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# Influence of hydration status in normal subjects: fractional analysis of parameters of Tc-99m DTPA and Tc-99m $MAG_3$ renography

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***Rationale and Objectives:*** The purpose of this study was to evaluate the influence of hydration status upon renogram patterns and renal physiological parameters and clarify the differences between DTPA and $MAG_3$ studies in normal volunteers. ***Material and Methods:*** The study populations were 22 kidneys of 11 volunteers with no history of hypertension or renal disease with normal serum creatinine levels. They were 6 men and 5 women aged from 24 to 48 yrs (mean age: 33.4 yrs). Renal scintigraphies with both 185 MBq (5 mCi) of Tc-99m DTPA and Tc-99m $MAG_3$ were performed after dehydration (urine specific gravity > 1.025) and adequate hydration (urine specific gravity < 1.010) in each subject at least with a 5–7-day interval. Renograms were generated from the whole kidney and cortical ROIs. We analyzed the clearance, renogram pattern, mean transit time, time to maximum activity, time from maximum activity to half activity, and residual cortical activity. Paired t-test and Wilcoxon signed rank test were used as statistical analysis methods. Statistical analysis was considered significant at $p < 0.05$. ***Results:*** In the dehydrated state, with Tc-99m DTPA and whole kidney ROI, parameters such as time to maximum activity, time from maximum activity to half activity, residual cortical activity, and mean transit time were delayed as compared to parameters in the adequately hydrated state, but the clearance was not changed. With the cortical ROI, the changes of parameters due to dehydration were partially offset. There were insignificant differences between most parameters of Tc-99m DTPA and Tc-99m $MAG_3$ with the whole kidney and cortical ROIs. ***Conclusions:*** Dehydration may bring about a false positive curve pattern on renograms which can be prevented or minimized by using the cortical ROI. There were insignificant differences between most parameters of Tc-99m DTPA and Tc-99m $MAG_3$.

**Key words:** renal scintigraphy, hydration, dehydration, DTPA, $MAG_3$

## INTRODUCTION

IT IS WELL KNOWN that the hydration status can influence the renogram pattern and physiological parameters of the kidney including clearance rate. The dehydrated renal scintigraphy has a higher kidney to background ratio at 1 to 2 minutes (min) than the hydrated one, and it is most likely secondary to a small amount of excreted tracer by 2 min, with a greater amount of tracer remaining in the calyces and pelvis and, thus, in the renal region of interest in the dehydrated state. Therefore, the degree of hydration is important in the analysis of renal scintigraphy.[1–3] The effects of varying degrees of dehydration or hydration on the Tc-99m-diethylenetriaminepentaacetic acid (DTPA) and I-131-orthoiodohippurate (OIH) studies of normal human kidney have been reported.[3–6]

Levey CS et al.[5] reported that a false-positive result occurred because of inadequate patient hydration on the captopril renogram. Dehydration, with secondary hypotension, can cause a diminished glomerular filtration rate and mimic bilateral renovascular hypertension on the

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captopril renal scan. Dore et al.[7] reported that a fluctuating renogram was shown in the case of chronic pyelonephritis or temporary ureteral spasm. This pattern is accentuated in the dehydrated state. Therefore, in the dehydrated state, quantitative and qualitative analysis of the renogram is difficult, and it is difficult to classify pathologic conditions. To resolve these problems, cortical region of interest (ROI) or diuretics can be used.

Recently, Tc-99m-mercaptoacetyltriglycine ($MAG_3$) has been used with DTPA for dynamic renal imaging. $MAG_3$ has the advantage of a high extraction rate. But, the effects of varying degrees of hydration on $MAG_3$ study of normal kidney are not yet clearly defined.[8,9]

In this study, we determined the influence of hydration status on renogram patterns and renal physiological parameters with the whole kidney and cortical ROIs and clarified the differences between DTPA and $MAG_3$ studies in healthy volunteers.

## MATERIALS AND METHODS

### *1. Study Population*

The study populations were 22 kidneys of 11 volunteers. They were 6 men and 5 women aged from 24 to 48 yrs (mean age: 33.4 yrs). Each volunteer had a normal serum creatinine level, a normal urinalysis, no history of renal disease, and no other disease at the time of the study. All volunteers gave informed consent and no volunteer was used more than once.

