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Article

Use of diffusion tensor imaging in assessment of renal fibrosis in lupus nephritis: cross sectional study

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Abstract

Background: Lupus nephritis (LN) is a major risk factor for morbidity in systemic lupus erythematosus (SLE) and 10% of patients with LN will develop end stage renal disease. Renal biopsy is mandatory in almost all patients with LN, but sometimes it is not feasible and may be associated with complications. Therefore, the identification of a non-invasive tool for assessment of renal structure and function is vital. The aim of our study is to explore the association of diffusion tensor magnetic resonance imaging (MRI) parameters as apparent diffusion coefficient (ADC) and fractional anisotropy (FA) with measurements of renal functions and renal histopathological changes especially markers of fibrosis in a cohort of patients with LN.

Methods: The study was conducted on thirty patients diagnosed with LN and thirty healthy volunteers representing the control group. All candidates were subjected to measurements of renal functions, estimated glomerular filtration rate (eGFR), SLE disease activity index (SLEDAI) score and underwent diffusion tensor MRI of kidneys. Renal biopsy was done for the cases group within one week of the MRI. In addition to the routine histological examination, immunohistochemical staining using anti-collagen III antibody was done as a measure of fibrosis.

Results: The mean cortical ADC, medullary ADC, cortical FA and medullary FA in patients with LN were significantly lower than the control group and they correlated positively with eGFR. These markers also correlated negatively with the pathological chronicity index and they showed a downward trend with increasing interstitial fibrosis score. Δ ADC can somehow differentiate between some classes of LN. *Conclusions:* Diffusion tensor imaging (DTI) is a useful non-invasive tool which can help in assessment of renal impairment in patients with LN, it can also give an idea about the degree of fibrosis and chronicity which can influence treatment decisions.

Keywords: Lupus nephritis, Diffusion tensor, Magnetic resonance imaging, Renal fibrosis

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect nearly any organ of the body. The course of the disease is extremely variable ranging from asymptomatic to life threatening. Patients with SLE have a defective immune system with loss of self-tolerance which leads to formation of autoantibodies against different cellular antigens and subsequently production of immune complexes that may injure many organs.(1) Lupus nephritis (LN) is clinically apparent in more than half of the patients with SLE, and it is histologically evident in most of lupus patients.(2) LN is a major risk factor for morbidity in SLE and 10% of patients with LN will develop end stage renal disease.(3)

Renal biopsy should be considered in any patient with SLE who has active urinary sediment or abnormal renal functions, especially upon the first attack of nephritis.(4) However, it is an invasive procedure associated with many complications as perinephric haematoma, macroscopic haematuria, infection, arteriovenous fistula, damage to adjacent organs and even death. In addition, it might be difficult to repeat the biopsy whenever the clinical course is changed or on treatment failure. This may be due to patient refusal, pregnancy, critically ill patients, or persistent thrombocytopenia.(5) Therefore, the identification of a non-invasive tool for assessing renal structure and function is vital.

Routinely used imaging modalities nowadays especially ultrasound (US) and Computed Tomography (CT) provide adequate information on structural changes but little on functional impairment of the kidney. Magnetic resonance imaging (MRI) has the unique ability to show both structure and function. Techniques for functional renal imaging may be contrast-enhanced such as MR renograms, or unenhanced modalities, such as diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) which have shown promising results in the evaluation of renal functions.(6)

The aim of our study is to explore the association of DTI parameters as apparent diffusion coefficient (ADC) and fractional anisotropy (FA) with measurements of renal functions in a cohort of LN patients and to correlate these findings with renal histopathological changes and markers of fibrosis.

Methods

This was an observational cross-sectional study which was conducted on 60 subjects. Thirty patients diagnosed with LN representing the cases group and thirty healthy age and sex matched volunteers representing the control group. Patients in the study group were adults diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria and they have evidence of renal involvement suggested by presence of active urinary sediment or impaired renal functions.(7) Those patients were admitted in the nephrology or rheumatology department in the period between October 2018 and March 2020. Exclusion criteria included pyelonephritis, diabetes mellitus, patients with metallic implants incompatible with MRI and patients with claustrophobia.

An informed consent was signed from all candidates and approval of the ethics of committee was obtained before the beginning of the study. Patients were subjected to detailed history taking, full clinical examination and routine laboratory investigations which included complete urine analysis, urinary protein/ creatinine ratio, renal function tests and estimated glomerular filtration rate (eGFR) calculation by CKD-EPI equation.(8) SLE disease activity index (SLEDAI) score was assessed as a measure of disease activity.(9)

Renal histopathology

Renal biopsies were taken from the cases group within one week of the MRI. They were mostly done before the MRI but some cases were after. Each biopsy was routinely stained and classified according to the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) classification that was modified in 2018, also activity and chronicity indices were calculated. (10)

