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MAG3 Renogram Deconvolution in Kidney Transplantation: Utility of the Measurement of Initial Tracer Uptake

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The study of renal retention function by deconvolution analysis of renographic curves is useful to calculate quantitative parameters in renal studies. The aim of the work is to evaluate the usefulness of ^{99m}Tc-MAG3 renogram deconvolution in renal function monitoring of kidney graft recipients. **Methods:** Forty-three kidney grafts and 112 renograms were studied: 41 were diagnosed as functioning graft, 35 as acute tubular necrosis, 24 as acute rejection, 8 as obstruction and 4 as cyclosporin toxicity. The parameters calculated were mean transit time (MTT), time at 20% of renal retention function (T20) and initial uptake (IU). **Results:** MTT and T20 were significantly longer in obstructives than in functioning grafts ($p < 0.001$). Initial uptake was significantly lower in acute tubular necrosis (ATN) and acute rejection ($p < 0.001$) and in obstructives ($p < 0.05$) than in functioning grafts. The joint evaluation of MTT and IU allowed to diagnose cases with graft function severely impaired. **Conclusion:** Initial uptake is useful in evaluating post-transplantation complications and in combination with MTT and T20 reflects renal dysfunction severity.

Key Words: renal transplantation; technetium-99m-MAG3; deconvolution analysis

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Dynamic renal scintigraphy is routinely applied in most nuclear medicine departments to study renal transplants (*1*). The technique is accurate for the functional evaluation of kidney function and is a useful tool for clinicians in the postoperative follow-up of transplanted patients (*2,3*). Since its introduction in 1987, the use of mercapto-acetyl-triglycine (MAG-3) labeled with ^{99m}Tc has increased and progressively replaced ^{131}I-OIH and ^{99m}Tc-DTPA as tracer for renal functional studies.

Several different parameters are used to follow the kidney's progress. This fact suggests that there is not one that is ideal. Nevertheless, it can be agreed that to determine the intrarenal kinetics and to calculate quantitative parameters, the study of the renal retention function (RRF) is useful. The RRF is calculated by deconvolution analysis of the renographic curves (*4*). There is little experience in deconvolution in renal transplanted patients (*5–7*) and even less with ^{99m}Tc-MAG3 (*8*).

In 1992, we developed a deconvolution method for MAG3 renography, for which initial results in normal volunteers and functioning kidney grafts were promising (*9*). The aim of this work was to study the usefulness of that deconvolution method with ^{99m}Tc-MAG3 in kidney graft monitoring. We evaluated the RRF derived parameters: initial uptake (IU) and two transit times of the tracer: mean transit time (MTT) and time at 20% of the RRF (T20). We analyzed if they reflect the graft function accurately and also compared the RRF with the effective renal

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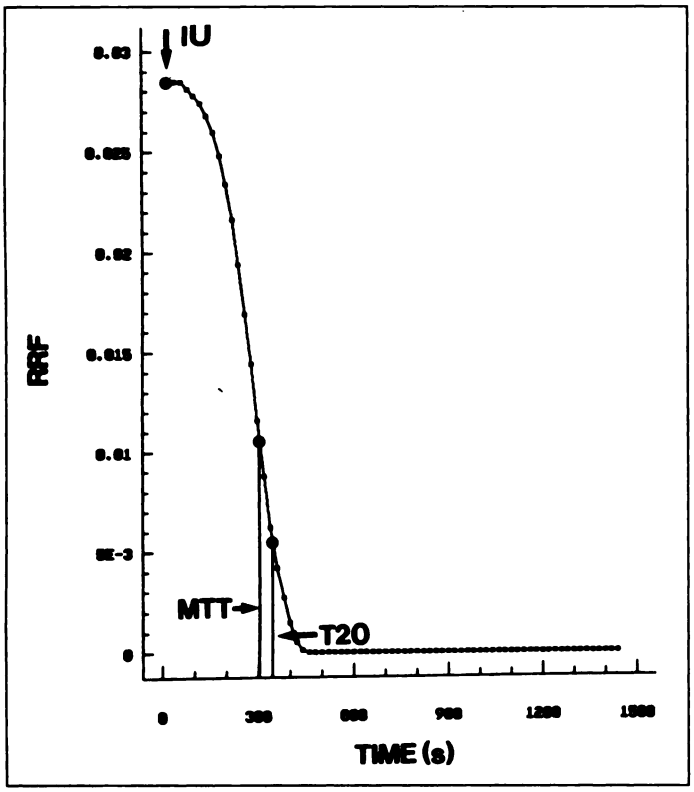

