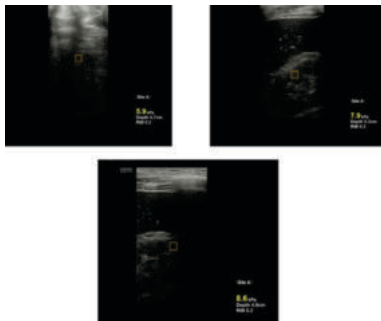


Image : 2 :- In a patient with Grade II renal parenchymal disease the Young's Modulus was calculated using Samsung RS80 EVO equipment. It was found to be increased (7.4 kPa) more than the normal reference value (i.e. approximately 5 kPa)^[24].

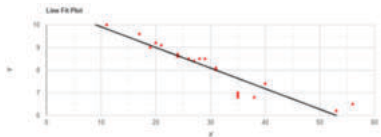


Image : 3 Line Fit plot shows the negative correlation between the degree of decrease in e-GFR value to the increase in the renal parenchymal stiffness or Young's modulus.

OBSERVATIONS

Demographic Data Obtained

| Age (years) | Gender (M/F) | Weight (kg) | B-mode Ultrasound Grade Of RPD (Grades) | eGFR (ml/min/1.73m ²) | Stage Of CKD According To eGFR (Stages) | Serum Creatinine (mg %) | Young's modulus (kPa) | Renal cortical cysts (+/-) |
|-------------|--------------|-------------|-----------------------------------------|-----------------------------------|-----------------------------------------|-------------------------|-----------------------|----------------------------|
| 55 | M | 45 | I | 35 | 3b | 2.2 | 6.8 | - |
| 67 | M | 65 | II | 28 | 4 | 2.0 | 8.5 | + |
| 60 | M | 45 | II | 29 | 4 | 2.5 | 8.5 | + |
| 59 | M | 42 | II | 26 | 4 | 2.7 | 8.5 | - |
| 63 | M | 65 | II | 35 | 3b | 2.1 | 7 | - |
| 72 | M | 75 | I | 53 | 3a | 1.8 | 6.2 | - |
| 50 | M | 50 | I | 56 | 3a | 1.5 | 6.5 | - |
| 56 | F | 60 | II | 27 | 4 | 1.9 | 8.4 | + |
| 57 | M | 65 | III | 24 | 4 | 2.1 | 8.6 | - |
| 48 | F | 58 | II | 24 | 4 | 2.2 | 8.7 | - |
| 52 | M | 67 | I | 35 | 3b | 1.8 | 6.9 | - |
| 54 | F | 59 | III | 21 | 4 | 2.4 | 9.1 | - |
| 59 | M | 58 | III | 20 | 4 | 3.1 | 9.2 | - |
| 61 | F | 55 | II | 31 | 3b | 1.6 | 8.1 | - |
| 57 | M | 65 | I | 38 | 3b | 1.9 | 6.8 | + |

| | | | | | | | | |
|----|---|----|-----|----|----|-----|-----|---|
| 51 | M | 58 | I | 31 | 3b | 2.2 | 8 | + |
| 50 | F | 68 | II | 40 | 3b | 1.5 | 7.4 | - |
| 62 | F | 65 | III | 17 | 4 | 2.8 | 9.6 | + |
| 60 | F | 70 | III | 11 | 5 | 4.1 | 10 | - |
| 54 | F | 54 | II | 19 | 4 | 2.5 | 9 | - |

* Young's modulus were taken as average of kPa values at upper, mid and lower pole.

Abbreviations

- CKD : Chronic kidney disease
- RPD : Renal parenchymal disease
- SWE : Shear Wave Elastography
- eGFR : Estimated glomerular filtration rate
- M : Male
- F : Female
- + : Present
- : Absent

CONCLUSION

The correlation between renal tissue elasticity and B-mode ultrasound suggests that shear wave elastography (SWE) has the potential to serve as an indicator of chronic kidney disease (CKD) severity. While renal biopsy remains the gold standard for grading renal cortex stiffness or fibrosis, SWE can complement this by providing staging information for renal parenchymal disease (RPD). Although SWE cannot entirely replace biopsy, it offers a cost-effective means of measuring renal cortical stiffness and, consequently, assessing RPD.

Utilizing shear wave elastography allows for the grading of fibrosis based on Young's modulus values, similar to liver elastography. This approach facilitates early detection of renal fibrosis and holds promise for reducing the necessity of renal biopsy and its associated complications in the future. When combined with B-mode ultrasound and correlated with its findings, shear wave elastography emerges as a valuable, easily accessible, and cost-effective tool for more effective staging of RPD.

