Original Research Article

A study on radiological nomogram of renal cortical elasticity using dynamic shear wave ultrasound elastography

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Abstract

Background: Renal fibrogenesis is the final common pathway to all renal injuries that leads to Chronic Kidney Disease (CKD) consequently. Renal fibrosis encompasses glomerulosclerosis, interstitial fibrosis, tubular atrophy, and vascular changes. Chronic kidney injury is manifested by a variety of histological structural alterations, including the accumulation of extracellular matrix (ECM). The accumulation of ECM is colloquially termed Interstitial fibrosis. Tubular atrophy (TA) often accompanies IF and, when occurring together, IF and TA are collectively termed IFTA Imaging of the kidney is mainly based on the evaluation of the renal parenchyma, excretory system, and renal vasculature using imaging modalities such as USG, CT, and MRI.

Aim and objective: To establish the normal values of renal cortical elasticity using dynamic shear wave elastography and to establish the influence of factors affecting the renal cortical elasticity.

Materials and methods: The study was conducted in our institute for 6 months and included 177 normal population in the year 2019 at Barnard Institute of Radiology, Madras Medical College. Patients underwent abdominal sonographic examination and shear wave ultrasound elastography using a convex probe (1-5 MHz) in the HITACHI ALOKA ARIETTA S70 machine. The renal measurements such as length, width, parenchymal thickness, cortical thickness, and skin to cortex distance are measured by a single observer. Before the study, All patients were screened for any residual urine in the supine position. All measurements were taken in the lateral decubitus position after emptying the urinary bladder. The length of the kidney was measured from the superior pole of the kidney to the inferior pole of the kidney on the coronal plane. The width of the kidney was measured from the renal hilum to the renal capsule at the mid pole on the coronal plane. Parenchymal thickness was measured on the coronal plane at the mid pole between the outer margin of the renal sinus and the renal capsule. The measurement from the renal capsule to the medullary pyramid base at the mid pole gives the cortical thickness. At last, the distance of skin to the outer margin of the renal cortex was measured at the mid pole. The probe was placed steadily with minimum compression in lateral decubitus position and the person was asked to hold his/her breath for a few seconds in full inspiration. This is to minimize the movement of the kidney with respiration. Then, a predefined region of interest (ROI) box (predefined by the manufacturer) of 1 x 1.5 cm was placed in the renal cortex at the mid pole of the kidney excluding the renal medulla as much as possible. The axis of the ROI box should be kept parallel as much as possible to the main axis of the pyramids of the renal medulla in the mid pole and SWV values are measured in terms of m/s in each kidney. Six valid elasticity measurements in terms of shear wave velocity were measured for the right kidney followed by the left kidney.

Results: The mean parenchymal thickness of the right and the left kidney was 1.81 ± 0.34 and 1.92 ± 0.31 cm respectively. On statistical analysis, there exists a highly significant statistical difference between the parenchymal thickness of the right and left kidneys. The mean cortical thickness of the right and the left kidney was 0.90 ± 0.17 and 0.95 ± 0.19 cm respectively. On comparison between right and left kidneys by statistical analysis using paired t-test, it was found that there is a highly significant statistical difference between the cortical thickness of both kidneys (p-value 0.0005). The mean skin to cortex distance of the right kidney was 4.42 ± 1.01 cm and the left kidney was 4.37± 1.02. However, there was no statistically significant difference observed between skin to cortex distance of right and left kidneys. The average renal elasticity value of the right kidney was 1.53 ± 0.20 m/s and the left kidney was 1.51 ± 0.15 m/s. There was no significant statistical difference between the mean renal cortical shear wave velocities of the right and left kidney (p-value 0.341). There was no statistically significant correlation noted between the renal cortical plasticity (expressed in m/s) and the length of the right and left kidneys. The p-value was 0.906 and 0.958 in right and left kidney when analyzed using Pearson’s correlation. There was a statistically highly significant negative correlation noted between renal cortical elasticity and width of the right kidney (p-value 0.002), when analyzed using Pearson’s correlation. However, no statistically significant correlation was noted between renal elasticity and the width of the left kidney (p-value 0.186).