FIGURE 1. Graphic representation of MTT, T20 and IU calculation.

plasma flow (ERPF) (measured with ^{131}I-OIH) and with the serum creatinine values.

MATERIALS AND METHODS

We studied 43 kidney graft recipients (22 men, 21 women; range 15–63 yr; mean age 41 yr). All patients were referred for renogram studies and underwent transplantation between 24 hr and 6 mo before the study began. One hundred-twelve renogram studies were obtained and analyzed.

Patients were categorized into five groups including:

1. Functioning graft (FG) (n = 41). Patients with adequate diuresis, without clinical signs of rejection on the day of study or the following week and serum creatinine <200 mmol/liter.
2. Acute tubular necrosis (ATN) (n = 35) was diagnosed on the clinical and biochemical requirement of hemodialysis, absence of rejection signs and clinical and renographic improvement after only supportive therapy. In some cases, graft biopsy was also obtained.
3. Acute rejection (AR) (n = 24). Diagnosis was always based on histological data, and only the exams performed before rejection treatments began were included.
4. Obstruction (OBS) (n = 8). Ultrasonography demonstrated the urinary tract dilatation, and subsequently obstruction was the clinical diagnosis.
5. Cyclosporin toxicity (CTX) (n = 4) was diagnosed by exclusion of other diagnoses. The presence of high serum levels of CyA as well as renal function recovery and clinical improvement after cyclosporin withdrawal were the main criteria (*10*).

The diagnosis was established by the nephrologist without knowledge of deconvolution results.

A basal study performed within 24–72 hr of kidney transplantation was initially obtained and follow-up examinations were obtained when required, depending on the clinical evolution. In 18 patients, a study was made 3 mo post-transplantation at the time of a control kidney graft biopsy.

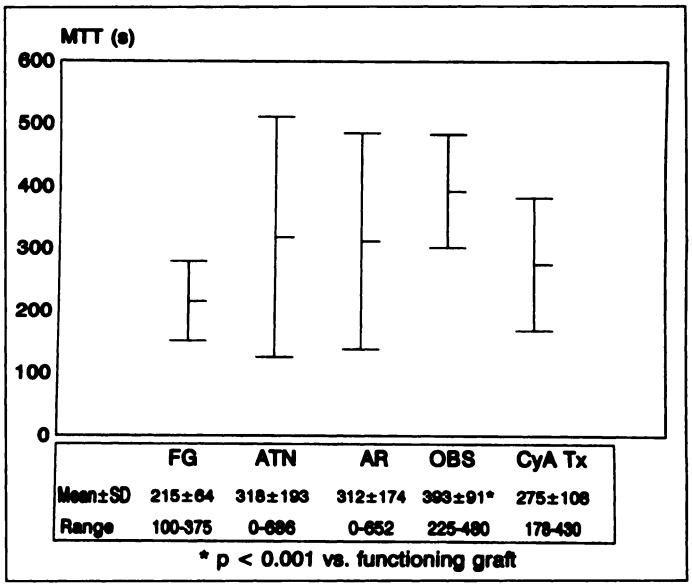

FIGURE 2. Mean ± 1 s.d. and range of MTT.