### *2. Study Design and Imaging Protocol*

Each subject was studied four times and each study was performed with a 5–7-day interval. The subjects were injected with 185 MBq (5 mCi) of Tc-99m DTPA and studied twice, once adequately hydrated and once dehydrated with a 5–7-day interval. And after 5–7 days, the subjects were injected with 185 MBq (5 mCi) of Tc-99m $MAG_3$ and studied twice, once adequately hydrated and once dehydrated with a 5–7-day interval. For the hydrated study, the subject had drunk 1,500 m*l* of water 30 min to 1 hour before the examination began and urine specific gravity was examined. Adequate hydration was considered present only when the urine specific gravity was less than 1.010. For the dehydrated study, the subject had drunk or eaten nothing for 8 hours before the examination began and the urine specific gravity was examined. Dehydration state was considered present when the urine specific gravity was more than 1.025. For each study, the volunteers were placed in the supine position. Following a bolus injection, dynamic images were acquired for 26 min using a gamma camera (Orbiter, Siemens) with high-resolution collimator. We acquired continuous images for 26 min: 24 frames with each frame for 15 seconds for the 6 min and 24 frames with each frame for 50 seconds for the remaining 20 min.

### *3. Data Analysis*

The obtained data were transferred to an IBM PC using the file transfer protocol (FTP), and then post-processing and analysis of data by renal processing software (IDL version 5.2) were performed. The renograms were obtained by placing the ROI over the whole kidney and cortex. And the renogram was classified as showing a normal pattern when the renal parenchymal radioactivity decreased continuously with time, regardless of decreasing slope, in the excretory phase, and the renogram was classified as showing a fluctuation pattern when the renal parenchymal radioactivity went up and down repeatedly in the excretory phase, showing a step-like curve pattern.

Background correction was performed. We put the ROI 2 pixels away from the inferolateral margin of the kidney with crescent shape for background correction. And the renal parameters were obtained as follows: time to maximum activity (T max), time from maximum activity to half activity (T half), residual cortical activity (RCA: activity at 20 min/activity at 3 min), mean transit time (MTT: measured with deconvolution analysis), clearance (measured with Gates method in case of Tc-99m DTPA, and camera method in case of Tc-99m $MAG_3$).[10–12] We obtained the retention function value by the kidney function itself after we deconvoluted the renogram from the kidney with the renogram from the renal artery, from which we obtained mean transit time.

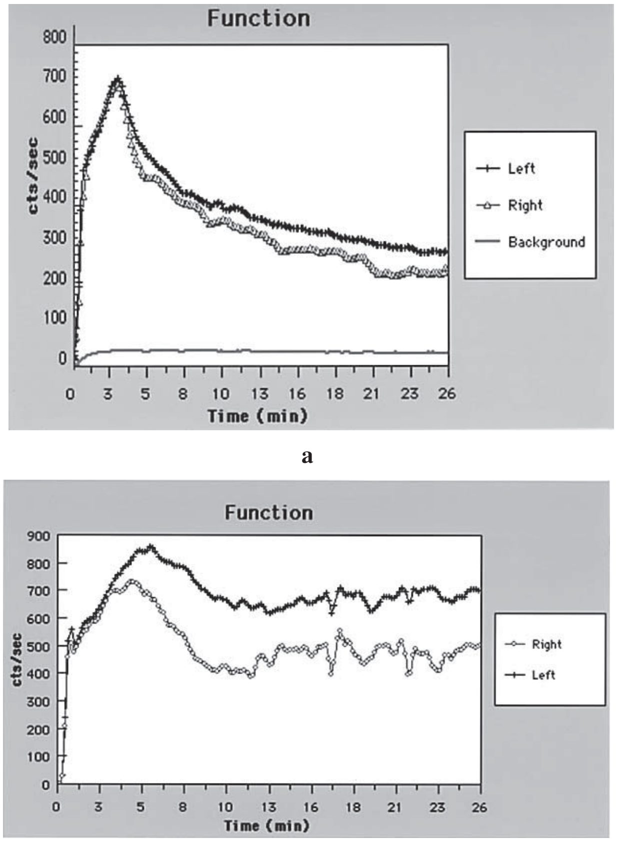
$$R(t) = \int_0^t I(t-\tau) \cdot H(\tau) d\tau$$