Conclusion: Normal Renal cortical shear wave values can be used as reference values to assess early renal damage and assess renal disease progression Renal cortical shear wave velocity can be used as a non-invasive biomarker of renal disease.

Key words

Renal fibrogenesis, Chronic Kidney Disease (CKD), Tubular atrophy (TA).

Introduction

Chronic kidney disease (CKD) is one of the major diseases which causes a high economic burden to health systems. 10% of the world population is affected by chronic kidney disease (CKD). It is estimated that cases of kidney failure will increase disproportionately in developing countries, such as China and India. Chronic kidney disease (CKD) is defined as an alteration in function and/or structure of the kidney that lasts for more than 3 months [1]. Chronic kidney disease (CKD) is associated with age-related renal dysfunction, which becomes accelerated in systemic diseases such as hypertension, diabetes, obesity, and also in primary renal disorders. Cardiovascular disease (CVD) is an accelerator of CVD risk and an independent risk factor for CVD events and has indeed become a strong contributor to mortality and morbidity Decreased renal function is a predictor of hospitalization cognitive dysfunction and poor quality of life. Renal fibrogenesis is the final common pathway to all renal injuries that leads to Chronic Kidney Disease (CKD) consequently [2]. Renal fibrosis encompasses glomerulosclerosis, interstitial fibrosis, tubular atrophy, and vascular changes. Chronic kidney injury is manifested by a variety of histological structural alterations, including the accumulation of extracellular matrix (ECM). The accumulation of ECM is colloquially termed Interstitial fibrosis. Tubular atrophy (TA) often accompanies IF and, when occurring together, IF and TA are collectively termed IFTA Imaging of the kidney is mainly based on the evaluation of the renal parenchyma, excretory system, and renal vasculature using imaging modalities such as USG, CT, and MRI. It has been found that there exists a significant correlation between renal fibrosis and renal length, renal parenchymal thickness, and resistive index (RI) [3]. However, these are neither sensitive nor specific in the evaluation of renal disease, as the morphology of renal tissue can still appear normal in the early stages of CKD. The severity of CKD and the degree of kidney cortical interstitial fibrosis have a strong correlation. The biopsy is currently the gold reference standard for assessing fibrosis with histological techniques. Although renal biopsies have become safer over recent years, complications and limitations of this procedure remain. Like any invasive procedure, renal biopsies carry the risk of several complications, like pain, infection, and bleeding. Bleeding complications such as peri-renal hematoma, hematuria, or formation of arteriovenous fistulas can occur, though infrequent [4]. These complications, when severe and associated with drop-in hemoglobin may require blood transfusion and may lead to loss of the kidney or even death. Hence, new non-invasive techniques are necessary for the evaluation and follow-up of CKD patients. Imaging methods such as ultrasound and magnetic resonance imaging are emerging for the assessment of kidney fibrosis by elastography. These two techniques have advantages but also limitations. In addition to the radiological assessment of fibrosis, urinary and plasma biomarkers are being developed and tested as predictive tools for histological lesions in the kidney [5].

Materials and methods

The study was conducted in our institute for 6 months and included 177 normal population in the year 2019 at Barnard Institute of Radiology, Madras Medical College.

Inclusion criteria: Both sexes, Patients attending OP ultrasound, Patients attending IP ultrasound, Patients attending Master health check-up, Attenders of the patients attending OP, IP ultrasound, and Master health check-up, Age between 20 and 60 years.

Exclusion criteria: Unwilling patients, Patients with deranged renal function (serum urea higher than 40 mg, creatinine level higher than 1.3 mg/100 ml), Presence of abnormal findings in greyscale ultrasonography such as renal calculus /vesical calculus, unilateral/bilateral Hydronephrosis, ascites and diabetics, hypertension, and renal cyst.