Renograms were obtained in anterior view, using a large field of view gamma camera fitted with a 140 KeV, LEAP collimator positioned over the patient in the supine position. A bolus of 222–259 MBq ^{99m}Tc-MAG3 was injected intravenously into an antecubital vein. During 24 min, 114 frames were recorded: a first group at 2.5 sec intervals for 120 sec, followed by a second group of 66 frames at 20 sec intervals. At the same time, in the contralateral antecubital vein, 1.85 MBq of ^{131}I-OIH was injected to calculate the ERPF. The ERPF was measured using the three blood samples method (7, 17 and 30 min) used routinely in our institution as previously published (*11*). Regions of interest (ROIs) were defined for the whole kidney, abdominal aorta (before aortic bifurcation) and background (graft mirror in the contralateral iliac fossa, avoiding vascular and urinary tract structures if present). By deconvolution analysis of renal output (renogram curve) with renal input (aortic curve), the renal retention function was obtained. The deconvolution method used was developed in our department (*9*). It is based on the matrix algorithm and uses a three-point linear filter (1:2:1).

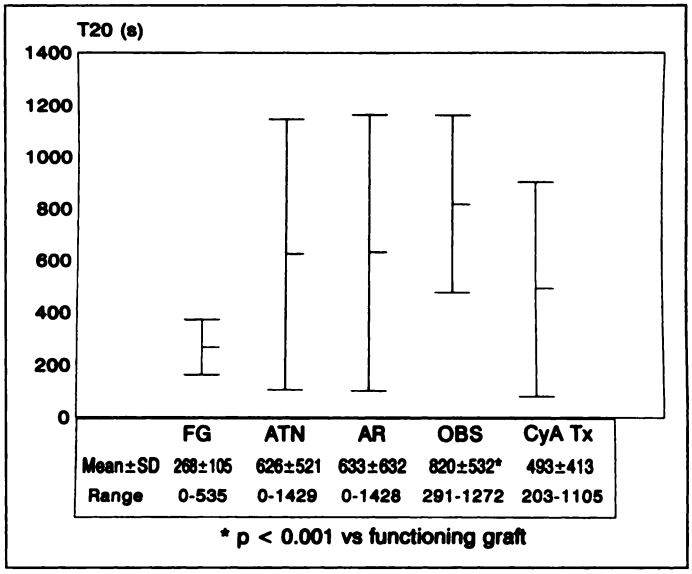

FIGURE 3. Mean ± 1 s.d. and range of T20.

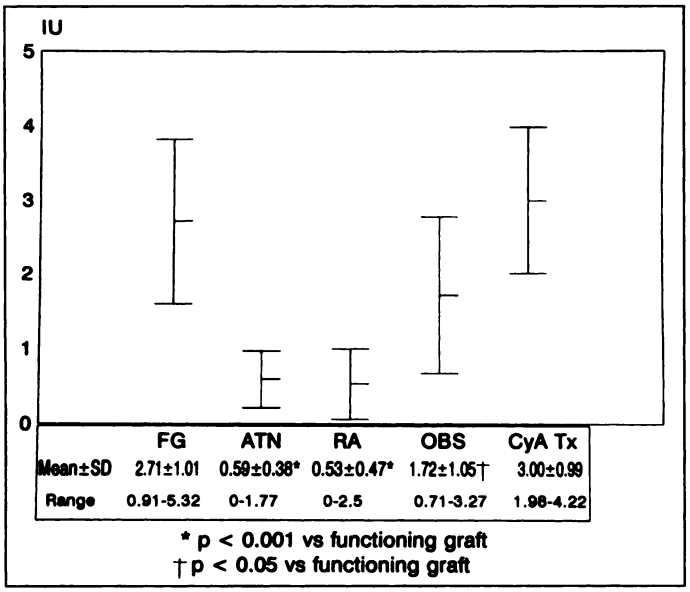

FIGURE 4. Mean ± 1 s.d. and range of IU.

