The Role of Diffusion-Weighted MRI and Apparent Diffusion Coefficient in the Evaluation of Early Renal Allograft Dysfunction

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ABSTRACT:

BACKGROUND:

The most common complication of allografted kidney is renal allograft dysfunction which in some cases results in graft loss, the Diffusion Weighted-Magnetic Resonant Imaging (DW-MRI) and Apparent Diffusion Coefficient (ADC) value may provide a useful insight into the underlying pathology of renal allograft dysfunction.

OBJECTIVE:

To evaluate the utility and diagnostic performance of the DW-MRI and its ADC value in patients with early renal allograft dysfunction.

PATIENTS AND METHODS:

An analytic prospective study was conducted at MRI unit of Al Shaheed Ghazi Al Hariri Teaching Hospital from February 2015 to the end of November 2015, a total of 57 cases were included in this study, they divided in to two groups; control group: including 30 cases with stable or normal renal allograft function and patients group: including 27 cases with early renal allograft dysfunction. All study cases underwent DW-MRI with b value=1000 sec/mm^2. The ADC was reconstructed and mean ADC values were correlated with histopathological biopsy results which is done for all patients group to determine the underlying etiology.

RESULTS:

The mean ADC values of the patients group (1.7±0.2) *10^{-3} mm^2/s were significantly lower (p=0.001) compared with the mean ADC values in the control group (2.2±0.1) *10^{-3}mm^2/s. The cutoff ADC value between the control group and the patients group was (2.06*10^{-3} mm^2/s). According to the morphological appearance in DWI and ADC map we can differentiate acute tubular necrosis (ATN) cases which expressed a heterogeneous appearance/mosaic pattern from acute renal allograft rejection cases and calcinurin inhibiter (CNI) nephrotoxicity cases where both expressed a homogenous morphological pattern.

CONCLUSION:

DW-MR and its ADC were valuable in the assessment of the underlying etiology of early renal allograft dysfunction and there was a Cutoff ADC value between stable or normal renal allograft function cases and early renal allograft dysfunction.

KEY WORDS: renal allograft dysfunction, magnetic resonance imaging, diffusion weighted imaging, apparent diffusion coefficient.

INTRODUCTION:

The most common complication of renal transplantation is allograft dysfunction which in some cases results in graft loss, early deterioration in function of renal allograft and it's a diagnostic and therapeutic challenge. In the early post transplantation period (up to 12 weeks) the allograft dysfunction or abrupt reduction in renal allograft function (within 48 hr) currently define as an absolute increase in serum creatinine of ≥0.3 mg/dl (≥26.4 mmol/l), a percentage of increase in serum creatinine of ≥50% (1.5-fold from baseline), or a decrease in urine output (documented oliguria of less than 0.5 ml/kg/hr for more than 6 hr) [(1)]. The major underlying causes of the early renal allograft dysfunction

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are: acute rejection, which is most common underlying cause, calcineurin inhibiter nephrotoxicity, post renal obstructive uropathy, vascular causes including thrombosis of the renal artery or renal vein, infection (pyelonephritis) and acute tubular necrosis (ATN) [2,3]. The final diagnosis and confirmations will found after renal biopsy, However; the biopsy may be associated with serious morbidity, such as hematuria (up to 40%) that may require transfusion, obstruction of the allograft by clots, hypovolemic shock, arterial injury as arteriovenous fistulae or pseudo aneurysm and intraperitoneal hemorrhage that may lead to graft nephrectomy, together with absolute contraindications of the renal allograft biopsy as uncorrectable bleeding diathesis, uncontrollable sever hypertension, active renal or perirenal infection and skin infection at biopsy site [4, 5]. Diffusion-weighted imaging (DWI) provides quantification of Brownian motion of water protons by calculating the apparent diffusion coefficient (ADC), and can be used for in vivo quantification of the combined effects of capillary perfusion and diffusion.