Patients and attendees attending USG outpatient, USG inpatient, and Master Health check-up units were the study population. The individuals were screened using the drawn inclusion/ exclusion criteria. Relevant entries were made in the proforma for each patient after reviewing his/her case sheet and previous medical records. Patients underwent abdominal sonographic examination and shear wave ultrasound elastography using a convex probe (1-5 MHz) in the HITACHI ALOKA ARIETTA S70 machine. The renal measurements such as length, width, parenchymal thickness, cortical thickness, and skin to cortex distance are measured by a single observer. Before the study, all patients were screened for any residual urine in the supine position. All measurements were taken in the lateral decubitus position after emptying the urinary bladder. The length of the kidney was measured from the superior pole of the kidney to the inferior pole of the kidney on the coronal plane. The width of the kidney was measured from the renal hilum to the renal capsule at the mid pole on the coronal plane. Parenchymal thickness was measured on the coronal plane at the mid pole between the outer margin of the renal sinus and the renal capsule. The measurement from the renal capsule to the medullary pyramid base at the mid pole gives the cortical thickness. At last, the distance of skin to the outer margin of the renal cortex was measured at the mid pole. The probe was placed steadily with minimum compression in lateral decubitus position and the person was asked to hold his/her breath for a few seconds in full inspiration. This is to minimize the movement of the kidney with respiration. Then, a predefined region of interest (ROI) box (predefined by the manufacturer) of 1 x1.5 cm was placed in the renal cortex at the mid pole of the kidney excluding the renal medulla as much as possible. The axis of the ROI box should be kept parallel as much as possible to the main axis of the pyramids of the renal medulla in the mid pole and SWV values are measured in terms of m/s in each kidney. Six valid elasticity measurements in terms of shear wave velocity were measured for the right kidney followed by the left kidney.

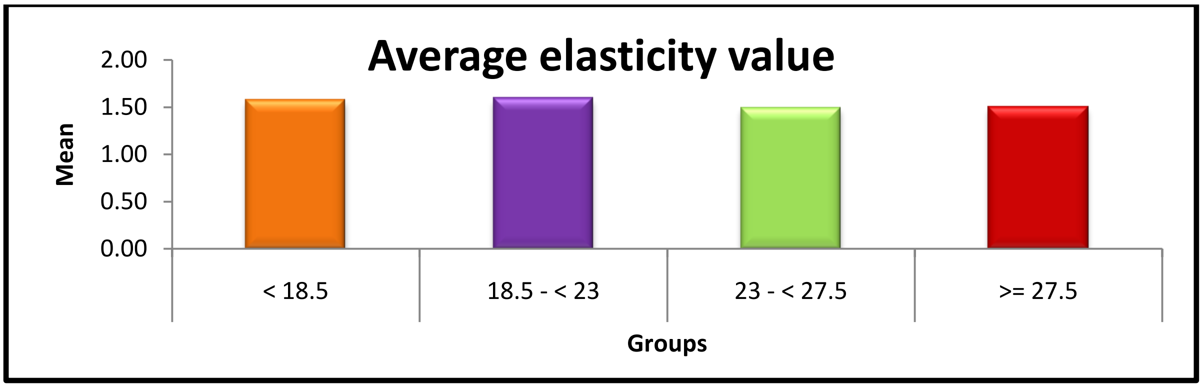
Statistical analysis

The data collected were statistically analyzed using IBM.SPSS statistics software 23.0 Version. To describe the descriptive statistics of the data, frequency analysis and percentage analysis were used for categorical variables, and S.D and mean was used for continuous variables. The Paired sample t-test was used to find the significant difference between the bivariate samples in Paired groups, and the Unpaired sample t-test was used for independent groups. The one-way ANOVA test is used for the multivariate analysis. To assess the relationship between the variables Pearson's Correlation was used. The ICC was used to find the efficacy of the tool. The multiple regression analysis with the enter method was used to find the influencing factors for the elasticity value. In all of the above statistical analyses, the probability value .05 was considered significant.

