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Significance of Elastography In Renal Allograft Correlation Between S. Creatinine, Biopsy Result, Doppler Ri Value And Elastography

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Abstract

Introduction: To establish and determine the significance of shear wave elastography technique as a non-invasive alternative to biopsy in early detection of renal graft fibrosis or histological changes in comparison to Banff classification, serum creatinine, and resistive index as measures of color doppler study.

AIM: The aim of the study was to asses elastography as a non-invasive tool and alternative to biopsy in early diagnosis in renal allograft failure. Elastography can be easily performed as an out patient department with much lesser complications and hence may help in early detection of fibrosis or rejection and hence aid in treatment modification.

Methods And Material: Approximately 200 patients with diagnosed or suspicious renal allograft dysfunction underwent ultrasound and elastography examination in Department of Radio-diagnosis and imaging at Institute of Kidney Diseases & Research Centre (IKDRC) & Dr. H. L. Trivedi Institute of Transplantation Sciences (ITS), Ahmedabad from 1st January 2022 to 31th october 2022 were included in the study. The doppler and elastography results were than compared with biopsy results and serum creatinine at the time of ultrasound examination.

Results: There were 166 male (78%) patients and 46 (21.6%) female patients among 212 transplanted patients included in the study. The average age of patients was 33 years, the maximum was 64 years and the minimum was

18 years. 76 (35.8%) patients received a kidney from deceased donor and rest 136 patients received it from live donors. Maximum creatinine value being 11.54 and minimum of 0.64 [Table 1]. A significant difference was obtained for the age of patients where patients with abnormal RI were significantly older (39.95±12.24) than those with normal RI (33.27±9.71). However, the mean serum creatinine (p=0.056) and mean elastography value (p=0.725) was similar [table2]. a weak, insignificant correlation was observed between mean elastography value and RI (r=-0.018, P=0.804). [table3] No significant difference was obtained between different Banff types and mean elastography value (p=0.135), mean elastography value was similar across the Banff types. No significant difference was obtained between donor types and mean elastography value (p=0.113), the mean elastography value was similar in both deceased and live donors.

Conclusions: On ultrasound examination, Ri value appears to correlate with serum creatinine and hence with graft dysfunction however with elastography we could not establish positive correlation with biopsy results, as SWE values were similar across the Banff classification. As well elastography results did not show positive correlation to elevated Ri value on doppler.

Keywords: Banff Classification, Biopsy, Doppler Ri Value, Elastography, Renal Allograft, Serum Creatinine**.**

Introduction

Kidney transplant has become the treatment of choice in patients with end-stage renal disease, with the availability of better diagnostic tools and better immunosuppression treatment it has now become possible to increase the graft survival rate. Renal graft fibrosis remains the most common cause of graft failure. [1,2] Graft nephropathy is a broad entity encompassing glomerulosclerosis, vascular obstruction, and acute/chronic rejection early diagnosis which will provide better treatment management.

Despite the availability of wide clinical parameters, analysis of laboratory tests, and ultrasound examination to determine early allograft dysfunction, renal biopsy remains the gold standard. [3]. Percutaneous allograft biopsy is an invasive procedure is associated with minor complications like local hematoma and haematuria and major complications like aneurysm formation, arteriovenous malformation, and major hematoma formation leading to graft nephrectomy. [4]

Ultrasound evaluation with the doppler study has become the primary choice of non-invasive investigation in outpatient departments as well as for immediate post-transplant observation. Being a fast and easily available bed site tool, it helps in the early diagnosis of the vascular cause, peri graft collection, and obstructive uropathy. However, there is still an ongoing debate on the importance of doppler examination by using the resistive index as a parameter to evaluate the vascular changes that occur in renal parenchyma. [5]

However, ultrasound evaluation fails to address the morphological changes in renal parenchyma.

With recent advances, elastography has emerged as a non-invasive alternative to assess the progression of fibrosis in renal grafts. Elastography in its inception is a tool to evaluate tissue stiffness. Being a fast, easily available, and non-invasive tool elastography can be used to assess the progression of fibrosis in renal allograft and hence the early diagnosis of graft allopathy.

This study aims to evaluate the role of real-time shear wave elastography in the early detection of renal graft fibrosis, correlating the value of tissue stiffness (measured in kPa) with the stages of Banff classification.

Material and Method

Ethics statement: written informed consent was taken from all patients undergoing graft biopsy. The ethics committee of IKDRC-ITS Ahmedabad in the state of Gujarat in India approved the study.

Patient Population: Two hundred and twelve patients undergoing grey mode ultrasound, doppler, and SWE examination with graft biopsy at IKDRC between January to October 2022 were included in the study. Histopathological reports were then compared with elastography results. Elastography was performed by a radiologist blinded to pathological reports.

