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Review Article

ROLE OF MRI CORTICOMEDULLARY DIFFERENTIATION IN THE ASSESSMENT OF RENAL POST TRANSPLANTATION COMPLICATIONS

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Abstract

Objective: To evaluate MR features of renal corticomedullary differentiation in the assessment of renal allograft complications.

Patients and Methods: Ten individuals with normal renal functions as a control group and thirty patients with post transplantation complications underwent MR examination. The signal intensity of the cortex and medulla were measured on coronal plane and the corticomedullary contrast (CMC) was calculated according to the equation:

$$\%CMC = \frac{SI(cortex) - SI(medulla)}{SI(cortex) + SI(medulla)}$$

Results: All the patients with acute rejection showed loss of the corticomedullary differentiation CMD with a negative corticomedullary contrast CMC%, with sensitivity 75%, specificity 31%, positive predictive value 11% and negative predictive value 92%.

One of the 2 cases with acute tubular necrosis (ATN) showed a decreased CMD with a CMC% of 6% and the other one showed a negative CMC% of -3%, having sensitivity 100%, specificity 36%, positive predictive value 15% and negative predictive value 100%.

The cases with cyclosporine toxicity (Cs T)showed a wide variability in their CMD, where 40% showed normal CMC% of >9%, 17% showed a decreased CMD ranging between 0-9% and 43% showed loss of CMD. The MR assessment by this modality showed sensitivity 63%, specificity 28%, positive predictive value 18% and negative predictive value 75% detecting this type of medical complication.

On the other hand, all patients with chronic graft rejection (CGN) showed decreased CMD ranging from 0-9%, with sensitivity 100%, specificity 32%, positive predictive value 7% and negative predictive value of 100%.There was a statistically significant decrease in the CMD seen in patients with chronic allograft rejection and those of the controls (p=0.02).

Conclusion: Alteration in MRI corticomedullary differentiation can be pointer for impairment of renal function in renal allograft assessment, it is a sensitive but nonspecific indicator of renal disease.

Keywords: Renal allograft complications, MRI corticomedullary differentiation

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INTRODUCTION

The renal allograft complications comprises medical functional, vascular and urological complications as well as perinephric collections.(1)

Medical functional complications after renal transplantation include acute rejection(AR), acute tubular necrosis (ATN), cyclosporine toxicity(CsT) and chronic graft rejection(CGR).(2)

Various modalities are used for evaluation of the transplanted kidney, ultrasound, Doppler, Radioisotope imaging and MRI. Ultrasound is mainly used for assessment of morphological changes, Doppler for vascular changes, Radioisotope for functional changes, while MRI can be used as one stop imaging technique for assessment of all complications of the transplanted kidney(3).

MR advantages comprise Superior contrast resolution, multiplanar capability, lack of operator dependence, different applications including MRA and MRU., evaluation of renal function through perfusion studies which provides morphological and functional data(4).

On magnetic resonance imaging (MRI) T1-weighted images (TI WI), the cortex in a healthy kidney is easily differentiated from the medulla, a trait known as corticomedullary differentiation (CMD). This difference in tissue contrast on T1 WI results from the shorter T1 relaxation time of the cortex relative to the medulla, attributed mainly to differences in water content between the two tissues, causing the cortex to appear hyperintense compared to the medulla(5)&(6).

This study aimed to evaluate MR features of renal corticomedullary differentiation in the assessment of renal allograft complications.

PATIENTS AND METHODS

Patients

Control group of 10 patients with normal renal allografts and normal renal functions together with thirty patients with post transplantation complications subjected to different imaging and laboratory investigations. Complain was mainly deteriorating renal function, (23 patients) or other reasons as pain, swelling at the site of the graft, fever or hypertension (7 patients) all were subjected to MRI of the renal allograft to assess corticomedullary differentiation.

MR Imaging Examination protocol

MR Imaging Examination

MR imaging was performed on a 1.5T MR system (Philips) operating at 1.5T using a body coil. An axial, coronal and sagittal T1WI locator was performed upon which the rest of the examination was planned, as follows:

(a) T1 weighted images of the pelvis (from the level of the upper border of the renal graft down to the urinary bladder neck) by use of a non-fat suppressed magnetization gradient echo technique (TR/TE/slice thickness/n = 600/19/10mm/15) in the

coronal plane, and matrix size was 128x128; T1 fat sat SSFP with IR pulse.

