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Validity of Strain Elastography in Renal Allograft Infection

Moataz Fatthy[1], Abd ELrahman Marzouk[1], Ahmed Fathy[1], Sameh Abouzeid[2], Ahmed Fayed[1]

[1]Nephrology division, Kasr al ainy school of medicine Cairo University, Cairo, Egypt

[2]Nephrology division, Theodor Bilharz institute

**Corresponding author's E-mail: Abdo.elmaghraby75@gmail.com*

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Abstract

***Background**: Strain elastography is not routinely used by many clinicians to determine allograft dysfunction. Validity of strain elastography and renal histopathologic characteristics especially infected allograft have not been sufficiently evaluated in renal transplant recipients. **Objective**: To study the correlation between strain elastography and renal allograft infection in Kasr Al Ainy school of medicine -Cairo University. **Design/Methods**: In a single-center, prospective study involving 109 renal-allograft recipients, the strain elastography was evaluated in 109 renal transplant recipients to be correlated with renal allograft infection that was proved in (64 patients) by the laboratory and histopathological finding and (45 patients) without allograft infection. **Results**: There was no statistically significant difference between renal allograft infection and strain elastography (P value 0.447). Causes of allograft infection were CMV in (30.3%), UTI in (18.3%),) and BK polyomavirus in (10.1%). Histopathological findings in renal allograft biopsy were active ABMR in (6.4%), acute interstitial nephritis with neutrophils with bacterial infection in (18.3%), Acute TCMR in (6.4%), BK polyomavirus nephropathy with SV40 positive in (10.1%), chronic ABMR in (17.4%), chronic active ABMR in (7.3%), CMV nephropathy in (13.8%), mixed rejection in (3.7%) and tubular injury with viral infection in (16.5%).Conclusion: Strain elastography may not be useful in renal allograft infection evaluation*

Keywords: *Strain elastography, Renal allograft infection, Kidney transplant recipients*

1. Introduction

Ultrasound is a frequently utilized technique in a range of clinical applications because it is a safe, simple, affordable, and readily available technology that may be used as a bedside test. These characteristics also apply to sono-elastography, which has lately been used in numerous clinical applications, including the detection of lymph nodes, liver fibrosis, kidney, thyroid, breast, and prostate tumors. By using tissue stiffness as a supplementary technology to traditional ultrasound, elasticity imaging in Sono elastography adds information to the latter**. (1)**

The diagnosis of renal allograft fibrosis and chronic allograft failure requires noninvasive techniques to replace renal allograft biopsy. One of these appealing substitutes is sono-elastography; a cutting-edge imaging technique that assesses tissue stiffness. Renal stiffness following tissue expansion during acute rejection is not captured by conventional ultrasonography methods. Sono-elastography (SE), in contrast, enables the indirect assessment of changes to renal function by providing quantitative information on tissue elasticity distribution for the assessment of renal pathological alterations. **(2)**

Sono-elastography, an imaging technique that assesses tissue stiffness, is particularly useful for superficial organs, it can be further divided as: (1) Shear wave elastography, also known as

quantitative elastography, includes real-time elastography, transient elastography, and acoustic radiation force impulse. (2) Strain elastography is also known as quantitative and qualitative elastography, including real-time elastography**. (3)**

Principles and Techniques of Ultrasound Elastography
Strain Sono-elastography is subdivided into two main methods

1) First method, where the operator performs compression manually on the tissues using US transducer. This approach gives fair results for superficial organs as thyroid and breast but not good results on deeper structures as the liver. **(4)**

2) The second method, where the operator holds the transducer steadily and displace the tissues through internal physiologic motion as cardiovascular and respiratory systems, as this approach is not depending on superficial compression, it can be used in detection of deeper structures. The same-direction stress that causes tissue displacement is then measured using a variety of techniques, including radiofrequency echo correlation-based tracking, depending on the manufacturing firms. Processing done using ultrasound or a mix of those two techniques. **(5)**

The strain data are shown on an elastogram, a semi-transparent color map that is superimposed over the B mode image. Although the color scale can vary based on the ultrasound machine, low strain, which indicates rigid tissue, takes the color blue, while high strain, which represents soft tissue, takes the color red. **(6)**

The ratio of the strain measured in surrounding tissue (normal tissue) to the strain measured in the target lesion (region of interest), or strain ratio, is a pseudo-quantitative measurement that can be used. If the strain ratio is greater than 1, the ROI is less than normal, indicating lower strain and greater stiffness. **(7)**