Results

A total of 177 individuals were included in this study after screening for inclusion and exclusion criteria. The age group between 20 -29 years were 40 individuals, 30-39 years were 46 individuals,40 -49 years were 52 individuals and 60 years were 8 patients. Out of a total of 177 individuals included in the study, 135 were male (76.3%) and 42 were female (23.7%). Of the study group, 4 (2.3%) individuals had BMI < 18.5, 59 (33.3%) individuals had BMI 18.5 - <23, 80 (45.2%) individuals had BMI 23- < 27.5%, 34 (19.2%) individuals had BMI >27.5. The mean length of the Right kidney and the left kidney were 9.46 ± 0.93 cm and 9.65 ± 0.78 cm respectively. On comparison of length of right and left kidneys by statistical analysis using paired t-test, it was found that there was a highly significant statistical difference between both kidneys (p-value 0.03). The mean width of the right kidney was 4.54 ± 0.65 cm and the left kidney was 4.93 ± 0.57cm. There was a significant statistical difference noted between the renal width of both kidneys using statistical analysis by paired t-test (p-value 0.0005). The mean parenchymal thickness of the right and the left kidney was 1.81 ± 0.34 and 1.92 ± 0.31 cm respectively. On statistical analysis, there exists a highly significant statistical difference between the parenchymal thickness of the right and left kidneys. The mean cortical thickness of the right and the left kidney was 0.90 ± 0.17 and 0.95 ± 0.19 cm respectively. On comparison between right and left kidneys by statistical analysis using paired t-test, it was found that there is a highly significant statistical difference between the cortical thickness of both kidneys (p-value 0.0005). The mean skin to cortex distance of the right kidney was 4.42 ± 1.01 cm and the left kidney was 4.37± 1.02. However, there was no statistically significant difference observed between skin to cortex distance of right and left kidneys. The average renal elasticity value of the right kidney was 1.53 ± 0.20 m/s and the left kidney was 1.51 ± 0.15 m/s. There was no significant statistical difference between the mean renal cortical shear wave velocities of the right and left kidney (p-value 0.341). There was no statistically significant correlation noted between the renal cortical plasticity (expressed in m/s) and length of right and left kidneys. The p-value was 0.906 and 0.958 in right and left kidney when analyzed using Pearson's correlation. There was a statistically highly significant negative correlation noted between renal cortical elasticity and width of the right kidney (p-value 0.002), when analyzed using Pearson's correlation. However, no statistically significant correlation was noted between renal elasticity and width of the left kidney (p-value 0.186). There was a highly significant statistical negative correlation noted between renal elasticity and parenchymal thickness of the right kidney (p-value 0.001) when analyzed using Pearson's correlation. However, no significant statistical correlation was noted between renal elasticity and parenchymal thickness of left kidney (p-value 0.902). No statistically significant correlation was noted between renal elasticity and cortical thickness of right/left kidneys (p-value was 0.140 and 0.177 for right and left kidney respectively). No statistically significant correlation noted between renal elasticity and skin to cortex distance of right/left kidneys (p-value was 0.794 and 0.551 for right and left kidney respectively). Multiple regression analysis was done to establish the influence of factors affecting renal cortical elasticity. The multiple regression analysis of the right kidney showed a statistically significant influence of BMI (p-value 0.002), width (p-value 0.049), and parenchymal thickness (p-value 0.012) on renal cortical elasticity. However, no statistically significant influence of age, gender, length, cortical thickness, and skin to cortex distance on renal elasticity was established. The multiple regression analysis of the left kidney showed a statistically significant influence of BMI on renal elasticity (p-value 0.041). However, no statistical significance was noted between age, gender, length, width, parenchymal thickness, cortical thickness, and skin to cortex distance (**Graph – 1 to 9**).