- (IR) pulse can emphasize subtle differences in T1 values between the renal cortex and medulla. A series of topographically identical SSFP sequences with selective IR pulse were performed. Using variable inversion times (TI) (700, 800, 900, 1000, 1100, 1200, 1300, 1400, and 1500 msec).

(b) T2 weighted images (planned on the coronal images) by means of the fast spin echo technique (TR/TE/slice thickness/n = 1600/100/10mm/25) in the axial plane.
(c) Post processing work-up was done either using the MR machine or by using a separate workstation.

MRI Data analysis
Morphological evaluation
Measurement of the renal size (longitudinal, anteroposterior, transverse and parenchymal thickness) the signal intensity of the sinus fat, the size of the collecting system and the presence of focal parenchymal changes were assessed on the baseline T1 and T2 weighted images.

The signal intensity of the cortex and medulla were measured on the coronal scans and the corticomedullary contrast (CMC) was calculated according to Marotti proposed equation:

$$\%CMC = \frac{SI(cortex) - SI(medulla)}{SI(cortex) + SI(medulla)}$$

Optimal TI was defined as TI showing the highest corticomedullary contrast ratio among serial SSFP images.

The signal intensity data for each region of interest at 78 consecutive points were acquired in a spread sheet format. Mean signal intensity values for each group (normal and different types of complications) for these 78 points were computed and plotted

against time using the graphics module of Microsoft excel software. Comparison between peak signal intensities (Amax) was made for analysis.

The results were correlated with histopathological biopsy results in the twenty patients with suspected medical renal complications, the other vascular and urological complications as well as perirenal collections were diagnosed by different imaging techniques.

Statistical Analysis
All values are expressed as means ± standard deviation (SD).
Data were analyzed by use of Student t test analysis, correlations
For data analysis the patient population was divided into two groups: the normal control group and the group with different renal transplant complications.
All variables that were statistically significant if p≤0.05 level and r>0.3 were included in our final analysis.

RESULTS
Ten individuals with normal renal allografts as a control group (6 males and 4 females) and thirty renal transplant recipients with different types of complications were examined by MRI examination (20 males and 10 females), with a mean age of 40 ± 11 years.

Table (1) shows sizes of the renal allograft in control group and patients with graft complications.

Table (1): Sizes of renal allografts (in cm) by MRI in normal control group and patients with graft complications.

	longitudinal	AP	Transverse	Parenchymal Thickness
Normal (n=10)	11±1.3	4.7±0.6	5.1±0.3	1±0.2
Medical Renal complications (n= 20)				
AR(acute rejection) (n=5)	12.6	5.2	5.8	1.3
Cs T(cyclosporine toxicity) (n=8)	11.6	5.7	6.4	1.46
CGN(chronic graft nephropathy) (n=4)	10.9	5.8	6.5	1.25
ATN(acute tubular necrosis) (n=2)	13.8	5.8	5.8	1.25
Transplant glomerulopathy (n=1)	13	5.5	6	1.5
Vascular Complications (n=4)				
RAS(renal artery stenosis) (n=1)	12	5	6	1.2
Graft AVF(arteriovenous fistula) (n=1)	11	7	6.5	1.5
Cortical infarct (n=1)	11.75	5	5.25	1
Dissection (n=1)	12	5	6	1.5
Urological complications (n=4)				
PCS dilatation (n=2)	11.5	5	5.55	1
Stones (n=2)	11.5	4.75	5.5	1.25
Perinephric collections (n=2)	11.3	4.9	5.8	1.1

According to the student *t* test, the renal grafts with acute rejection had a significantly larger longitudinal diameter than those seen in the controls (p= 0.005), those with cyclosporine nephrotoxicity (p= 0.036) and those with chronic allograft nephropathy (p=0.0039)

The renal allografts with cyclosporine toxicity were significantly smaller than those with acute tubular necrosis (p=0.003), while those with chronic graft nephropathy were significantly smaller in size than those seen in ATN (p=0.002).