REFERENCES

1. Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med.* 2013;158(11):825-30.
2. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the global burden of disease study 2010. *Lancet.* 2012;380(9859):2095-128.
3. Rajapurkar MM, John GT, Kirpalani AL, Abraham G, Agarwal SK, Almeida AF, et al. What do we know about chronic kidney disease in India: first report of the Indian CKD registry. *BMC Nephrol.* 2012;13:10.
4. Modi GK, Jha V. The incidence of end-stage renal disease in India: a population-based study. *Kidney Int.* 2006;70(12):2131-3.
5. Anonymous Kidney Disease. Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013; 3: 1-150.
6. Mostbeck GH, Kain R, Mallek R, et al. Duplex Doppler sonography in renal parenchymal disease. Histopathologic correlation. *J Ultrasound Med* 1991; 10: 189-194.
7. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. *Am J Kidney Dis* 2014; 64: 510-533.
8. Stevens PE, Levin A; Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med* 2013; 158: 825-830.
9. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet.* 2013;382(9889):339-52.
10. The Look AHEAD Research Group, et al. Effect of a long-term behavioural weight loss intervention on nephropathy in overweight or obese adults with type 2 diabetes: a secondary analysis of the Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol.* 2014; 2(10):801-9.
11. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ.* 1998;317(7160):703-13.
12. Xie X, Liu Y, Perkovic V, Li X, Ninomiya T, Hou W, et al. Renin-angiotensin system inhibitors and kidney and cardiovascular outcomes in patients with CKD: a Bayesian network meta-analysis of randomized clinical trials. *Am J Kidney Dis.* 2016;67(5):728-41.
13. Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (study of heart and renal protection): a randomised placebo-controlled trial. *Lancet.* 2011;377(9784):2181-92.

14. Flynn C, Bakris GL. Blood pressure targets for patients with diabetes or kidney disease. *Curr Hypertens Rep.* 2011;13(6):452-5.
15. Shurraw S, Hemmelgarn B, Lin M, Majumdar SR, Klarenbach S, Manns B, et al. Association between glycemic control and adverse outcomes in people with diabetes mellitus and chronic kidney disease: a populationbased cohort study. *Arch Intern Med.* 2011;171(21):1920-7.
16. Cummings DM, Larsen LC, Doherty L, Lea CS, Holbert D. Glycemic control patterns and kidney disease progression among primary care patients with diabetes mellitus. *J Am Board Fam Med.* 2011;24(4):391-8.
17. Ferguson TW, Tangri N, Tan Z, James MT, Lavallee BDA, Chartrand CD, et al. Screening for chronic kidney disease in Canadian indigenous peoples is cost-effective. *Kidney Int.* 2017;92(1):192-200.
18. McGill JB, Brown WW, Chen S-C, Collins AJ, Gannon MR. Kidney early evaluation program (KEEP): findings from a community screening program. *Diabetes Educ.* 2004;30(2):196-206.
19. Komenda P, Ferguson TW, Macdonald K, Rigatto C, Koolage C, Sood MM, et al. Cost-effectiveness of primary screening for CKD: a systematic review. *Am J Kidney Dis.* 2014;63(5):789-97.
20. Stevens PE, Levin A; Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med* 2013; 158: 825-830.
21. Cosgrove D, Piscaglia F, Bamber J, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: Clinical applications. *Ultraschall Med* 2013; 34: 238-253.
22. Rizzo L, Calvaruso V, Cacopardo B, et al. Comparison of transient elastography and acoustic radiation force impulse for non-invasive staging of liver fibrosis in patients with chronic hepatitis C. *Am J Gastroenterology* 2011;106(12):2112e20.
23. Friedrich-Rust M, Wunder K, Kriener S, et al. Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. *Radiology* 2009;252(2):595e604.
24. Kuttancheri T, Krishnan K, Das SK, Shetty MS. Shear wave elastography: usefulness in chronic kidney disease. *Pol J Radiol.* 2023 Jun 14;98:e286-e293. doi: 10.5114/pjr.2023.128694. PMID: 37404549; PMCID: PMC10317009.
25. Samir AE, Allegretti AS, Zhu Q, et al. Shear wave elastography in chronic kidney disease: a pilot experience in native kidneys. *BMC Nephrol* 2015; 16: 119. doi: 10.1186/s12882-015-0120-7.
26. Ahmed S, Bughio S, Hassan M, Lal S, Ali M. Role of Ultrasound in the Diagnosis of Chronic Kidney Disease and its Correlation with Serum Creatinine Level. *Cureus.* 2019 Mar 12;11(3):e4241. doi: 10.7759/cureus.4241. PMID: 31131164; PMCID: PMC6516621.
27. Levey AS, Stevens LA, National Kidney Foundation. 2021, <https://www.kidney.org/professionals/KDOQI/gfr_calculator>.
28. Stats Kingdom. (n.d.). Retrieved from <https://www.statskingdom.com/index.html>
29. Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences* (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates, Publishers.