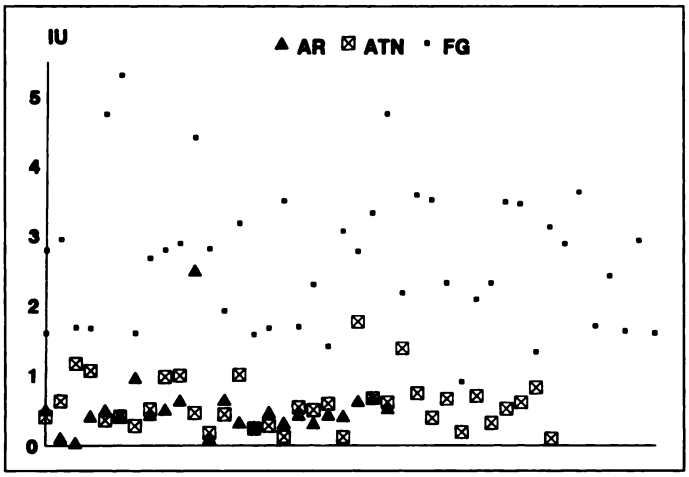

FIGURE 5. Distribution of IU in FG, ATN and AR. The cutoff value for IU is 1.6.

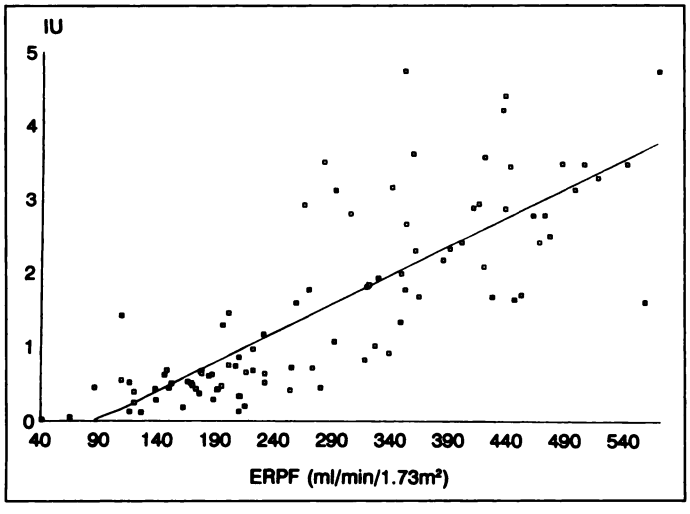

FIGURE 6. Significant correlation was found between ERPF and IU (n = 98, r = 0.73, p < 0.01).

From the RRF, the following parameters were calculated: the MTT, or the average time that the tracer stays in the kidney, was calculated by dividing the area under the RRF by the first value of the curve (H_0); T20, or the time at 20% of the maximum height of the RRF (H_0); IU, or retention at zero time (H_0), multiplied by 100 (Fig. 1).

Statistical significance of differences between groups was determined by U Mann-Whitney test. The correlation between IU and ERPF and serum creatinine was calculated by the Pearson Coeficient.

RESULTS

Figures 2, 3 and 4 show mean ± s.d. of MTT, T20 and IU in the groups studied.

MTT and T20 were prolonged in all groups in relation to functioning grafts. Nevertheless, differences were statistically significant only with obstructed kidneys ($p < 0.001$). IU was significantly lower in ATN ($p < 0.001$), AR ($p < 0.001$) and