Table (2): Calculated MRI %CMD in the normal renal graft function and different types of graft complications.

	Number	Corticomedullary Differentiation		
		Normal	Decreased	Absent
Normal renal graft	10	100%	0%	0%
Medical Renal complications (n=20)				
Acute rejection	5	0%	0%	100%
Cyclosporine Toxicity	8	40%	17%	43%
Chronic graft nephropathy	4	0%	100%	0%
Acute tubular necrosis	2	0%	50%	50%
Hypertrophic glomerulonephritis	1	0%	0%	100%
Vascular Complications (n=4)				
Renal Artery Stenosis	1	0%	0%	100%
Graft AVF	1	0%	0%	100%
Cortical infarcts	2	100%	0%	0%
Aortic & iliac dissection	1	0%	0%	100%
Urological Complications (n=4)				
hydronephrosis	2	100%	0%	0%
Stones	2	100%	0%	0%
Perirenal graft collections	2	25%	50%	25%

Table (3) shows the sensitivity, specificity and predictive values of the measurement of CMD by MRI in the different medical complications:

Disease	Sensitivity	Specificity	+ve predictive value	-ve predictive value
AR (n=5)	75%	31%	11%	92%
CAN (n=4)	100%	36%	15%	100%
CsA T (n=8)	63%	28%	18%	75%
ATN (n=2)	100%	32%	7%	100%

There was a statistically significant decrease in the CMD seen in patients with chronic allograft rejection (p=0.02).

There was a statistically significant negative correlation between the corticomedullary differentiation measured by MRI and the cortical thickness of the renal grafts when measured by conventional MRI (r=-0.45).

The MRI appearance of the patients with ATN could not be differentiated from that seen in cases with acute rejection.

Given that only single patient with post transplantglomerulopathy was incorporated in this study, this case was expelled from further statistical analysis. Fig (1)

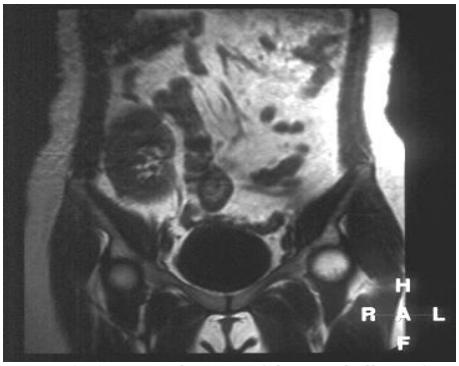


Fig. (1a): Coronal T1WI of the renal allograft (normal).

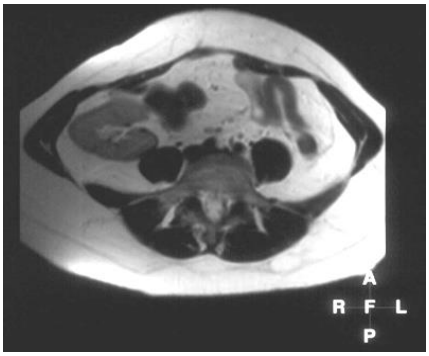
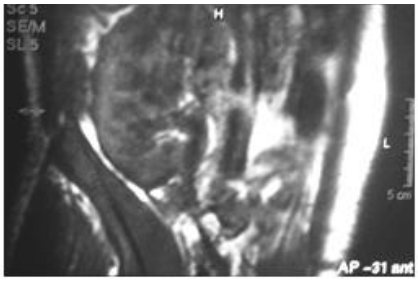


Fig. (1b):Axial T2WI of the renal allograft (normal)

The corticomedullary differentiation measured was: $\frac{(1435-970)}{(1453+970)}=19\%$; one of the control group. Fig (2)



