ORIGINAL ARTICLE

ROLE OF SONOELASTOGRAPHY IN EVALUATION OF RENAL ALLOGRAFT DYSFUNCTION TAKING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

BACKGROUND: Renal Transplant is a lifesaving surgery for patients with renal failure. There is myriad of complications which can result in failure of the grafted kidney. In order to avoid these, close watch is kept on patient s general heath, blood and urine parameters. However, these complications often develop sub clinically and before any abnormality shows up in blood investigations, the damage is already done and possible irreversiblility in functional parameters. Hence, any noninvasive and practical method of keeping check on earliest changes in renal graft parenchymawill be renal graft saving and so, lifesaving. **OBJECTIVE:** The objective of this study is to evaluate the diagnostic accuracy of shear wave elastography in the diagnosis of chronic allograft nephropathy taking histopathological findings as gold standard. **METHODS:** A total of 176 patients and control group of 176 were included in this study conducted from April 2021 to September 2021. Patients with reduced GFR and having increased creatinine levels along with already biopsy proven chronic renal allograft nephropathy were enrolled in this study. Shearwave sonoelastography was performed and findings of sonoelastography were correlated with biopsy and recorded on proforma. **RESULTS:** The average age of the patients was 36.23 – 10.09 years. The sensitivity, specificity, PPV and NPV and diagnostic accuracy of sonoelastography for detection of chronic allograft dysfunction was 90.90%, 97.27%%, 95.23% and 94.69% and diagnostic accuracy was 94.88% respectively. **CONCLUSION:** Shearwave sonoelastography is very useful non-invasive technique in evaluation of chronic allograft dysfunction which may alarm change in ongoing treatment and therefore invasive technique like biopsy can be avoided.

Key words: Shearwave, Sonoelastography, Chronic allograft dysfunction, Biopsy, Histopathology

Introduction

The recipients of renal transplants are being monitored both clinically and through lab investigations for any developing abnormality and to ensure proper functioning of the graft. In spite of a thorough approach towards the patient s well-being, renal damage often sets in and goes undiagnosed as early abnormalities are either undetected or the lab investigations and clinical presentation often lag behind in raising a red flag.[1-3]

Rejection occurring in first year of transplant is des-

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cribed as early, occurring mostly due to ischemia reperfusion injury resulting in tubular damage in renal parenchyma which causes glomerulosclerosis.[3] Any damage beyond first year of transplant is described as late phase and can be due to many confounding factors having both immunologic and non-immunologic origins.

Ultrasound has been a beneficial tool in detection of immediate correctable complications like development of collections and hematomasin post-surgery period. Needless to mention the immense role of doppler ultrasound in vascular assessment of graft post-transplant. Using the same noninvasive approach, sonoelastography is used to detect tissue stiffness through the ultrasound probe.[4,5] It has been used in detection of possible malignancies in soft tissue organs like breast, thyroid and prostate. There has been considerable benefit in evaluation of atherosclerosis[6-9] and in delineating cirrhotic from non-cirrhotic liver.[10] In literature we have come across 2 studies that have used shear-wave sonoelastography in evaluation of native kidneys.[11,12] Conventionally, anatomical assessment of the allografts have been done using grey scale and doppler ultrasound, CT scans and MRIs which now provide added information regarding function of the graft.

Sonoelastography is a practical tool for studyingthe early morphological changes that will help to detect development of fibrosis by studying the stiffness of the renal graft parenchyma. It is a promising tool for early detection of fibrosis which can be correlated with creatinine levels, glomerular filtration rates and biopsy results. Of special mention is the non-invasive nature of this tool being much safer compared to the biopsy of these already damaged kidneys prone to bleeding.

The aim of this study is to see the utility of this non-invasive technique in detection of chronic allograft dysfunction which may modify the present line of investigation and treatment by avoiding unnecessary possible complications secondary to biopsies.