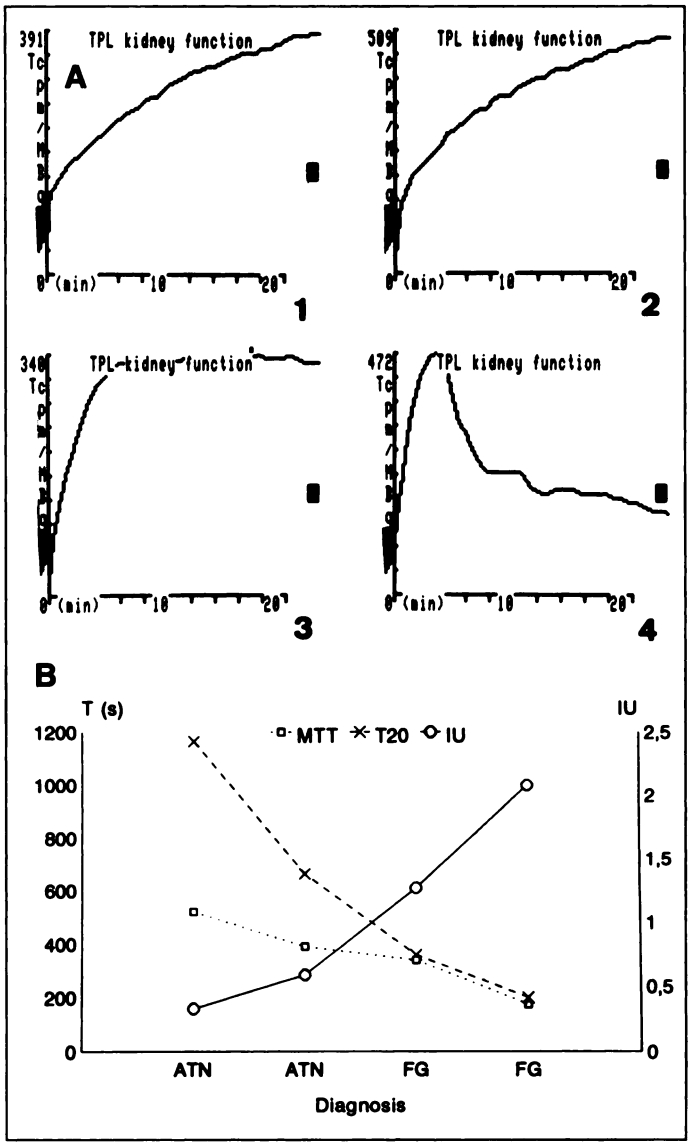

FIGURE 7. Clinical evolution of a 44-yr-old patient who received a renal graft. (A) Renograms with ^{99m}Tc-MAG3 of the four studies performed on this patient. (B) RRF parameters evolution. The first study was performed within 24 hr of kidney transplantation, reflecting an ATN in the renogram and the RRF. The second study was performed 7 days later on the following day of the last hemodialysis session. The third study was performed 9 days posthospital discharge. Renogram and RRF improve remarkably.The fourth study was performed 2 mo later. Renogram and RRF were normal.