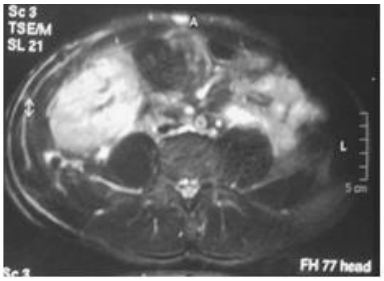


Fig. (2a): Coronal T1W1 Fig. (2b): Axial T2W1

Showing graft in the right iliac fossa with average size and diminished corticomedullary differentiation.
The corticomedullary measured was; $\frac{(980-1050)}{(980+1050)} = -3\%$. the biopsy showed Massive intracapillary glomerular thrombosis (Cs toxicity) with normalization of the renal function after reduction of the cyclosporine A dose Fig. (3)

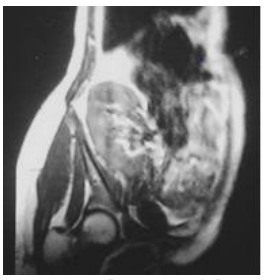
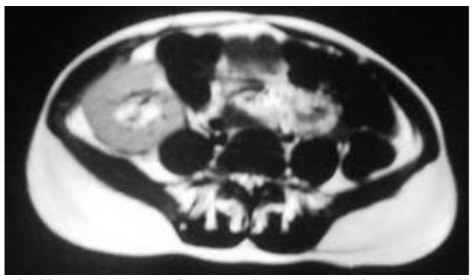
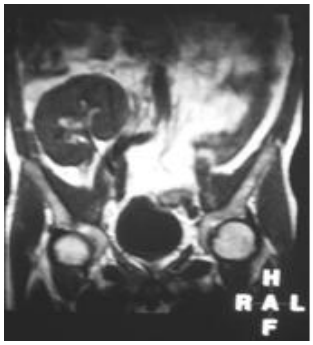



Fig. (3a): Coronal T1W1 of the renal allograft Fig. (3b): Axial T2W1 of the renal allograft showing diminished corticomedullary differentiation

The corticomedullary differentiation measured was $\frac{(620-670)}{(620+670)} = -4\%$. ; the biopsy showed acute rejection of the graft Fig (4)



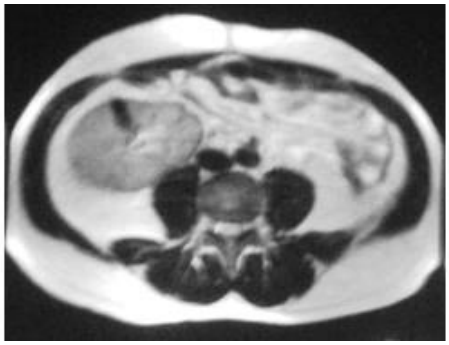


Fig. (4a): Coronal T1W1 of the renal allograft Fig. (4b): Axial T2W1 of the renal allograft

Showing dilated tortuous signal void areas noted of the cortical region of the renal graft suggestive of a renal AVF
The corticomedullary differentiation measured was $\frac{(1140-1080)}{(1140+1080)} = 3\%$; final diagnosis by biopsy and imaging is chronic graft rejection with renal AVF

DISCUSSION

The kidney is the most frequently transplanted organ. Advances in surgical methods, immunosuppression courses of therapy, scrutiny imaging, and histopathological conclusion of rejection have permitted prolonged graft survival times. On the other hand, the requirement for kidneys continues to outgrow the obtainable supply, and there is hard work to increase use of donor kidney with moderate or high-risk profile (7).

This declares importance of assessing the renal transplant patient in perspective of both donor and recipient risk factors. In the situation of allograft dysfunction, advanced imaging techniques including MRI may be of help for giving more specific diagnosis and ruling out non rejection causes of renal dysfunction (8)&(9).

Our study showed that the renal grafts with acute rejection had a significantly larger longitudinal diameter than those seen in the normal functioning renal allografts (p= 0.005), those with cyclosporine nephrotoxicity (p= 0.036) and those with chronic graft rejection (p=0.0039).

The renal allografts with cyclosporine toxicity were significantly smaller in size than those with acute tubular necrosis (p=0.003), while those with chronic allograft nephropathy were significantly smaller in size than those seen in ATN (p=0.002).

By this we can demonstrate that the smallest sized renal allografts were seen in cases of chronic allograft nephropathy while the largest were seen in cases with ATN. There was no significant difference in the characteristics of the renal sinus fat in the studied cases.