2. Materials and Methods

One hundred and nine kidney transplant recipients (aged between 16 and 56 years old, males 64, females 45), presented with renal allograft dysfunction with suspicious of allograft infection to the department of nephrology at Cairo University Hospital in Egypt were included consecutively in this study. Informed consent was taken from all cases. All patients in this study received a living donor renal transplantation. Inclusion criteria includes renal transplant patients, rising kidney function tests and suspected renal allograft infection. Exclusion criteria includes chronic allograft rejection

All the patients were subjected to the following: Detailed medical history, transplantation history, duration of renal transplantation, induction therapy, immunosuppressive drugs, any history suspected of allograft infection, complete physical examination to detect any source of infection. Laboratory investigations including; serum creatinine, TLC, CRP, serum procalcitonin, urine analysis and urine culture, drug level (FK or C0 level), CMV PCR. BK Polyomavirus PCR, HBsAg, HCV Abs, HIV Abs and PCR for Covid19. Imaging: graft ultrasonography, strain elastography. The ultrasound technique: Patients were placed in the supine position with the abdominal wall over the transplant renal graft side fully exposed. B-mode ultrasound was performed to observe transplant renal shape, size, and parenchymal echo, space occupation, collecting system, ureter dilatation, and perinephric effusion.

Sono-elastography: Strain wave elastography was performed for the assessment of parenchymal elasticity for all patients in this study by using a 5-1 MHz trans-abdominal transducer to assess the following: Elasticity value at the upper zone, elasticity value in the middle zone, elasticity value at a lower zone, the mean for these measurements was calculated. The measurements of kidney stiffness were expressed in terms of young's modulus (Kpa). The results obtained by strain wave Sono-elastography will be correlated with those obtained by US and color Duplex Doppler.

Renal allograft biopsy was taken for all patients
All measurements were performed by the same operator who has more than 16 years' experience in interventional nephrology practice. Renal parenchyma stiffness of each transplant recipient using linear probe (high frequency probe 8-12 MHz logic F8 expert, ultrasound and Duplex were assessed cautiously. Renal resistive index and Sono-elastography findings were compared with the

histopathological proven renal allograft infection. Percutaneous ultrasound guided renal allograft biopsy were performed using 16-gauge automatic needles. These biopsy specimens were fixed in formalin and examined under light microscopy using hematoxylin and eosin stain and in some cases immunofluorescence or even Electron microscope were required. Histopathological diagnosis of biopsy specimens was obtained and served as reference standards.

Statistical analysis: Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired test in normally distributed quantitative variables while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables. For comparing categorical data, Chi square (x2) test was performed. Exact test was used instead when the expected frequency is less than 5.

Consent: consents were taken from the patient

3. Results and Discussion

In our study, there are one hundred and nine kidney transplant recipients with living related donors, presented with renal allograft dysfunction with suspicious of renal allograft infection to the department of nephrology at Cairo University Hospital in Egypt, we evaluated the correlation between the strain elastography and renal allograft infection that proved with laboratory work up and histopathological finding. There were two groups, infected renal allograft group (64 patients) and non-infected group (45 patients).

Table 1. Comparison between the infected and non-infected group regarding: V.a: Descriptive parameter results

	Infected group		Non-infected group		
	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**	**P value**
Age (years)	32.25	8.41	32.71	7.58	0.770
Duration of transplantation (years)	4.91	1.70	4.71	1.46	0.517
Creatinine (mg/dl)	3.88	1.13	3.88	1.00	0.984
TLC $\times 10^9$/L	8.72	4.78	7.10	1.29	0.012
Serum Procalcitonin (ng/ml)	0.95	1.66	0.02	0.01	< 0.001
CRP (mg/dl)	98.22	69.85	4.22	1.88	< 0.001
C0 level (ng/ml)	90.70	15.30	87.38	5.68	0.359
FK level (ng/ml)	6.92	1.49	5.85	1.17	0.001