In a single-center observational prospective cross-sectional study of patients undergoing renal transplant at IKDRC from the period between January 2022 to September 2022 attending the outpatient department of nephrology and were referred to the radiology department for doppler evaluation and further planned for renal biopsy.

Inclusion criteria

Patients who underwent live/cadaveric transplants sent for doppler evaluation who came for a general health check-up. Patients undergoing biopsy with abnormal doppler Ri value, and S.Creatinine.

Exclusion Criteria

1. Patients with age < 18 years.
2. Skin graft distance >3cm.
3. Obstructive uropathy or parenchymal thickness <1cm.
4. Peri graft collection
5. Patients having vascular complications – AVF / arterial stenosis / venous thrombosis.
6. Clinical and biological variables - age, sex, date of transplantation, donor, HLA match, and creatinine were collected at the time of inclusion.

Allograft dysfunction was defined as >50% (1.5-fold from baseline) increase in serum creatinine, reduced urine output - <0.5 ml/kg/hr for more than 6hr), or proteinuria>1gm/day.

Imaging Techniques: Greyscale and doppler examination: Patients referred from the nephrology department on IPD and OPD basis were evaluated by ultrasonography with a grey scale. Kidney dimension, echogenicity, peri graft collection, hydronephrosis – parenchymal thickness was determined followed by color doppler evaluation to evaluate for RVT, RAS, AVM, and to measure Ri at lobar, segmental, hilar, and anastomotic levels in the transplanted renal artery.

Findings supporting graft dysfunction were – graft edema/enlargement, edema within sinus fat causing obliteration of sinus echo complex and reduced cortical echogenicity leading to swelling of pyramids.

Acute rejection may be accompanied by edema of the collecting system wall and focal echo-poor areas of parenchymal infarction and per graft fluid due to necrosis and haemorrhage

Shear wave elastography examination: The patient is placed in a supine position with an empty bladder and regular breathing, SWE was determined using a curved array transducer C5 in a Philips affinity 70 machines, and dynamic excitation was used to generate shear waves in the tissue shear wave speed then calculated as young's modulus (as a measure of stiffness – kPa, kilopascals) in a predefined region of interest (ROI).

The examination was performed by the same radiologist by selection ROI (rectangular tool, around 1cm length) after obtaining a B-mode image with a clear determination of the cortex and medulla. mean Tissue stiffness was measured in YM at the level of medulla and cortex at the upper, mid, and lower poles of the allograft. The value of YM was calculated by affinity software for each SWE examination in selected ROI.

Renal allograft biopsy

Tru-cut biopsy was performed under local anesthesia with an 18-gauge needle guided by a radiologist and performed by a nephrologist. A biopsy was performed from the lower pole and the patient was evaluated for post-biopsy complications. Two adequate tissue samples were taken and sent for electron microscopy, light microscopy, and immunofluorescence study. Results were evaluated according to the upgraded Banff classification.

The Radiologist performing elastography was blinded to biopsy results.

Statistical Analysis

All the data analysis was performed using IBM SPSS ver. 25 software. A descriptive analysis was performed to obtain the general characteristics of the study population. Quantitative data were expressed as mean and standard deviation whereas categorical data were expressed as proportions. One-way ANOVA was used to compare the mean. Pearson correlation was performed to obtain the association between quantitative parameters. A p-value of <0.05 is considered significant.

Results

There were 166 male (78%) patients and 46 (21.6%) female patients amongst 212 transplanted patients included in the study.

Average age of patients was 33years, maximum was 64years and minimum was 18 years.

76 (35.8%) patients received kidney from deceased donor and rest 136 patients received from live donors including mother, father, siblings and cross matched donors.

Maximum creatinine value being 11.54 and minimum 0.64.

Table 1: General characteristics of the patients undergoing renal graphs

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age; years	200	18	65	34.57	10.56
Sex (Male/Female)	200	157/43			
HLA Match/6	152	0	8	2.22	1.55
Serum Creatinine; µmol/L	199	0.68	11.54	3.33	2.29
RI	200	0.55	1.00	0.74	0.091
Mean elastography value- lower pole	200	4.60	64.50	25.79	14.34

Table 1 shows the general characteristics of the patients undergoing renal graphs. Mean age was 34.57±10.56 with male preponderance (n=157).