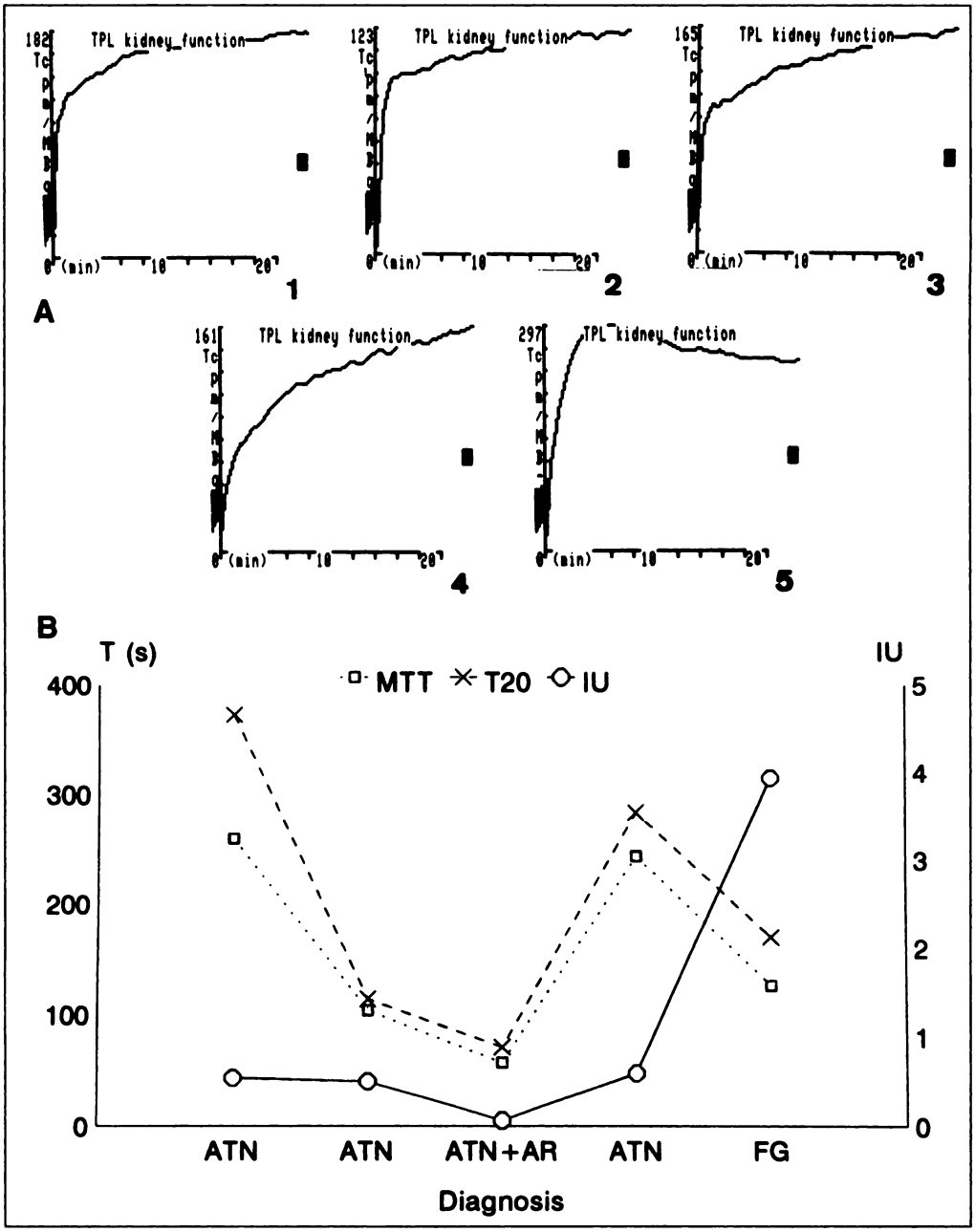

FIGURE 8. Serial studies of a 49-yr-old patient who suffered an ATN and AR mixed. (A) Renograms with ^{99m}Tc-MAG3 of the five studies performed on this patient. (B) RRF parameter evolution. The first study reflects an ATN in the renogram and in the RRF on the first day post-transplantation. In the second study, 7 days later, renogram has not changed, but MTT and T20 have decreased below the normal range. In the third study, 3 days later, renogram continued without change and RRF parameters became still shorter. A biopsy shows severe ATN and AR, and the patient receives specific treatment the following day. In the fourth study, 7 days later, the renogram is similar to the previous ones. RRF parameters increased. After 4 days urine production began. In the fifth study, 3 mo later, renogram improves notably, and RRF parameters were within the normal range.

OBS ($p < 0.05$) than in functioning grafts. There were no significant differences between ATN and AR. In functioning grafts, IU was equal or greater than 1.6 in all cases but three. In these three cases, IU was 1.4, 1.3 and 0.9, respectively. In the last case, a routine ultrasonographic study disclosed a perirenal liquid collection.

In ATN and AR patients, IU was lower than 1.7 in all cases but two. In a case of a very mild acute rejection and a case of ATN, IU was 2.16 and 1.77, respectively. Figure 5 shows the distribution of IU in FG, ATN and AR.

Using the cutoff value of 1.7, the sensitivity for the detection of ATN was 97.1%, the detection of AR was 95.8%. Specificity was 60.0% and 51.3%, respectively. There was a significant inverse correlation between serum creatinine and IU ($n = 103$, $r = -0.78$, $p < 0.01$), that is IU decreases when serum creatinine increases. The correlation between ERPF and IU is also significant ($n = 98$, $r = 0.73$, $p < 0.01$), that is ERPF increases when IU increases (Fig. 6).

In the follow-up of patients, IU and transit time evolution corresponded with clinical evolution. Figures 7 and 8 show the results for two patients with different diagnosis and evolution in whom the conventional renogram does not change significantly while IU, MTT and T20 do.

DISCUSSION

The results obtained show the strength of the deconvolution method used in renal transplant. The method is potent enough and was applied to all the renograms, the mathematical process failed only in 3 cases, and that was usually due to the severity renal function impairment.