Material & Methods

The quasiexperimental case-control study is conducted from April 2021 to September 2021 in department of radiology, SIUT, Karachi after approval from the research and ethical committee of the institution. Informed consent was taken from both the cases and control group. Based on the previous estimate of renal allograft dysfunction was observed in 25.6%[13] patients. The sensitivity and specificity 73.68% and 80%[14] respectively, with margin of error 13% and 95% confidence level. A total of 176 patients were needed for this study and control group of 176 patients were also included. Both male and female patients were selected with age range from 20 to 60 years. The cases (patients) were included who have chronic renal allograft dysfunction (more than 3 months of post renal transplant) with reduced eGFR < 50 ml/min, increase serum creatinine level >50% above baseline and who are biopsy proven cases of chronic allograft nephropathy while control group were included with more than 3 months post-transplant with no evidence of renal dysfunction clinically and as per labs and who did not went renal allograft biopsy to compare with patients having above laboratory findings. The patients having skin-allograft distance greater than 3 cm, parenchymal thickness <1cm and having perigraft fluid collection were excluded from the study. The patients and control group were referred from outpatient department and urology transplant ward. All patients in this study received a renal transplant from a living related donor. All measurements were per-formed by the same observer having more than 10 years of experience in abdominal US, including 5 years of experience with shearwave sonoelastography), who will be blinded to the patient data. A check ultrasound examination was performed to evaluate the allograft morphologic characteristics and vascularity, perigraft collection, and skin-allograft distance. Measurements were then performed with the patient lying in a supine position. The sampling for point-based shear-wave sonoelastography was performed after the patient was instructed to hold his or her breath. A total of six measurements of shear-wave sonoelastography (ultrasound systems (CANON; APLIO i800) based parenchymal stiffness of two measurements each from the upper polar, lower polar, and midinterpolar regions were performed and recorded in kilopascals. The mean value of parenchymal stiffness was included for each patient. Shear wave elastography findings was compared with histopathologically proven renal graft fibrosis. Inclusion and exclusion criteria were strictly followed as to control

the biasness and effect modifiers. The whole study was statistically evaluated to determine the sensitivity and specificity of shearwave sonoelastography in diagnosing renal graft fibrosis taking histopathological findings as gold standard.

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS 21.0) as to obtain sensitivity and specificity of shear wave elastography in the diagnosis of renal graft fibrosis and taken histopathology as gold standard. Frequency and percentage were calculated for qualitative variables, i.e., presenting complains, detailed history of presenting complains; shear wave elastography findings and histopathological findings.

Mean – SD was computed for quantitative variable, i.e. Age of the patient. Taking histopathological findings as gold standard, all statistical parameters, (sensitivity, specificity, positive predictive value, negative predictive value) were calculated to obtain diagnostic accuracy of shear wave elastography.

Results

In our study 176 patients of both genders were included having chronic renal allograft dysfunction for more than 3 months as presented with reduced GFR and raised serum creatinine levels were included. The average age of the patients was 36.23 – 10.09 years (20-60 years). Histopathological confirmation of chronic allograft dysfunction was 37.5% while sonoelastography was diagnostic in 35.79% cases as shown in table 90.90%, 97.27%%, 95.23% and 94.69% respectively were the sensitivity, specificity, PPV and NPV of sonoelastography for detection of chronic allograft dysfunction. 94.88% was the diagnostic accuracy of sonoelastography for detection of chronic allograft dysfunction as shown in (Tab.1). (Fig.1a) is showing sonoelastography of a patient with abnormal labs having suspicion of allograft dysfunction. The elastography is demonstrating the non-homogeneous color codding of area in renal allograft as has multiple colors with predominantly red color which signifies the significant loss of elasticity while increasing stiffness in renal parenchyma and increased mean kPa of 20.8 suggestive of renal allograft dysfunction. Sonoelastography findings were correlated with histopathology (Fig.1b) of same renal

Sonoelastography Finding	Histopathological Finding		Total
	Positive	Negative	
Positive	60(TP)	3(FP)	63 (35.79%)
Negative	6(FN)	107(TN)	113 (64.20%)
Total	66 (37.5%)	110 (62.5%)	176

Sensitivity	=60/66	90.90%
Specificity	=107/110	97.27%
PPV	=60/63	95.23%
NPV	=107/113	94.69%
Diagnostic Accuracy	=60+107/176	94.88%

Table 1: Diagnostic accuracy of sonoelastography finding in chronic renal allograft dysfunction