Routine assessment of interstitial fibrosis by Masson's trichrome stain has some limitations as it stains the basement membranes, interstitial oedema and sometimes the brush borders, which should not be included in measurement of interstitial fibrosis. (11) Moreover, Masson's trichrome may not be sensitive for mild fibrosis. (12) For these reasons, assessment of fibrosis by 2 methods (trichrome and collagen measurement) could help improve the efficiency, reproducibility and functional correlation for best interpretation of renal fibrosis. (11) (**Figure1**)

IHC by anti-collagen III antibody

IHC was done using Collagen III alpha 1/COL3A1 Antibody (1E7-D7/Col3) – BSA Free by NOVUS biologicals. It is a monoclonal antibody derived from a mouse host that's highly specific for type III collagen. Immunostaining steps included fixing the slides in 50°C oven overnight, deparaffinization in xylene and rehydration in a graded alcohol series. Then the slide was incubated in hydrogen peroxide block for 10 minutes followed by antigen retrieval in sodium citrate buffer for 17 minutes. The primary antibody was diluted 1:50 in phosphate buffered saline (PBS) and the intensity of staining was estimated semi-quantitatively.

MRI Kidneys

All the patients and healthy volunteers underwent MRI of kidneys using a super-conducting 1.5 Tesla closed MRI scan (Model Ingenia CX) by Philips (Netherlands). There was no requirement for the patients to fast, and they remained hydrated on the day of the examination. They lied in a supine position and a body coil was used and placed anterior to the abdomen. The following sequences and scanning parameters were applied: T2 coronal oblique (field of view (FOV) 330x330 mm, slice thickness 3 mm, slice gap 0.4 mm, repetition time (TR) 1000 msec, echo time (TE) 100 msec and matrix 200x227 mm) and renal coronal oblique (DTI) (FOV 450x401 mm, slice thickness 2.5 mm, slice gap 0.4 mm, TR 1788 msec, TE 84 msec and fat suppression SPIR). The total scan duration was 4 minutes including 15 seconds survey. Respiratory gating was used to minimize the respiratory motion artifact.

Imaging analysis

The ADC and FA values of the kidneys were calculated on a Philips workstation using the ADC and FA maps generated from the DTI sequence. In the coronal ADC map (nearest to the renal hilum) regions of interest (ROIs) were placed manually on the parenchyma of the renal cortex and medulla. Fat within the renal sinus was excluded. Those ROIs (ranging 5-10 mm^2) were placed, one in the upper, middle, and lower poles on each kidney and the mean of these six values were calculated for both ADC and FA. The size of ROI was set to reduce the noise and the influence of partial volume effects. Avoiding visible vessels, any haematomas post biopsy, renal cysts, or susceptibility artifacts, ROIs were placed manually on the clear corticomedullary differentiation (CMD) image. (**Figure 1**)

For nephropathic kidneys with indistinct CMD, cortical ROIs were placed as near as possible to the outer boundary of the cortex and medullary ROIs were placed between the expected area of the cortex and renal pelvis. Imaging analysis was performed by a radiologist with more than 10 years of experience in abdominal and genitourinary MRI who was blinded to both the laboratory and histopathological findings.

Statistical analysis of the data

Data were fed to the computer and analysed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to verify the normality of distribution. Student t-test was used for normally distributed quantitative variables and Mann Whitney test was used for abnormally distributed quantitative variables, to compare between the two studied groups. The correlation between quantitative parameters was done using Spearman's correlation test. Significance of the obtained results was judged at the 5% level.

Results

Cohort characteristics

The LN group included 3 males (10%) and 27 females (90 %) with their age ranging between 18 and 50 years (mean = 30.40 ± 9.42 years), while the control group included 5 males (16.7 %) and 25 females (83.3 %) with their age ranging between 21 and 44 years (mean = 29.53 ± 5.73 years).
Serum creatinine in the LN group ranged between 0.4 and 8 mg/dl with a mean of 1.72 ± 1.76 mg/dl, while in the control group it ranged between 0.6 and 1.1 mg/dl with a mean of 0.74 ± 0.12 mg/dl. Estimated GFR calculated by CKD-EPI in the LN group ranged between 5.7 and 151 ml/min with a mean of 72.07 ± 45.78 ml/min, while in the control group it ranged between 90.60 and 135.3 ml/min with a mean of 110.9 ± 14.1 ml/min. SLEDAI score in the LN group ranged between 8 and 32 with a mean of 20.73 ± 6.38.