		Infected group		Non-infected group		P value
		Count	**%**	**Count**	**%**	
Sex	Female	23	35.9%	18	40.0%	0.666
	Male	41	64.1%	27	60.0%	
HCVAb	Neg	64	100.0%	45	100.0%	------
HBsAg	Neg	64	100.0%	45	100.0%	------
HIV	Neg	64	100.0%	45	100.0%	------
Covid 19 PCR	Neg	64	100.0%	45	100.0%	------
CMV PCR	Positive	33	51.6%	0	0.0%	< 0.001
	Neg	31	48.4%	45	100.0%	
BK PCR	Positive	11	17.2%	0	0.0%	0.002
	Neg	53	82.8%	45	100.0%	
urine culture	UTI	20	31.3%	0	0.0%	< 0.001
	no growth	44	68.8%	45	100.0%	
Causes of infection	UTI	20	31.3%	0	0.0%	< 0.001
	CMV	33	51.6%	0	0.0%	
	BK polyoma virus	11	17.2%	0	0.0%	
	No infection	0	0.0%	45	100.0%	

[Table 1] shows, comparison between the infected renal allograft group and non-infected group was highly significant (P <0.001) regarding serum procalcitonin and CRP, causes of renal allograft infection.

Figure (1): Causes of renal allograft infection in our study

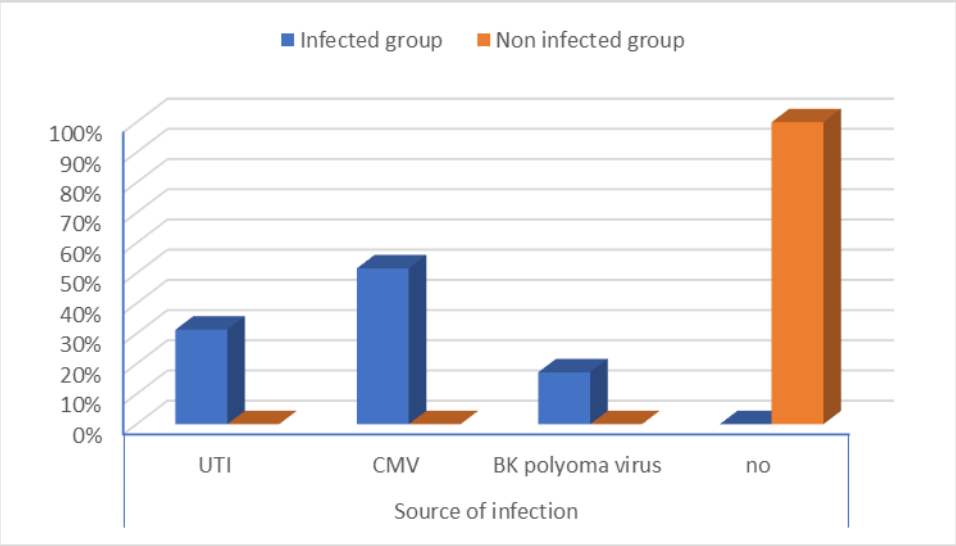

Figure (2): Renal allograft biopsy results

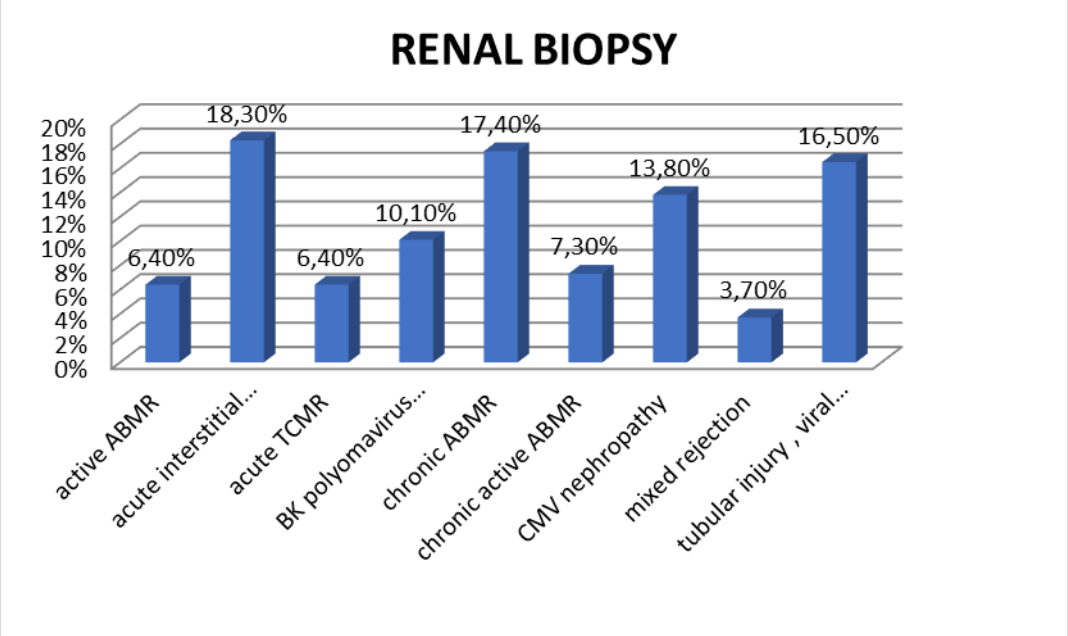

Table 2. Cortical strain score electrography

	Infected group		Non-infected group		
	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**	**P value**
Cortical strain score elastography	2.34	0.72	2.44	0.62	0.447

[Table.2] shows, there is no statistically significant difference with cortical strain score elastography (P 0.447).