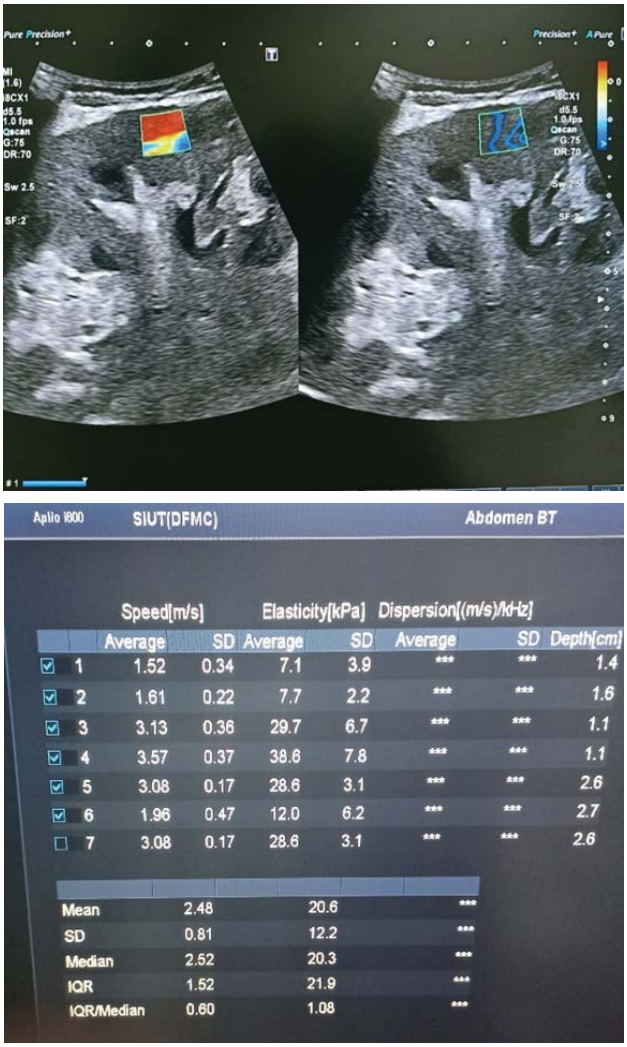

Figure 1(a): Renal allograft dysfunction (increased parenchymal stiffness) with mean kPa of 20.8

allograft which showed severe tubular atrophy and interstitial fibrosis involving more than 50% parenchyma of the particular field of biopsy taken.

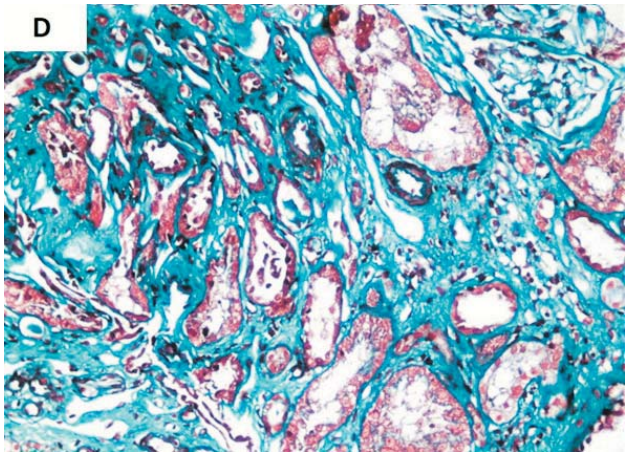

Figure 1(b): Histopathology demonstrates severe tubular atrophy and interstitial fibrosis.

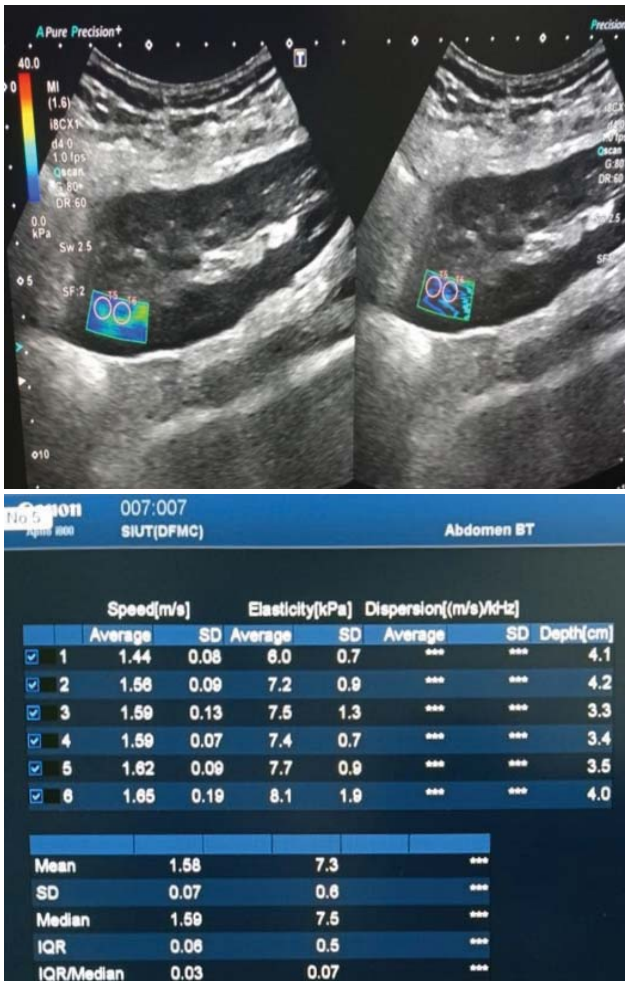

Figure 2: Normal renal allograft function (preserved parenchymal stiffness) with mean kPa of 7.3

(Fig.2) is showing sonoelastography of a patient with normal labs (control group) which is demonstrating the homogeneous color codding of area in renal allograft with complete blue color which signifies the complete preserved elasticity in renal parenchyma and normal mean kPa of 7.3 suggestive of normal renal allograft functioning.