AIM OF THE STUDY:

To evaluate the utility and diagnostic performance of the DW-MRI and its ADC value in patients with early renal allograft dysfunction.

PATIENTS AND METHODS:

An analytic prospective study was conducted during the period from February 2015 to the end of November 2015, A 57 patients were examined in the Radiology Department at Al Shaheed Ghazi Al Hariri Teaching Hospital- Medical City, we divided them in to two main groups: control group; includes 30 patients with stable or normal renal allograft function and patients group; includes 27 patients with early renal allograft dysfunction. All patients group underwent ultrasound-guided needle biopsy to determine the underlying etiology of graft dysfunction. We included any patient with renal allograft and within the early period (up to three months after renal transplantation) post renal transplantation either with stable or normal renal allograft function or with renal allograft dysfunction (and with allograft biopsy) and we exclude patients with complete vascular obstruction (as complete renal artery obstruction or renal vein thrombosis), patients with urinary obstruction (obstructed hydronephrosis) and patients with pyelonephritis which can be diagnosed with clinical picture and ultrasonography .

All case were underwent clinical examination and B.urea, S.creatinine and ultrasonography were done to them, then they were examined with MRI using Achieva 1.5 tesla scanner Philips Medical system, DW-MRI were obtained in the coronal plane by using a body coil and a gradient multi shot spin-echo echo planar sequence TR 2.4 sec, TE 68 m sec, flip angle 90˚, section thickness 7 mm; intersection gap, 1 mm; FOV(field of view) 375 mm; b-value1000 mm2 /s, ADC maps were derived automatically with the MR system and Calculated ADC values are expressed in square millimeters per second.

The ADC value of the renal allograft is calculated in three circular regions of interest (ROI) measuring 25 mm² for each, placed on upper, mid and lower poles of renal allograft parenchyma for all cases.

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 20, The Chi-square test was used to assess the association between categorical data, Pearson's correlation test was used to assess the correlation between the continuous variables, Receiver operator curves were used to assess reliability values (Sensitivity, specificity and accuracy) as well as calculating cutoff values, P – Value less than 0.05 was used as the alpha level of significance.

RESULTS:

The final diagnose in patients group (27 cases) according to histopathology results were acute renal allograft rejection in 20 cases (74.1%), ATN in 3 cases (11.1%) and CNI nephrotoxicity in 4 cases (14.8%).

1. Morphological evaluation: in control group cases the morphological analysis of DW MRI and ADC map was homogenous (figure: 1) and in patients group cases, the ATN cases express a heterogeneous pattern with multiple patchy /tubular hypo intense areas with mosaic pattern in the DWI and the ADC map (Figure: 2), this may be due to filling the tubules with debris. However, both acute renal allograft rejection (figure: 3) and CNI nephrotoxicity cases (figure: 4) reveal a homogeneous pattern.

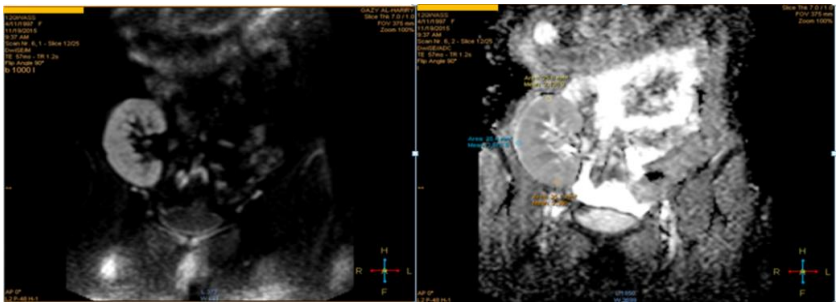

Figure 1: Coronal DWI and ADC for patient with stable or normal renal allograft function, the ADC map showing homogenous pattern with high mean ADC values of the renal parenchyma.