Histopathological results

Histological examination classified class II LN in 4 cases, class III LN in 4 cases, class III + V LN in only 1 case, class IV LN in 13 cases, class IV+ V LN in 6 cases, and class V LN in 2 cases. The activity index in the studied cases ranged between 0 and 11 with a mean of 6.43 ± 3.67 and the chronicity index ranged between 0 and 8 with a mean of 2.40 ± 2.40. 12 cases had interstitial fibrosis score of 0/3, 11 cases had a score of 1/3, 7 cases had a score of 2/3, and no cases had a score of 3/3. Anti-collagen III antibody failed to demonstrate the stain in 11 cases, 8 cases stained from > 0 to less than 5%, 4 cases stained from 5 to < 10%, and 7 cases stained about 10%. (Figure 1)

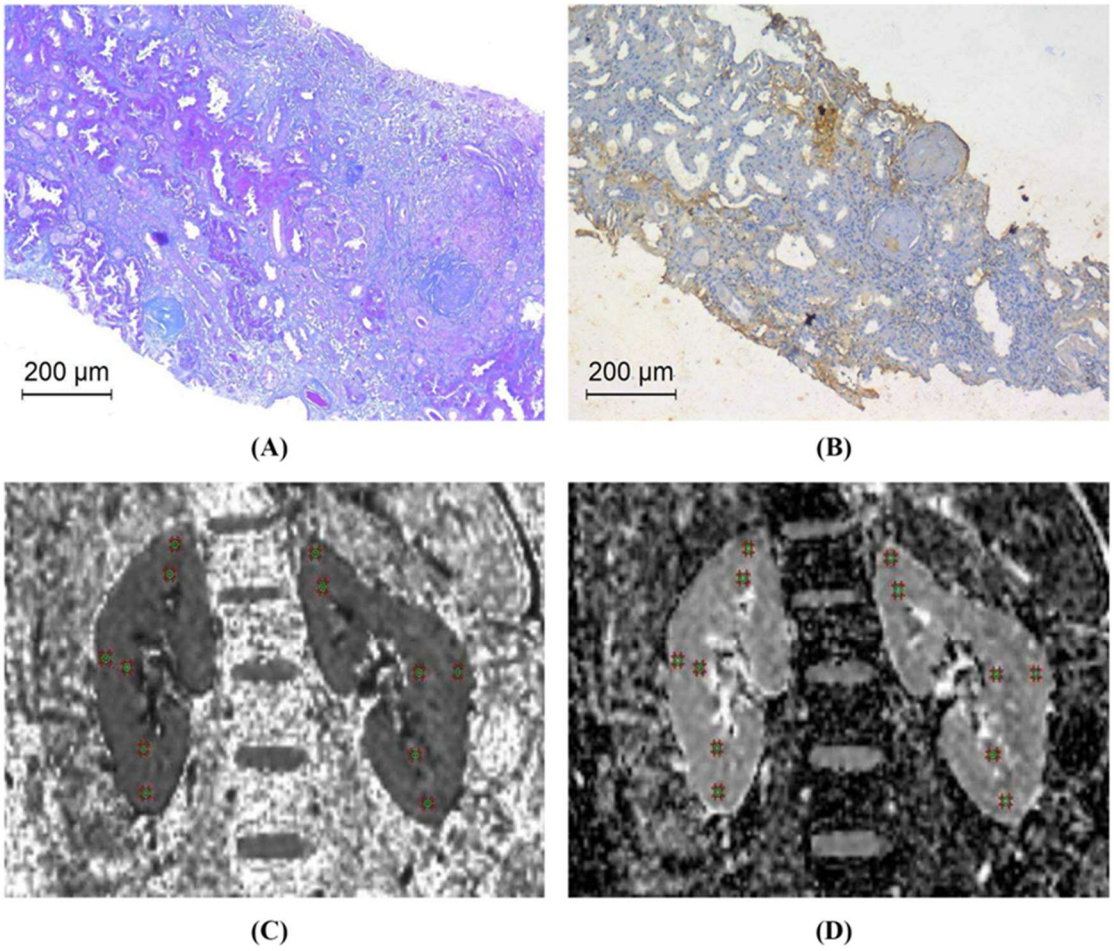

Figure 1: **Renal histopathology and MRI kidneys of a 32-year-old patient with LN, her eGFR was 54 ml/min and she was diagnosed as Class IV LN with chronicity index 4/12. Picture A) Masson's trichrome stain showing a moderate degree of interstitial fibrosis. B) Immunohistochemistry using anti-collagen III antibody showing around 10 % staining. C) ADC map showing the site of 6 ROIs used for calculation of cortical and medullary ADC values D) FA map showing the site of 6 ROIs used for calculation of cortical and medullary FA values.**

Imaging results

ADC and FA values of the cortex and medulla of the kidneys in LN patients and controls are shown in **Table 1**. The mean ADC value of the cortex and medulla of the kidneys were significantly lower in the LN group than in the control group (p=0.001, 0.004 respectively). The mean Δ ADC of the kidneys (difference between cortical and medullary ADC) was significantly lower in the LN group

than in the control group (p=0.003). The mean FA value of the cortex and medulla of the kidneys were significantly lower in the LN group than in the control group (p<0.001).