Discussion

24.7% of renal transplant recipients present with chronic graft failure 1 year post transplant and the percentage rises to 89.9% in recipients after 10 years of a renal transplant making chronic allograft nephropathy as the most frequent reason for renal graft failure.[15]

Present line of investigations for suspected failure include serum creatinine and eGFR measurement and vascular/ perfusion assessment by measuring resistive index (RI) using Doppler ultrasound.

RI is frequently used to assess adequate perfusion in renal graft with normal ranges between 0.4-0.7. RI more than 0.8 is abnormal and that between 0.7-0.8 is borderline.

A study done by, Boas et al[16] determined average RI of 0.71 – 0.11 as normal graft function and RI of 0.77 – 0.11 as acute rejection with average RI measurements showing considerable difference between normal and dysfunctional graft using cut off RI of 0.8 being 38% sensitive and 63% specific in detection of rejection.[16]

Limited work have been done on detection of fibrosis in kidney using sonoelastography using stiffness as a measure for fibrosis. There is vast number of researches available for superficial organs like breast and thyroid gland with kidney being deep seated is a relative drawback. A study done on native kidneys by Ozkan et al[17] reported normal elasticity values within renal cortex in 127 healthy volunteers aged 17-63 years, with mean elasticity values of 5.2 kPa 6 2.9 (range, 1-13 kPa) in men and 4.9 kPa 6 2.9 (range, 1-26 kPa) in women.

Exploiting the superficial position of the renal graft, like several studies done in past,[17-20] which is normally placed superficially in the abdomen, we have studied the ability of shear wave sonoelastography to assess for fibrosis by detecting graft parenchymal stiffness, a principal on which shear-wave sonoelastography

works. Mean shear-wave sonoelastography parenchymal stiffness was 6.52 kPa – 2.34 (range, 3.94 - 10.35 kPa) in patients with normal allograft renal functions (Control group) while 17- 32 kPa in patients with chronic allograft dysfunction. Parenchymal stiffness showed a negative correlation with eGFR (r = 20.725; P<, .001) and positive correlation with serum creatinine level (r = 0.714; P <, .001). We found a sensitivity of 90.90% and specificity of 97.27% for the differentiation of patients with stable allograft from those with chronic allograft dysfunction (threshold value, 10.11 kPa). The threshold value of 10.11 kPa has a sensitivity of 90.90% and specificity of 97.27% in distinguishing normal from chronically dysfunctional graft.

Some previously done work has reported that renal parenchymal elasticity values differ with anisotropy, vascular and urinary pressures, Gennison et al[18]

One such study, Brocchi et al[20] showed that there is no relationship between parenchymal stiffness and creatinine values. However, inverse relationship of renal parenchymal tissue elasticity with eGFR (r=20,.47) was found by another study, Arndt et al[19] This result is reproduced by our study redemonstrating the inverse relationship between the two variables (r=20.72) explained by the fact that fibrosis of the functioning cortex will affect the graft s excretory function.

In our study, parenchymal stiffness measurement also correlated with the serum creatinine values of the patients (r=0.71) demonstrating that parenchymal changes observed are helpful in bringing functional faults into light.

There are some limitations of this study. None of the patients in the control group (normal lab parameters) underwent renal transplant biopsy and the histopathological diagnosis was present only in cases (patients with chronic dysfunction) so this study cannot asses the false negatives for this modality. This technique is hand held and sonographic skill of users differ. In our study a single radiologist was asked to perform ultrasound of patients and record results once for each patient so heterogeneity between results of any two observers, has not been taken into account.

Conclusion

Shear-wave sonoelastography is a reliable noninvasive imaging modality that can diagnose the parenchymal stiffness in renal allograft and can help differentiate stable allograft from chronic dysfunction. On the basis of these results, we propose the use of US-based shear-wave sonoelastography as a noninvasive tool and it may be used in serial patient follow-up (in addition to the serum creatinine values, and eGFR). This is likely to help in clinical decision making regarding patient selection for allograft biopsy in the future.

Conflict of Interest: None

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