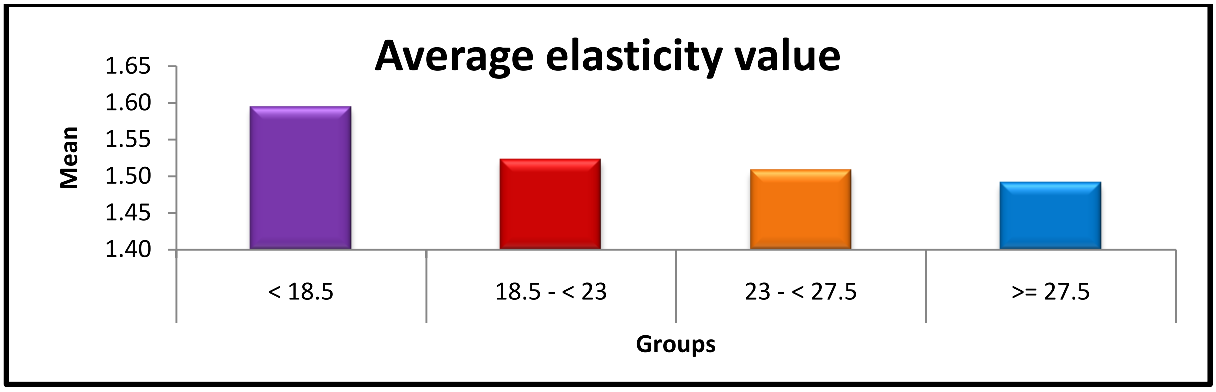
Graph – 1: Comparison of average elasticity value (SWV) with BMI by one-way ANOVA.



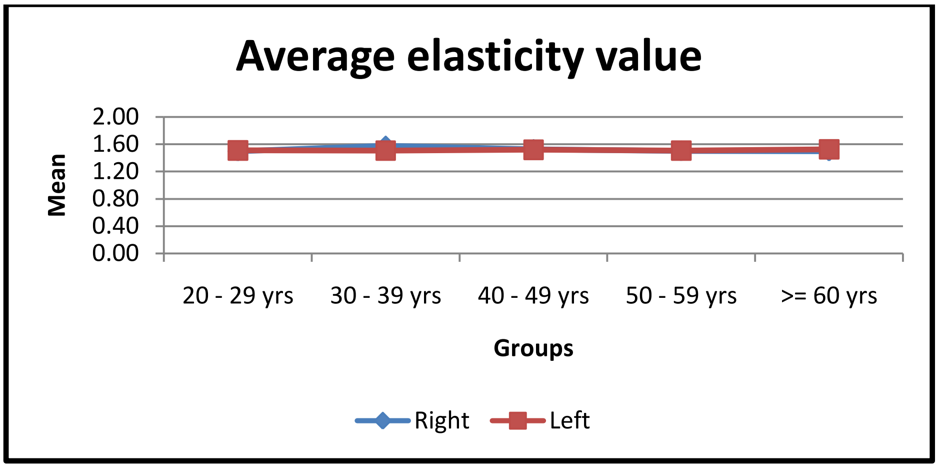
Discussion

There have been many studies for assessing tissue stiffness in solid viscera such as the liver using shear wave elastography. But there have been limited studies on renal shear wave elastography when compared to studies on the liver. Even among the studies using shear wave elastography in kidneys, most of the studies are conducted in transplant kidneys to assess renal allograft fibrosis and in CKD patients to quantify tissue fibrosis [6]. The range of normal renal shear wave velocity in our study was 1.18 to 2.52 m/s in the right kidney and 1.12 to 2.29 m/s in the left kidney. The range of shear wave velocities established in our study was the same as in other studies. However, the mean shear wave velocity in our study was 1.53 ± 0.20 m/s for the right kidney and the left kidney is 1.51 ± 0.15 m/s. However, no statistically significant difference (p-value 0.341) was observed between the mean renal cortical shear wave velocities of the right and left kidneys [7].