Our results are in agreement with previously published values with different tracers (*12–14*). MTT and T20 are prolonged in AR and ATN when compared with functioning grafts, as expected.

IU (defined as the first point of the RRF × 100) is, among the parameters studied, the most sensitive one to changes in parenchymal function. Mean value in FG was 1.6, and it significantly decreased in ATN and AR. Only 4 of the 41 FG cases studied were below the cutoff value of 1.6. Concerning abnormal groups, only 1 of 21 AR cases and 1 of 35 ATN studied were greater than 1.60. Obstructed graft and nephrotoxicity cases showed a wider range reflecting the renal function impairment of each case. Cyclosporin nephrotoxicity was suspected rather early when renal function was not severely damaged. CyA dosage rapidly decreased in all cases, and the clinical evolution with recovery of renal function confirmed the diagnosis. However, because of the small number of cases of CyA toxicity studied, no conclusion can be drawn. Obstructed kidneys show a significant decrease of IU, although less significantly than in AR and ATN. This may be due to varying degrees of pathologic changes that happen in obstructive problems.

A large overlap was found both for MTT and T20 between AR and NTA. The large s.d. found in both groups reflects the different degree of renal function impairment that can be observed in clinical practice in these patients. In some patients, we observed that MTT and T20 can be about the normal range or slightly below, while the IU significantly decreases. This fact reflects a more severe impairment of renal function. In these patients, tracer transit through the kidney is very fast, possibly because the MAG3 circulates only through the vascular renal network and neither glomerular filtration nor tubular extraction occurs significantly. In our experience the combination of an IU < 1.6 and a MTT < 160 were only seen in patients with very severe ATN and/or severe AR. In these patients, recovery began by a prolonged MTT over normal values, that was followed by IU increase and finally normalization of both MTT and IU. Figure 8 illustrates this hypothesis. It shows the evolution of a patient who begins with an ATN with prolonged transit times and low IU. A few days later, IU maintains while MTT and T20 decrease. This pattern is more dramatic some days later. A graft biopsy shows severe ATN and AR. In the following days, after specific treatment for AR, MTT and T20 increase, parallelly IU increases and finally, in the last control subject, MTT and T20 become normal and IU is about four. It is important to note that the RRF obtained with this method is faster in reflecting changes in renal function and is more accurate in showing the state of graft function than the typical renogram with ^{99m}Tc-MAG3.

Our findings with ^{99m}Tc-MAG3 are consistent with other reports (*7,14*) since MTT is significantly prolonged in the group of obstructions. Also, in our study, T20 is significantly prolonged.

Especially interesting is the significant correlation found between IU and blood creatinine. Though each agent is handled by the kidney in a different way, it shows the correlation between renal function and IU and how renal function can be quantified and standardized by using the IU. In the patient follow-ups, IU variations seem more useful than creatinine, especially if it is used in combination with MTT. Because MAG3 is a tubular tracer, we have looked for the correlation with ERPF and not with the glomerular filtration rate. The initial uptake of tracer corresponds with the kidney tubular function as shows the significant correlation found between ERPF and IU.

The IU usefulness as follow-up parameter increases too. A basal study should be obtained within the first 24–48 hr post-transplantation. Thereafter, posterior IU must be compared with the basal one. The decrease of the IU suggests renal function impairment, while its increase, at any moment, suggests renal function improvement. Concerning the conventional renogram, the IU measurement is a parameter that allows quantification of tubular renal function. It is less subjective than visual inspection of images or renographic curves and more accurate than the other parameters studied.

CONCLUSION

The parameter proposed is much more potent and less modifiable by tracer maladministration than the maximal uptake of tracer calculated in the usual renogram with ^{99m}Tc-MAG3. It can be used to monitor renal function graft evolution even in patient with ATN. The combined use of IU with MTT and T20 increases the accuracy of the method and reflects renal dysfunction severity. Decreased IU and under normal transit times reflect more severe graft damage than decreased IU and over normal transit times. Therefore, though a single value can be significant, it is recommendable to obtain a basal study and use the initial values of IU, MTT and T20 as reference in follow-up studies.

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