Table (1): Comparison between the two studied groups according to the calculated ADC and FA values of the kidneys

ADC (10^{-3} **mm²/s)**	**LN Patients (n = 30)**	**Controls (n = 30)**	**P**
Cortex			
Min. – Max.	1.57 – 2.59	2.12 – 2.84	0.001*
Mean ± SD.	2.11 ± 0.26	2.43 ± 0.22	
Medulla			
Min. – Max.	1.34 – 2.08	1.62 – 2.09	0.004*
Mean ± SD.	1.72 ± 0.21	1.86 ± 0.17	
Δ ADC			
Min. – Max.	0.10 – 0.66	0.26 – 1.13	0.003*
Mean ± SD.	0.39 ± 0.16	0.56 ± 0.22	
FA	**LN Patients (n = 30)**	**Controls (n = 30)**	**P**
Cortex			
Min. – Max.	0.19 – 0.29	0.26 – 0.34	<0.001*
Mean ± SD.	0.24 ± 0.03	0.30 ± 0.02	
Medulla			
Min. – Max.	0.27 – 0.47	0.39 – 0.53	<0.001*
Mean ± SD.	0.36 ± 0.05	0.45± 0.03	

Correlations of renal functions with different radiological parameters

Patients were divided into 3 groups according to eGFR. Group A included 7 patients with eGFR ≤29 ml/min (stages 4 and 5 CKD), Group B included 3 patients with eGFR 30-59 ml/min (stage 3 CKD) and Group C which included 20 patients with eGFR ≥60 ml/min (stages 1 and 2 CKD).

There was a downward trend of our measured radiological parameters with increasing stages of CKD in LN. Moreover, Cortical ADC, Cortical FA and Medullary FA were significantly lower in Group C than in the control group (p=0.009, p<0.001, p<0.001 respectively). This is shown in **Table 2**.

Table (2): Relation between eGFR of the studied groups and different radiological parameters (n = 60)

		eGFR by CKD-EPI (ml/min)				P
		Group A Stages 4 & 5 CKD (≤29) (n = 7)	**Group B Stage 3 CKD (30 –59) (n = 3)**	**Group C Stages 1 & 2 CKD (≥60) (n = 20)**	**Controls (n = 30)**	
ADC (10^{-3} mm^2/s)	**Cortex**					
	Min. – Max.	1.57 – 2.01	1.93 – 2.02	2.07 – 2.59	2.12 –2.84	<0.001*
	Mean ± SD.	1.75 ± 0.16	1.96 ± 0.05	2.25 ± 0.16	2.43 ±0.22	
	Significance between Groups	p_1= 0.387, p_2<0.001*, p_3<0.001*				
	P Control	<0.001*	0.001*	0.009*		
	Medulla					
	Min. – Max.	1.34 – 1.80	1.40 – 1.83	1.60 – 2.08	1.62 –2.09	<0.001*
	Mean ± SD.	1.50 ± 0.18	1.55 ± 0.25	1.82 ± 0.14	1.86 ±0.17	
	Significance between Groups	p_1= 0.977, p_2<0.001*, p_3<0.001*				
	P Control	<0.001*	0.011*	0.769		
FA	**Cortex**					
	Min. – Max.	0.19 – 0.24	0.22 – 0.25	0.21 – 0.29	0.26 –0.34	<0.001*
	Mean ± SD.	0.21 ± 0.02	0.23 ± 0.02	0.25 ± 0.02	0.30 ±0.02	
	Significance between Groups	p_1=0.515, p_2<0.001*, p_3<0.001*				
	P Control	<0.001*	<0.001*	<0.001*		
	Medulla					
	Min. – Max.	0.27 – 0.33	0.31 – 0.36	0.33 – 0.47	0.39 –0.53	<0.001*
	Mean ± SD.	0.31 ± 0.02	0.33 ± 0.03	0.38 ± 0.04	0.45 ±0.03	
	Significance between Groups	p_1=0.635, p_2<0.001*, p_3<0.001*				
	P Control	<0.001*	<0.001*	<0.001*		

p: p value for comparing between the different categories

p_1: p value for comparing between **Group A** and **Group B**

p_2: p value for comparing between **Group A** and **Group C**

p_3: p value for comparing between **Group B** and **Group C**

$p_{control}$: p value for comparing this group with the control group.

There was positive statistically significant correlation between ADC of the cortex and medulla of the kidneys in the LN group with eGFR (r=0.710, p<0.001, r=0.559, p=0.001 respectively). (**Figure 2**) There was negative statistically significant correlation between ADC of the cortex and medulla of the kidneys in the LN group and serum creatinine (r=-0.684, p<0.001, r=-0.616, p<0.001).

There was positive statistically significant correlation between FA value of the cortex and medulla of the kidneys in the LN group with eGFR (r=0.687, p<0.001, r=0.828, p<0.001 respectively). (Figure 2) The strongest correlation with eGFR among the 4 measured radiological parameters was with the medullary FA. There was negative statistically significant correlation between FA value of the cortex and medulla of the kidneys in the LN group and serum creatinine (r=-0.732, p<0.001, r=-0.830, p<0.001 respectively).