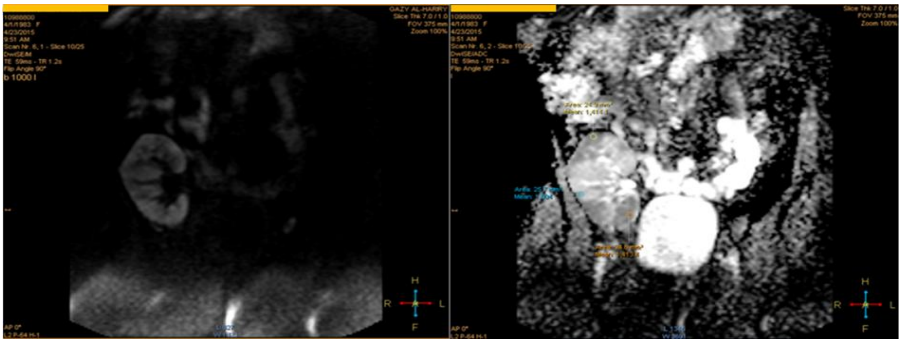

Figure 2: Coronal DWI and ADC for patient with ATN of renal allograft, the ADC map showing heterogeneous/ patchy mosaic pattern with low mean ADC values of renal parenchyma.

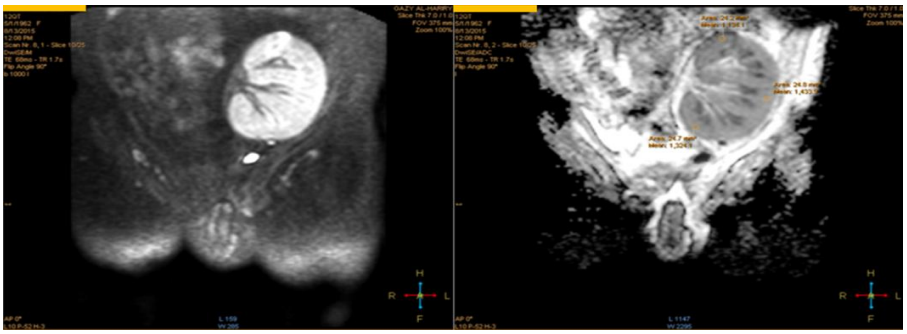

Figure 3: Coronal DWI and ADC for patient with acute renal allograft rejection, the ADC map showing homogeneous pattern with low mean ADC values of renal parenchyma.

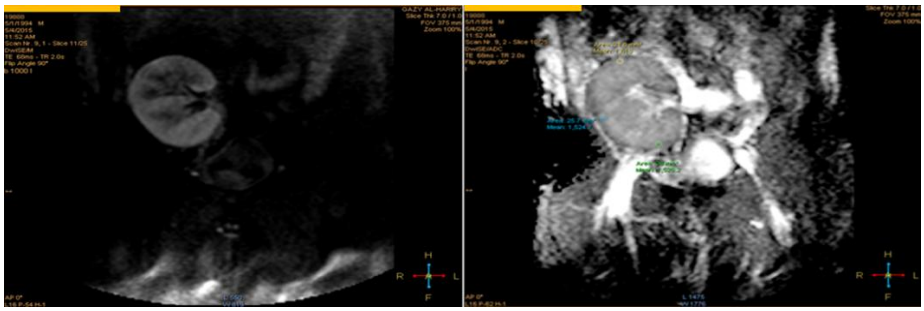

Figure 4: Coronal DWI and ADC for patient with CNI nephrotoxicity of renal allograft, the ADC map showing homogeneous low mean ADC values of renal parenchyma.