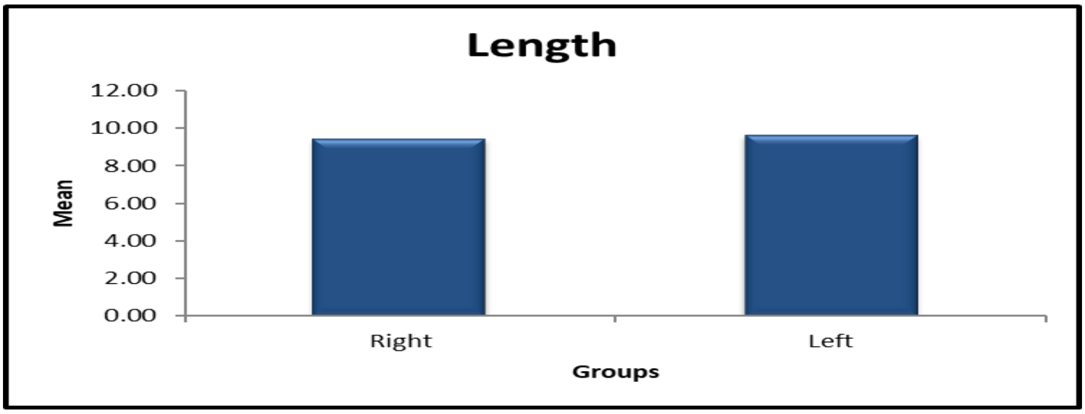
Graph – 2: Comparison of average elasticity value (SWV) with BMI in left kidney.



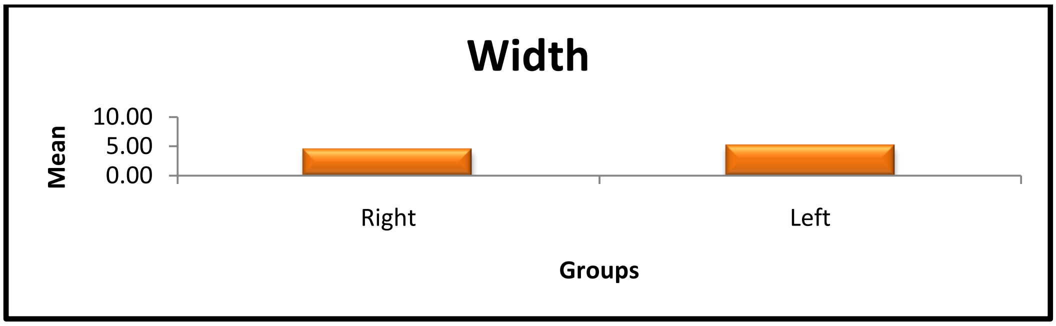
Graph – 3: Comparison of average elasticity value (SWV) with age by one-way ANOVA.
By using statistical analysis with a one-way ANOVA test, the average elasticity values of the Right and left kidneys are compared with age.



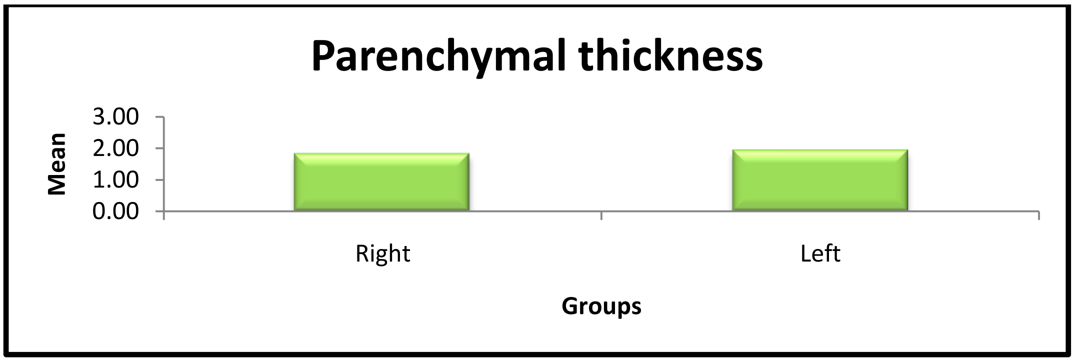
Graph – 4: Comparison of kidney length by paired t-test.
The length of the Right and left kidneys is compared by statistical analysis with paired t-test.