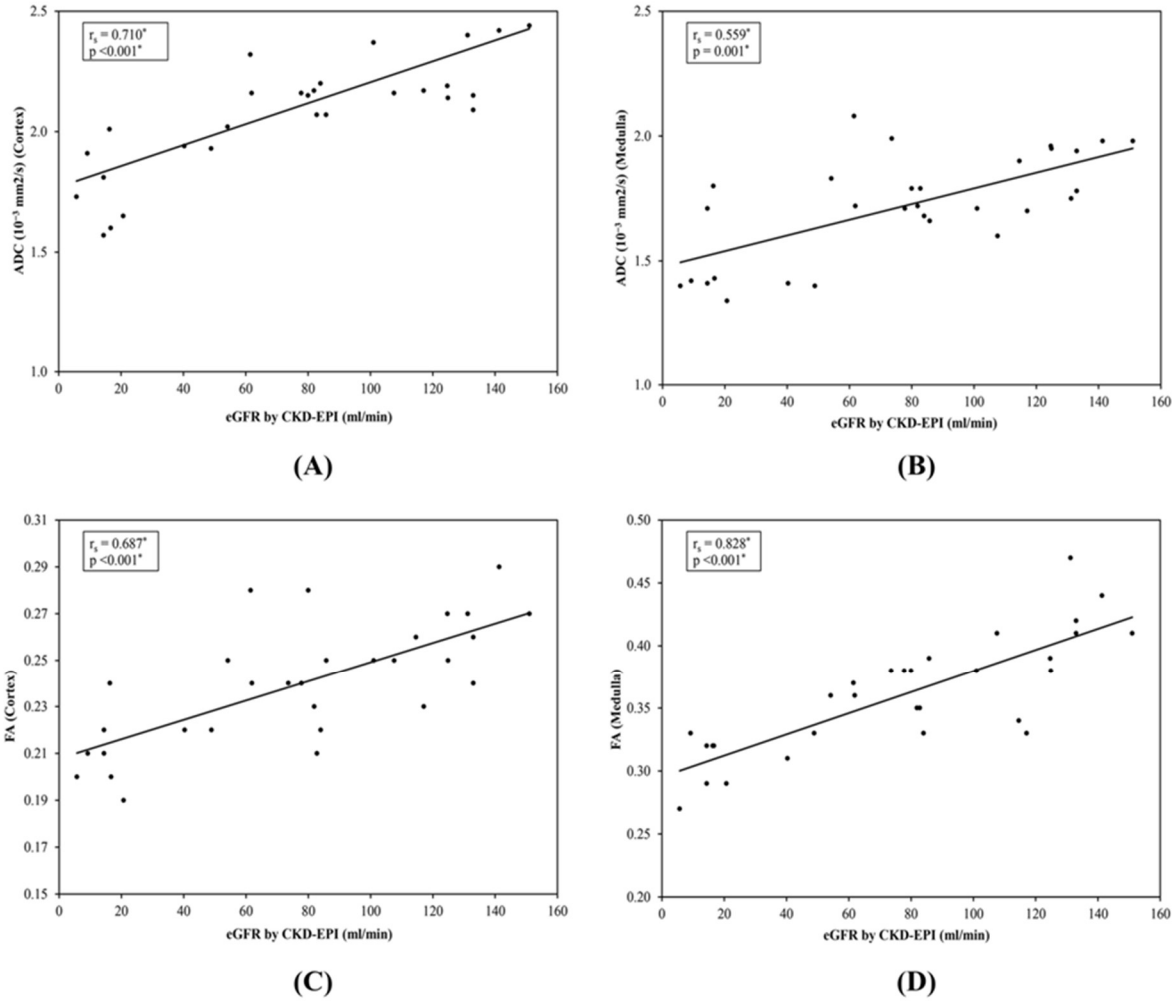

Figure 2: **Scatter plot diagrams showing correlations between eGFR by CKD-EPI in LN patients and different radiological parameters A) with Cortical ADC, B) with Medullary ADC, C) with Cortical FA and D) with Medullary FA. The strongest correlation was with Medullary FA.**

Pathological correlations with different radiological parameters

There were no statistically significant correlations between the pathological activity index and cortical ADC, medullary ADC, cortical FA or medullary FA of the kidneys (p=0.887, p=0.155, p=0.108 and p=0.498 respectively). There were negative statistically significant correlations between the pathological chronicity index and cortical ADC, medullary ADC, cortical FA and medullary FA of the kidneys (r=-0.707, p<0.001, r=-0.595, p=0.001, r=-0.606, p<0.001, r=-0.678 p<0.001 respectively). (**Figure 3**). The strongest correlation with chronicity index among the four measured radiological parameters was with the cortical ADC.