2. Quantitative evaluation: The mean ADC value in the upper, mid and lower poles for each case was measured and the results were as follow: in control group; the mean ADC value was (2.2±0.1) $*10^{-3}$ mm^2/s (figure: 1) while in patients group; the mean ADC values was (1.7±0.2) $*10^{-3}$ mm^2/s including ATN cases (1.74±0.48) $*10^{-3}$ mm^2/s (figure: 2), acute renal allograft rejection cases (1.64±0.18) $*10^{-3}$ mm^2/s (figure: 3) and CNI nephrotoxicity cases (1.79±0.06) $*10^{-3}$ mm^2/s (figure: 4). The mean ADC value for patients group was significantly lower compared with control group ($p< 0.001$) (Table: 1), although there were no significant difference between acute rejection, CNI nephrotoxicity and ATN, ($p< 0.353$) (Table: 2).
There was a significant statistical inverse correlation between the mean ADC values with blood urea and serum creatinine levels for all cases included in the study, with correlation coefficient R= -0.619, $p<0.001$ and -0.721, $p<0.001$ (Table: 3) respectively.

Table 1: Comparison of the mean ADC values between control group (n=30) and patients group (n=27).

Parameters	patients (N=27) Mean ±SD	Control (N=30) Mean ±SD	p-value
Mean ADC value/ROI –upper pole	(1.6±0.2) $*10^{-3}$	(2.2±0.1) $*10^{-3}$	<0.001*
Mean ADC value/ROI –middle	(1.7±0.2) $*10^{-3}$	(2.2±0.1) $*10^{-3}$	<0.001*
Mean ADC value/ROI –lower pole	(1.7±0.2) $*10^{-3}$	(2.2±0.1) $*10^{-3}$	<0.001*
average ADC values	(1.7±0.2) $*10^{-3}$	(2.2±0.1) $*10^{-3}$	<0.001*
Student t-test, SD=Standard deviation, * Significant at 0.01 level			

Table 2: Distribution of patients group, according to biopsy and morphological appearance in DWI and ADC map, n=27.

	Morphological appearance in DWI and ADC map		
Biopsy	Heterogeneous/ Tigroid No. (%)	Homogeneous No. (%)	Total No. (%)
ATN	3 (100%)	0 (0%)	3 (11.1%)
Drug toxicity	0 (0%)	4 (16.7%)	4 (14.8%)
Acute rejection	0 (0%)	20 (83.3%)	20 (74.1%)
Total	3 (100%)	24 (100%)	27 (100%)

Table 3: Correlation of the mean ADC value with B. urea and S. Creatinine in different ROI for all cases included in the study.

ADC values	B. Urea (mg/dl) Correlation Coefficient (r)	p-value	S. Creatinine (mg/dl) Correlation Coefficient (r)	p-value
Mean ADC_ROI upper pole	-0.625	<0.001	-0.719	<0.001
Mean ADC_ROI middle pole	-0.630	<0.001	-0.721	<0.001
Mean ADC_ROI lower pole	-0.591	<0.001	-0.709	<0.001
The average ADC values	-0.619	<0.001	-0.721	<0.001
** Correlation is significant at the 0.01 level.				

For the prediction of early renal allograft dysfunction using the DWI, ADC map and the mean ADC value, CI (confidant interval) 95%, the ROC curve for our study showed an AUC of 0.978 (0.951-1), with sensitivity of 96.3%, specificity of 100% and the cutoff ADC value between normal renal allograft function and early renal allograft dysfunction $2.06x10^{-3}$ mm^2/s (table: 4) (figure: 5).

Table 3: The cutoff ADC values and validity measures of the mean ADC values, for different positions and their average, N=57.

Parameters	Cutoff value	AUC (CI 95 %)	sensitivity	specificity	Accuracy	P-value
Mean ADC value /ROI-upper pole	2.04	0.979 (0.956-1)	96.3%	100%	0.982	< 0.0001*
Mean ADC value /ROI-middle pole	2.05	0.977 (0.948-1)	96.3%	100%	0.982	< 0.0001*
Mean ADC value /ROI-lower pole	2.09	0.978 (0.954-1)	96.3%	100%	0.982	< 0.0001*
Average ADC value	2.06	0.978 (0.951-1)	96.3%	100%	0.982	< 0.0001*
*Significant < 0.01 levels						