Table 3. Renal allograft biopsy results

	Infected group		Non-infected group		P value
	Count	%	Count	%	
Active ABMR	0	0.0%	7	15.6%	< 0.001
Acute interstitial nephritis with neutrophils, bacterial infection	20	31.3%	0	0.0%	
Acute TCMR	0	0.0%	7	15.6%	
BK polyomavirus nephropathy, SV40 positive	11	17.2%	0	0.0%	
Chronic ABMR	0	0.0%	19	42.2%	
Chronic active ABMR	0	0.0%	8	17.8%	
CMV nephropathy	15	23.4%	0	0.0%	
Mixed rejection	0	0.0%	4	8.9%	
Tubular injury, viral infection	18	28.1%	0	0.0%	

[Table.3] comparison between infected and non-infected renal allograft group, there was highly significant (P<0.001) regarding renal allograft biopsy results.

It is crucial to establish an early diagnosis to direct antimicrobial therapy because immunocompromised patients have poor tolerance to invasive infection and have significant morbidity and death rates. Viral infections are a major cause of morbidity, leading to graft dysfunction, graft rejection, systemic illness, and an increased risk for other opportunistic infections (like Pneumocystis and Aspergillus) and virally mediated cancers because of the predominate T-lymphocyte dysfunction inherent to transplant immunosuppression.

Renal elastography is an ultrasonographic method. It has recently been adopted since it clearly shows renal fibrosis in people with chronic kidney disease and kidney transplant recipients and is a useful technique that also provides important details on the type of renal masses. Typically, the strain index and a free-hand approach are used to evaluate kidney disorders. **(8)**

In the present study, we evaluated the correlation between the strain elastography with renal allograft infection that proved with laboratory work up and histopathological finding. one hundred and nine kidney transplant recipients with living related donors were included in our study, they presented with renal allograft dysfunction with suspicious of allograft infection, the mean age was 32.44 ± 8.05 years, (62.40%) were males (64 patients) and (37.60%) were females (45 patients). The mean value of duration of renal transplantation was 4.83±1.60 years, the mean values of laboratory work up results, serum creatinine was (3.88±1.08), TLC was **(**8.05±3.83**)** $\times 10^9$/L, serum procalcitonin was (0.56±1.35) ng/ml, C-Reactive protein (CRP) was (59.41±70.77) mg/dl, Tacrolimus (FK level) was (6.45±1.45) ng/ml, Cyclosporin (C0 level) was (89.50±12.68) ng/ml.

In our study there are two groups, infected renal allograft group (64 patients) and non-infected group (45 patients), the infection was proved with laboratory work up and histopathological renal allograft biopsy finding. The causes of allograft infection percent, UTI was (18.3%), CMV was (30.3%), BK polyomavirus was (10.1%) and there was no infection in (41.3%) and the mean value of cortical strain elastography score was (2.38±0.68)

The percentage of different results of renal allograft biopsies, active ABMR was (6.4%), acute interstitial nephritis with neutrophils with bacterial infection was (18.3%), Acute TCMR was (6.4%), BK polyomavirus nephropathy with SV40 positive was (10.1%), chronic ABMR was (17.4%), chronic active ABMR was (7.3%), CMV nephropathy was (13.8%), mixed rejection was (3.7%), and tubular injury with viral infection was (16.5%)

Our study clearly demonstrated that, the mean of cortical strain elastography score in infected group was (2.34±0.72), non-infected group was (2.44±0.62) with non-significant (P value - 0.447).

Limitations of the study: small sample size, more inflammatory markers should be done for better assessment of infections and there were no previous studies in the same topic

Recommendation of the study: Studies including larger number of patients to clarify the impact of strain elastography in diagnosis of renal allograft infection

4. Conclusion

Strain elastography may not be useful in renal allograft infection evaluation.

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