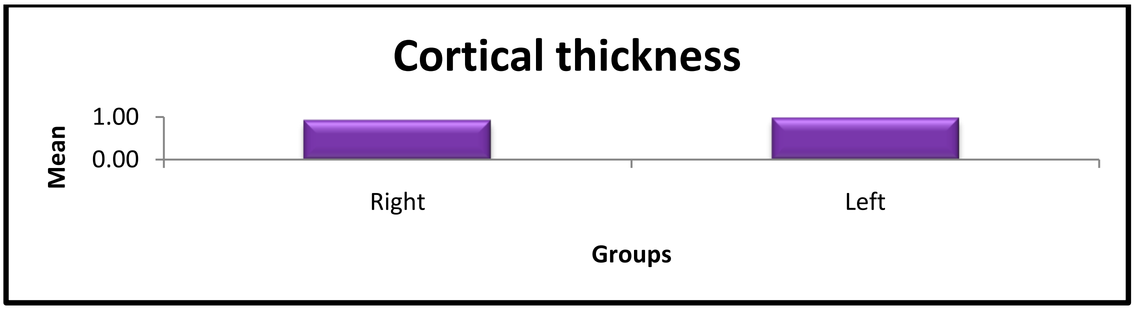
Graph – 5: Comparison of kidney width by paired t-test.



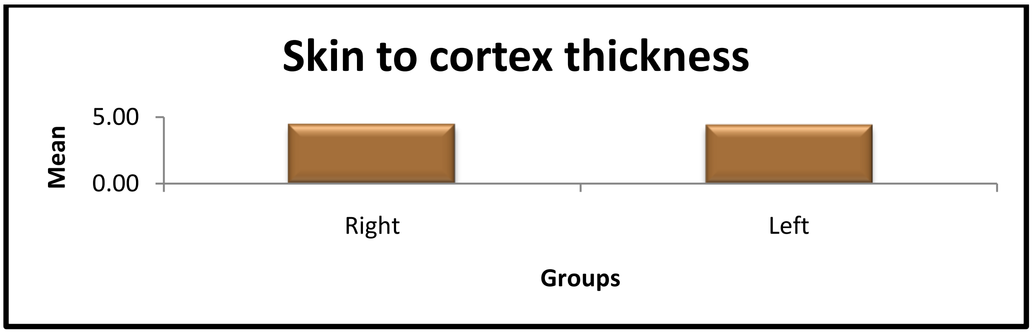
Graph – 6: Comparison of kidney parenchymal thickness by paired t-test.



Graph – 7: Comparison of kidney cortical thickness by paired t-test.

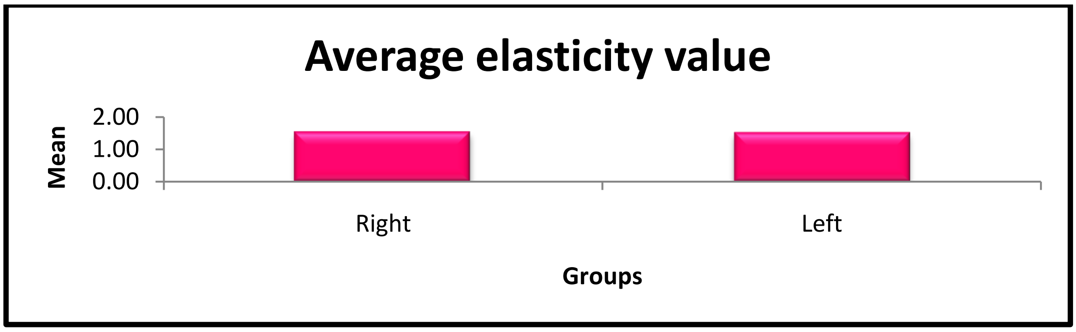


Graph – 8: Comparison of skin to cortex distance by paired t-test.



In a study by Caste, et al. 2012, the liver stiffness values assessed by ARFI elastography are lower in Asian versus European healthy volunteers. Another reason can be due to the technical difficulty in measuring SWV in kidneys because of the highly compartmentalized heterogeneous architecture of kidneys which is highly challenging especially placing the ROI box in the renal cortex. In our study, the ROI box was 1 x 1.5 cm which was predefined and not adjustable. Hence, even in normal subjects with normal RFT with cortical thickness <1.5 cm, we were not able to measure SWV [8]. The results of previous studies by Chin HJ, et al. showed that the renal poles showed lower SWV values when compared to the mid-portion of the renal parenchyma because of anisotropy. Hence, in our study, we measured the mid pole of the renal cortex. The lack of standardized methodology and technique across various studies might also be a reason for different results in various studies. Only a few studies have been conducted to assess the factors influencing renal shear wave velocity. The influence of age on elasticity was analyzed statistically in our study. We found that there is no statistically significant influence of age on elasticity in right and left kidneys with p-value 0.303 and 0.992 respectively [9].