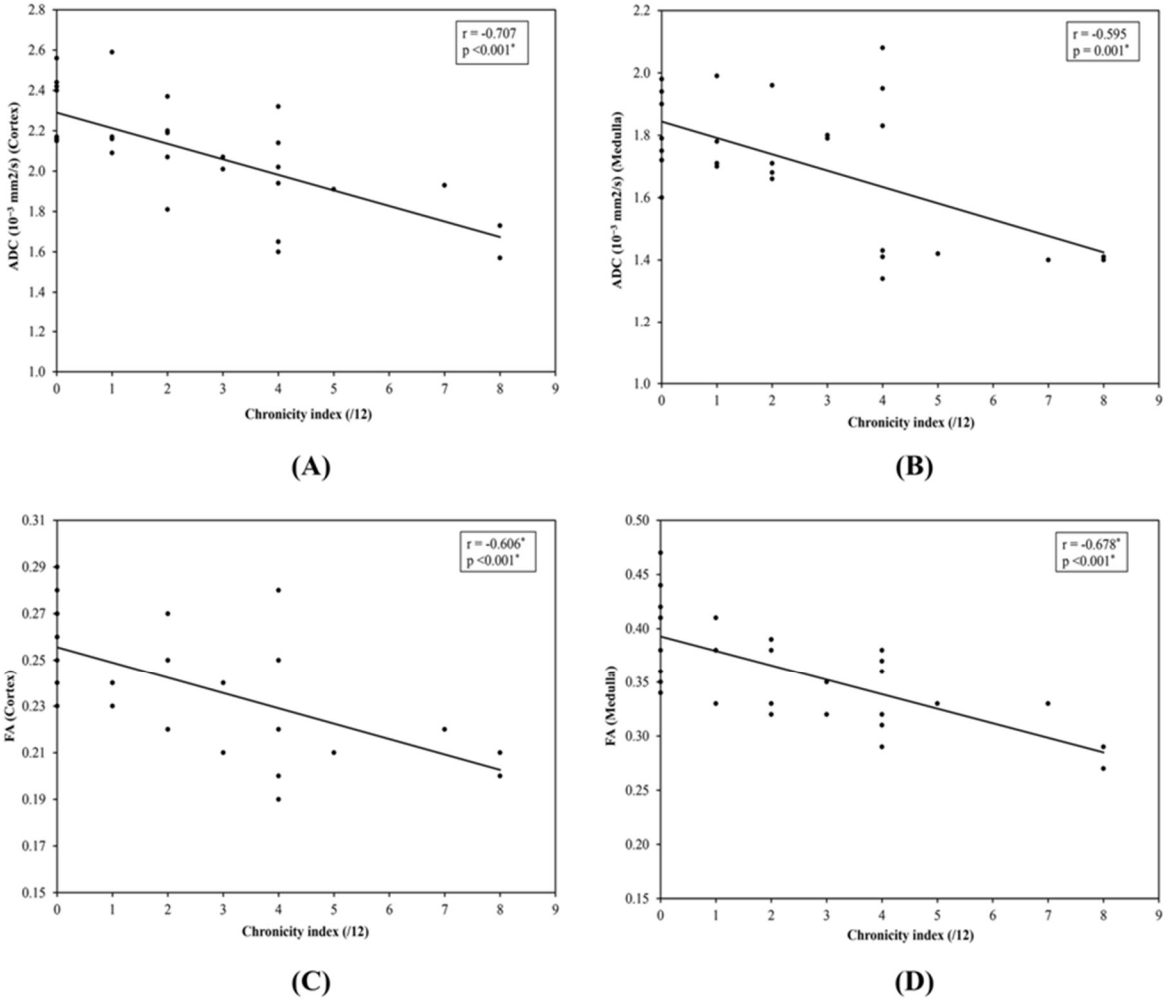

Figure 3: **Scatter plot diagrams showing correlations between the pathological chronicity index in LN patients and different radiological parameters A) with Cortical ADC, B) with Medullary ADC, C) with Cortical FA and D) with Medullary FA. The strongest correlation was with cortical ADC.**

The mean cortical and medullary ADC of the kidneys of patients with interstitial fibrosis score 0/3 were significantly lower than those with score 2/3 ($p<0.001$, $p=0.001$) but not significantly different from those with score 1/3 ($p=0.294$, $p=0.978$). The mean cortical and medullary FA of patients with interstitial fibrosis score 0/3 were significantly lower than those with score 2/3 ($p=0.001$) but not significantly different from those with score 1/3 ($p=0.460$, $p=0.432$). The mean cortical ADC, cortical FA and medullary FA of cases which failed to demonstrate the anti-collagen III antibody stain was significantly higher than cases which stain ≥ 5% ($p=0.003$, $p=0.014$, $p=0.021$ respectively). Nevertheless, the mean medullary ADC was less sensitive as it showed no significant difference between the non-stained cases and those which stain ≥ 5% ($p=0.109$) and it only showed significant difference with cases which demonstrated higher degree of fibrosis (around 10%) ($p=0.007$).