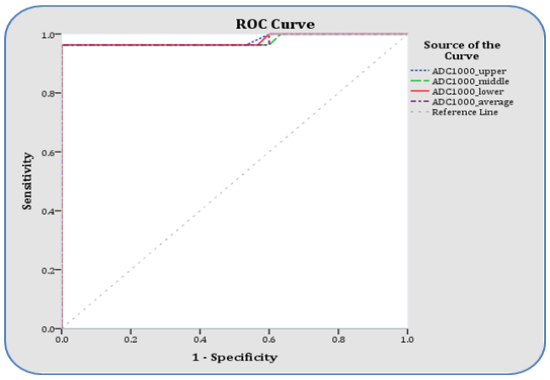

Figure 5: Receiver operator curve for validity measure of the mean ADC values, for different positions and their average, N=57.

DISCUSSION:

Although renal biopsy with histopathological assessment is the gold standard for diagnosing acute graft rejection, it is an invasive procedure and can have serious complications, thus non-invasive tools for detecting acute graft rejection are desirable[6].

In our study we found a significant inverse correlation p<0.001 between the mean ADC values and blood urea levels, the correlation coefficient (r) = -0.619, and between the mean ADC values and serum creatinine levels, correlation coefficient (r) = -0.721; this results agrees with a previous study done by Goyal et al [7] and Liu et al [8] they found a significant inverse correlation between ADC values of renal parenchyma and serum creatinine levels (correlation coefficient r = - 0.530) and similarly, a significant inverse correlation was also observed between ADC values of renal parenchyma and blood urea levels (r = - 0.502).

The mean ADC value in our study for patients group (1.7±0.2 $*10^{-3}$ mm^2/s) was significantly lower than that for control group (2.2±0.1 $*10^{-3}$ mm^2/s) (p<0.001), Similar results have been reported in previous studies done by Abou-El-Ghar et al [6], Liu et al [8], Blondin et al [9], Eisenberger and Thoeny et al [10] and Kaul et al [11] they found that the normally functioning renal allograft express significant higher ADC value (2.2*10^{-3} mm^2/s) compared with lower ADC value (1.9*10^{-3} mm^2/s) for renal allograft dysfunction.

Through our study we found that although all patients group showing low mean ADC value but there was no significant difference (p<0.3) in the mean ADC value between ATN, acute renal allograft rejection and CNI nephrotoxicity cases; which agrees with previous studies done by Abou-El-Ghar et al [6], Eisenberger and Thoeny et al [10] and Thoeny and De Keyzer et al [12].

ATN cases in our study showed a heterogeneous appearance with characteristic mosaic pattern on DWI and ADC map; whereas cases with acute renal allograft rejection and CNI toxicity have homogenous pattern, the CNI toxicity cases can be differentiated from acute renal allograft rejection cases by determining the blood level of the calcineurin inhibitor; this result is in agreement with Abou-El-Ghar et al [6] where they found that ATN appears heterogeneous with a characteristic mosaic pattern resembling the Tiger skin.

The cutoff ADC value between stable renal allograft function (control group) and early renal

allograft dysfunction (patients group) in our study was $2.06x10^{-3}$ mm^2/s; this result is comparable with Abou-El-Ghar et al [6] and Stefano Palmucci et al [13] as they found an ADC value of $2*10^{-3}$ $mm^2/$ s as a cut-off value to differentiate between normal and acutely impaired grafts.

CONCLUSION:

DW-MR and ADC are useful in the evaluation of early renal allograft dysfunction this will help to reduce the need for invasive ultrasound-guided biopsy, which has a high-risk of complications. There was a Cutoff ADC value between stable or normal renal allograft function and early renal allograft dysfunction. the ADC map (morphology) can differentiate ATN cases which express a mosaic pattern while cases of acute allograft rejection and CNI nephrotoxicity showing homogenous morphology, the CNI nephrotoxicity cases can differentiated from acute renal allograft reject cases by laboratory estimation of CNI level in the blood.

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DIFFUSION-WEIGHTED MRI AND APPARENT DIFFUSION COEFFICIENT