In normal kidney, non contrastSSFP MRI with spatially selective IR pulse can be used to assess renal corticomedullary differentiation and cortical thickness without the influence of aging(10)

The cortical and medullary parts of normal renal parenchyma could be differentiated by MR imaging. They found that on T1WIs of normal functioning kidney the signal intensity of the cortex was higher than the medulla, but lower than the renal sinus. This was attributed to greater free water content of the medulla. It was also marked that T1WIs were better than T2WIs in differentiating cortical and medullary parts of the transplanted kidney.

Kanki et al(11), concluded that SSFP MRI with Time-SLIP can advance renal corticomedullary differentiation without using contrast agents.

Significantly rejecting transplants have uniformly demonstrated sharply diminished or absent CMD. Diminished CMD is nonspecific for rejection as it has been reported to occur in several pathologic states including chronic renal insufficiency, obstructive hydronephrosis, and dehydration. The appearance of transplants undergoing ATN is somewhat controversial. Although some studies show transplants with ATN to have relatively preserved CMD, other reports have demonstrated a more variable pattern including many cases of ATN with sharply diminished CMD. The discrepancy in findings may be due to variability in criteria for diagnosis, variability in the severity of ATN seen in the different series, the presence of simultaneous processes affecting CMD distinction, the level of hydration, and variability in scanners and scan technique.

On the other hand, transplants with cyclosporine nephrotoxicity have generally shown preserved CMD.

In the current study, All the patients with acute rejection showed loss of the corticomedullary differentiation CMD with a negative corticomedullary contrast CMC%, with sensitivity 75%, specificity 31%, positive predictive value 11% and negative predictive value 92%.

One of the 2 cases with acute tubular necrosis (ATN) showed a decreased CMD with a CMC% of 6% and the other one showed a negative CMC% of -3%, having sensitivity 100%, specificity 36%, positive predictive value 15% and negative predictive value 100%.

The cases with cyclosporine toxicity (Cs T)showed a wide variability in their CMD, where 40% showed normal CMC% of >9%, 17% showed a decreased CMD ranging between 0-9% and 43% showed loss of CMD. The MR assessment by this modality showed sensitivity 63%, specificity 28%, positive predictive value 18% and negative predictive value 75% in detection of this type of medical complication.

On the other hand, all patients with chronic graft rejection (CGN) showed decreased CMD ranging from 0-9%, with sensitivity 100%, specificity 32%, positive predictive value 7% and negative predictive value 100%.There was a statistically significant decrease in the CMD seen in patients with chronic allograft rejection and those of the controls (p=0.02).

Given the now possible prolonged survival period for renal transplant recipients, it is more and more essential to innovate non-invasive techniques of screening these patients and evaluating their symptoms or signs of complications.

Noda et al(13), investigated 65 patients with and without chronic kidney diseases (CKD). They separated the patient according to the eGFR, into three groups. (Group 1, eGFR less than 60; Group 2, eGFR equals 60-90; and Group 3, eGFR more than 90). All patients performed non contrast SSFP MRI with spatially selective IR pulses and minimal renal cortical thickness was measured. The mean corticomedullary contrast ratio was significantly higher in SSFP images with optimal TI than in in-phase images in all three groups ($P = 0.001$). Positive connection was seen between the corticomedullary contrast ratio in SSFP images with optimal TI and eGFR ($P = 0.011$, $r = 0.314$). A significantly positive association was observed between minimal renal cortical thickness and eGFR ($P < 0.01$, $r = 0.495$). it was concluded that non contrast-enhanced SSFP MRI with a spatially Otsuka et al (12), correlated morphological parameters of the Kidney measured with SSFP MRI with the kidney function in patients with CKD, including those with sever kidney dysfunction.

selective IR pulse using optimal TI can improve the visibility of renal corticomedullary differentiation even in patients with renal insufficiency. The decrease in renal cortical thickness measured using this technique correlated significantly with eGFR.

CONCLUSION

Alteration in MRI corticomedullary differentiation could be pointer for impairment of renal function in renal allograft assessment, it is a sensitive but nonspecific indicator of renal disease.

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