For correlation of LN class with radiological parameters, we divided our patients into 2 groups, non-proliferative group which included classes II and V, and proliferative group which included classes III, IV, III + V and IV + V. The mean cortical and medullary ADC of the non-proliferative group were not significantly different from the proliferative group ($p=0.423$, $p=0.986$). The mean cortical and medullary ADC of the proliferative group were significantly lower than the control group ($p<0.001$, $p=0.022$). The mean Δ ADC of the non-proliferative group was significantly lower than the proliferative group ($p=0.044$), though it was not significantly different from the control group ($p=0.934$). The mean cortical and medullary FA of the non-proliferative group were not significantly different from the proliferative group ($p=0.859$, $p=0.933$). The mean cortical and medullary FA of the proliferative group were significantly lower than the control group ($p<0.001$, $p<0.001$ respectively). These findings should be considered preliminary. (**Table 3**)

Table (3): Relation between LN pathological class and different radiological parameters (n=60)

		Classes II & V (n = 6) (Non-proliferative LN)	Classes III & IV & III+V & IV+V (n = 24) (Proliferative LN)	Control (n = 30)	p
ADC (10^{-3} mm^2/s)	**Cortex**				
	Min. – Max.	1.65 – 2.59	1.57 – 2.44	2.12 – 2.84	<0.001*
	Mean ± SD.	2.22 ± 0.34	2.08 ± 0.24	2.43 ± 0.22	
	Significance between Groups	p_1=0.423, p_2=0.121, p_3<0.001*			
	Medulla				
	Min. – Max.	1.34 – 1.99	1.40 – 2.08	1.62 – 2.09	0.017*
	Mean ± SD.	1.71 ± 0.23	1.72 ± 0.21	1.86 ± 0.17	
	Significance between Groups	p_1=0.986, p_2=0.165, p_3=0.022*			
	Δ ADC				
	Min. – Max.	0.31 – 0.66	0.10 – 0.66	0.26 – 1.13	0.002*
	Mean ± SD.	0.51 ± 0.13	0.36 ± 0.16	0.56 ± 0.22	
	Significance between Groups	p_1=0.044*, $p_2$0.934, p_3<0.001*			
FA	**Cortex**				
	Min. – Max.	0.19 – 0.26	0.20 – 0.29	0.26 – 0.34	<0.001*
	Mean ± SD.	0.24 ± 0.02	0.24 ± 0.03	0.30 ± 0.02	
	Significance between Groups	p_1= 0.859, p_2<0.001*, p_3<0.001*			
	Medulla				
	Min. – Max.	0.29 – 0.41	0.27 – 0.47	0.39 – 0.53	<0.001*
	Mean ± SD.	0.36 ± 0.04	0.36 ± 0.05	0.45 ± 0.03	
	Significance between Groups	p_1=0.933, p_2<0.001*, p_3<0.001*			

p: p value for comparing between the different categories

p_1: p value for comparing between non proliferative LN and proliferative LN

p_2: p value for comparing between non proliferative LN and control group

p_3: p value for comparing between proliferative LN and control group

ROC analysis for prediction of proliferative versus non proliferative LN using mean Δ ADC was done. It showed that in prediction of proliferative LN using a threshold Δ ADC value of ≤ 0.44 × 10^{-3}

mm^2/s, the ROC curve showed an AUC of 0.781, a 95% Confidence Interval (CI) for the area= 0.594 – 0.968, with sensitivity of 66.7% and specificity of 83.3%.

Discussion

Although renal biopsy is mandatory in nearly all cases of LN, there are some conditions in which the biopsy is not feasible as in cases of bleeding diathesis, severe uncontrolled hypertension or patient refusal. Thus, the need arises for a non-invasive marker that could give us an idea about the progress of the disease, the need for treatment intensification or reduction and kidney prognosis. This is extremely valuable especially in cases when we need to repeat the renal biopsy throughout the course of the disease.

DWI is based on thermally induced Brownian motion of water molecules in tissue. The ADC calculation can be used for quantification of the summative effects of capillary perfusion and diffusion. Moreover, ADC measurements obtained by DWI have a scalar property, which means that they reflect only the strength of the diffusion but not its direction. However, diffusion of water molecules is a 3D process having both magnitude and direction. In DTI, diffusion gradients are applied in at least six directions. The directionality of diffusion is expressed as FA values which range from zero to one. Zero means totally scattered diffusion with no specific direction and one means completely anisotropic diffusion in only one direction.(13)