Table 2: Comparison between the renal graphs recipients with normal and abnormal RIs (< 0.79 and ≥ 0.79, respectively), in terms of sociodemographic and clinical variables

	<0.79		≥0.79		P value
	Mean	SD	Mean	SD	
Age; years	33.27	9.71	39.95	12.24	<0.001
Serum Creatinine; µmol/L	3.17	2.22	3.959	2.46	0.056
Mean elastography value- lower pole	25.62	14.33	26.52	14.51	0.725

Patients were grouped based on RI in to normal (<0.79) and abnormal (≥ 0.79) RIs. A significant difference was obtained for age of patients where patients with abnormal RI were significantly older (39.95±12.24) than those with normal RI (33.27±9.71). However, mean serum creatinine (p=0.056) and mean elastography value (p=0.725) was similar.

Table 3: Pearson correlation showing Pearson Correlation coefficient

		RI
Serum Creatinine	Pearson Correlation	0.151
	P value	0.034
	N	199
Mean elastography value- lower pole	Pearson Correlation	-0.018
	P value	0.804
	N	200

A significant correlation was obtained between serum creatinine and RI (r=0.151, p=0.034). This shows a positive correlation indicating an increase in RI with increasing serum creatinine values. However, a weak negative insignificant correlation was observed between mean elastography value and RI (r=-0.018, P=0.804).

Table 4: Comparing mean elastography value with diagnosis

Diagnosis	Mean	Std. Deviation	P value
Banff Type 3	29.8368	15.49632	0.135
Banff Type 4	27.7308	16.11368	
Banff TYPE 1	31.1500	29.62777	
Banff Type 2	23.8386	13.13145	
Banff TYPE 5	23.2727	15.23989	
Banff Type 6	28.8929	14.91321	
Tissue inadequate	18.4917	10.58339	
Total	25.7978	14.34136	

No significant difference was obtained between different Banff types and mean elastography value (p=0.135). This highlights that mean elastography value was similar across the Banff types.

Table 5: Comparing mean elastography value with donor

Donor	Mean	Std. Deviation	P value
Deceased	23.6282	12.39914	0.113
Live donor	26.9919	15.21958	
Total	25.7978	14.34136	

No significant difference was obtained between donor types and mean elastography value (p=0.113). This highlights that mean elastography value was similar in both deceased and live donor.

Discussion

In our single-center study at tertiary care hospital study, on evaluation of 200 patients with mean age 35+_10years and males being the majority, the mean serum creatinine, and elastography value increased as the value of mean RI increased >0.79, however, the P value not <0.001 to stamp it as significant. Ri value increased as the age of patients increased, this could be due to atherosclerotic and cardiovascular causes in higher age groups.

We found no positive correlation between the stiffness of the transplanted kidney and different categories of Banff classification, moreover, there was no evidence of a positive correlation between SWE parameters and the status of the donor being a diseased or live-related transplant. Similar results were observed in the previous study in the literature [6,7], contradicting these results study by chajjer et al [9] shows a positive correlation, this study had the limitation of a smaller sample size.

Further in our study, a weak negative insignificant correlation was observed between SWE and Ri value, contrary to this a study performed in brazil showed a positive correlation between SWE and RI value [8], this study had limitations of lack of biopsy results correlation and smaller study group.

A positive correlation was seen between the Ri value and serum creatinine, similar results were seen in a study conducted in china [10], in this study cut off value for Ri was taken as >0.75, and beyond which RI had a negative correlation, this study was conducted in immediate post-transplant patients with lack of follow up beyond one month, hence vascular causes were taken into consideration however parenchymal causes like fibrosis cannot be assessed in one month and hence lacked follow up.

It seems to be the need of the hour to find a non-invasive and fast diagnostic substitute for biopsy as a biopsy cannot be performed in patients with thrombocytopenia, patients on anticoagulants, and high serum creatinine. Recent advances in MR elastography and urinary biomarkers show promising results [11,12]

Elastography has its limitations as it detects stiffness of the graft kidney which can change with urinary pressure and renal blood perfusion besides the stiffness of the tissue can vary in various conditions that alter its histology and amount of focal fibrosis.

To boot there remains a void in guidance and standardization in the method to perform elastography and its capability to diagnose renal pathology is still limited yet there is a scope that renal elastography can be helpful to guide the location for sampling before performing the biopsy.

Conclusion

On ultrasound examination, Ri value appears to correlate with serum creatinine and hence with graft dysfunction however with elastography, we could not establish a positive correlation with biopsy results, as SWE values were similar across the Banff classification. Also, elastography results did not show a positive correlation to elevated Ri value on doppler.

Limitation of the study: Patients with graft dysfunction undergoing renal biopsy were selected as subjects with a lack of control group or patients with stable graft function. Moreover, the results were interpreted by a single observer.

Abbreviations

Ri – resistive index

CKD – chronic kidney disease

s.creatinine – serum creatinine

SWE -shear wave elastography

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