Graph – 9: Comparison of average elasticity values by paired t-test.



The influence of sex on elasticity was analyzed in our study. The mean elasticity value of the right kidney in males was 1.51 ± 0.19 m/s and in females was 1.58 ± 0.22 m/s. The mean elasticity value of the left kidney in males was 1.51 ± 0.14 m/s and female was 1.53 ± 0.17 m/s. Females had a higher SWV than males but we found that there was no statistically significant influence of sex on elasticity in both right and left kidneys (p-value 0.060 and p-value 0.390 for right and left kidney respectively [10]. The mean renal cortical shear wave velocity established in their study were high in females measuring 1.53 ± 0.21 m/s in the right kidney and 1.57 ± 0.18 m/s in the left kidney but without statistical significance. The SWV results were lower in men than in women: 2.22 ± 0.76 versus 2.70 ± 0.80, with a statistically significant value p 0.004. The influence of parenchymal thickness on elasticity was analyzed in our study. We found that there was a statistically significant negative correlation noted between the parenchymal thickness of the Right kidney and elasticity (r-value -0.245, p-value 0.001) However, there is no significant correlation noted between the parenchymal thickness of the left kidney and elasticity. The significant statistical correlation between the parenchymal thickness of the Right kidney and elasticity in our study was not observed in any other studies due to unclear reasons which may need further evaluation to detect if any additional factor plays a role [11]. The influence of cortical thickness on elasticity was analyzed in our study. We found that there was no statistically significant correlation noted between the cortical thickness of both rights (p-value 0.140) and left kidneys (p-value 0.177) with elasticity when analyzed by Pearson correlation. The influence of length on average elasticity was analyzed by Pearson correlation [12]. We found that there was no statistically significant correlation noted in right and left kidneys (p-value 0.906 and 0.958 in right and left kidneys respectively). When analyzing the influence of width on elasticity, we found that there was a highly significant negative correlation noted between renal width of right kidney and elasticity (p-value 0.002) due to unclear reasons which may need further evaluation to detect if any additional factor plays a role. However, no significant statistical correlation was noted between the width of the left kidney and elasticity. The influence of skin to cortex distance of right and left kidney on elasticity was analyzed in our study [13]. The study results showed no significant statistical correlation between skin to cortex distance and elasticity (p-value 0.794 for right and 0.551 for left kidney). The mean shear wave velocities of the right and left kidney was1.53 ± 0.20 m/s for the right kidney and the left kidney is 1.51 ± 0.15 m/s. ICC was used to assess the repeatability between the measurements in right and left kidneys. The ICC values were interpreted as poor agreement (ICC 0.00–0.20), fair agreement (ICC 0.21–0.40), moderate agreement (ICC 0.41–0.60), strong agreement (ICC 0.61–0.80) and excellent agreement (ICC.0.80-1.00). Intra class correlation coefficient of Right kidney is 0.649 (strong agreement) (which is statistically significant (p-value 0.0005) and Intra class correlation coefficient of the left kidney is 0.287 (fair agreement) which is also statistically significant (p-value 0.001) [14, 15].

Conclusion

The normal renal cortical shear wave elasticity of the kidney was established. We found that elasticity measured in terms of shear wave velocity is independent of age, gender, length, and cortical thickness. We also found a negative correlation between shear wave velocity and BMI in both kidneys. This study provides reference values that can be used for future clinical applications of elastography of the normal kidney. Further studies should be conducted in the future by taking into account the effect of renal perfusion also. Future studies in patients with renal diseases would help in assessing if renal cortical shear wave velocity can be used as a non-invasive biomarker of renal disease.

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