As regards the calculated ADC, the mean ADC values of both the cortex and medulla of the kidneys were significantly lower in the LN group than in the control group. There were positive statistically significant correlations between the ADC values of the cortex as well as the medulla of the kidneys and eGFR. These results were consistent with most of the published studies as Xu(14), Wang(15) and Emre et al(16) who found a linear correlation between the renal ADCs and the stages of CKD. However, Emre had found significant difference between stage 1 CKD and the rest of stages but Xu and Wang didn't.(14-16) Limiting the CKD patients into patients with LN only, our results also agreed with Li(17), Zheng(18) and Shi et al(19) where they found mean ADC values of LN patients significantly lower than healthy volunteers. This could be explained by the fact that all parenchymal diseases of the kidney which cause CKD end in a final common pathway which is glomerulosclerosis, interstitial fibrosis and tubular atrophy. ADC values reflect the movement of water molecules in all directions so it would be hindered by these pathological changes and thus ADC values decrease. (14, 15) Furthermore, renal physiological processes as blood flow in the small vessels and tubular fluid flow are affected in CKD patients whatever the stage and thus could change the ADC values.(20)

With respect to the Δ ADC of the kidneys which is the difference between the cortical and medullary ADC values, there was statistically significant difference between the LN group and control group. This was consistent with the results by Friedli et al(21) who concluded that Δ ADC can discriminate healthy from diseased kidneys in animal models and also in kidney allograft recipients where Δ ADC outperformed ΔT1 for interstitial fibrosis detection.

In view of FA of the kidneys measured by DTI, the mean FA values of both the cortex and medulla of the kidneys were significantly lower in the LN group than in the control group. There were statistically significant differences between both mean cortical and medullary FA of stages 1 and 2

CKD when compared to the control group which could help in early detection of cases of LN. Furthermore, both medullary and cortical FA correlated positively with eGFR and negatively with serum creatinine. Similar results were obtained by Wang et al(15) who found that FA values of both cortex and medulla were lower in CKD patients compared to healthy volunteers. (15) Also, Liu et al(22) who found statistically significant correlation between medullary and cortical FA with eGFR. This agrees partially with Lu(23) and Gaudiano et al(24) who stated that only medullary FA (not cortical) could discriminate between patients with renal impairment and control group. Similar results were deduced in renal allografts as in the studies by Lanzman(25) and Palmucci et al(26). These changes in FA values might be attributed to tubular damage, change in tubular flow, microcirculation and interstitial fibrosis. These processes decrease the number of radially oriented structures and thus diminish the FA values which is more reflected in the medulla.

In view of the pathological parameters, there were negative statistically significant correlations between cortical ADC, medullary ADC, cortical FA, medullary FA and chronicity index. Also, these radiological parameters could discriminate somewhat between different grades of interstitial fibrosis. On the other hand, there were no correlations with the activity index suggesting that the pathophysiological mechanisms that indicate activity such as endocapillary hypercellularity, hyaline thrombi and cellular crescents do not affect the ADC and FA values in a parallel manner compared to those processes which cause fibrosis and glomerulosclerosis. These results are in accordance with the results obtained by Li et al(15), who showed that the renal ADC values correlated negatively with the pathology scores in a heterogenous group of CKD patients. Also studies by Feng(27) and Liu et al(22) both in which showed a significant negative correlation between the percentage of glomerulosclerosis and cortical FA, as well as the degree of tubulointerstitial fibrosis with medullary FA. This is most likely because of multiple pathophysiological mechanisms as tubular atrophy, glomerulosclerosis and deposition of collagen which can directly decrease the diffusion of water molecules, distort the microvasculature and tubular flow leading to a decrease in both ADC and FA values. (27, 28)

The only radiological parameter which showed significant difference between proliferative and non-proliferative LN classes was Δ ADC, though there was no significant difference between the non-proliferative group and the control group. Limited number of studies addressed the use of DWI in distinctive classes of LN. A study by Zheng et al(18) divided LN classes into 3 main groups III, IV and V. Different from what was expected, ADC measurements were lower in the Class III group instead of the Class IV group (known by more aggressive pathological injuries) when compared to the Class V and healthy volunteer groups. Another study by Li et al(15) who divided LN patients into 2 groups: Group A which included 31 patients with LN class III, IV or V, and Group B which included 28 patients with LN class V + III or V + IV. The mean ADC values in Group A were higher than Group B. Our suggested classification into proliferative and non-proliferative LN was of clinical significance as each of them will benefit from different treatment protocols.

Yet there were still some limitations in our study. First, the small number of pathological classes that may not be enough to gain strong evidence when comparing them. Additionally, our study was a cross-sectional one without follow up that could have added to the significance of our results.

Conclusions

DTI is a useful non-invasive tool which could help in assessment of renal impairment in patients with LN. ADC and FA measurements by DTI especially cortical ADC can give an idea about the degree of fibrosis and chronicity of kidneys in LN patients which can influence treatment decisions.

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Research ethics

The research followed the principles of the Declaration of Helsinki. An informed consent was signed from all candidates before the beginning of the study and the research was approved by the Ethics Committee of Faculty of Medicine of Alexandria University (EC serial protocol number 0201165).

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