$$R_n = \sum_{k=0}^{n} I_{n-k} \cdot H_k \cdot \Delta t$$

Input function: $R_n$: renogram of the kidney
$H_k$: retention function of the kidney
$I_{n-k}$: radioactivity in the renal artery

When T half cannot be determined, we used 26 min for the T half (in the 3 cases: 26 min was the longest T half in the remaining cases).

Mean values and standard deviations were calculated. Comparison between these values were performed using the paired t-test (parametric analysis method: used when data are distributed following the normal distribution) and Wilcoxon signed rank test (nonparametric analysis method: used when data are not distributed following the normal distribution). Differences were considered significant at $p < 0.05$. And when we compared the influence of hydration status between the whole kidney and cortical ROIs and between Tc-99m DTPA and Tc-99m $MAG_3$, we obtained differences between the hydrated and dehydrated states under each condition, and we decided whether the values of difference are statistically significant between the whole kidney and cortical ROIs and between Tc-99m DTPA and Tc-99m $MAG_3$. As statistical methods, we also used paired t-test and Wilcoxon signed rank test. Differences were considered significant to be at $p < 0.05$.




a

b

**Fig. 1** Renogram patterns in a normal subject according to hydration status. a: A study in the adequately hydrated state with the $^{99m}$Tc-DTPA and whole kidney ROI shows normal perfusion, secretion and excretion of the radiotracers by both kidneys. b: A study in the dehydrated state with the $^{99m}$Tc-DTPA and whole kidney ROI shows fluctuation pattern.

## RESULTS

In the adequately hydrated state, all the renograms from the 22 kidneys of 11 persons in whom the ROI was placed over the whole kidney or the cortex showed normal pattern (normal perfusion, uptake and excretion phases) in both Tc-99m DTPA and Tc-99m $MAG_3$ renal scintigraphies (Fig. 1a).

In the dehydrated state, all the renograms showed normal perfusion, but some of them showed delayed uptake and excretion of radiopharmaceuticals by kidney. Some renograms, that were aquired by placing the ROI over the whole kidney, showed delayed and stack inclination of the uptake and the excretory phases. And they showed a fluctuating curve pattern in 7 kidneys when Tc-99m DTPA was used, and in 6 kindneys when Tc-99m $MAG_3$ was used (Fig. 1b). But all the renograms except in 1 case, that were acquired by placing the ROI over the cortex, showed normalized inclination of the curve (Table 1).

**Table 1** Curve patterns of renography according to the hydration status and ROI

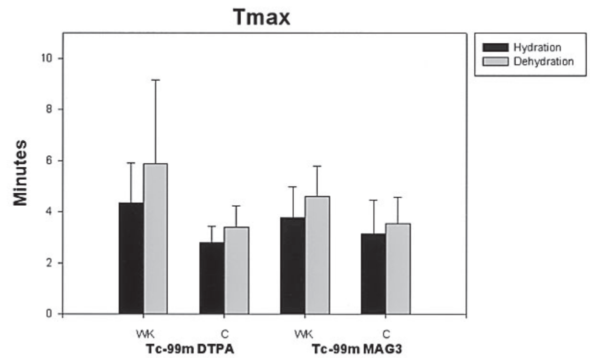
| | Dehydration | | | | Hydration | | | |
|---|---|---|---|---|---|---|---|---|
| | DTPA | | $MAG_3$ | | DTPA | | $MAG_3$ | |
| | WK* | C** | WK | C | WK | C | WK | C |
| Normal | 15 | 21 | 16 | 22 | 22 | 22 | 22 | 22 |
| Fluctuation | 7 | 1 | 6 | 0 | 0 | 0 | 0 | 0 |
| Total | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 |

*WK: Whole kidney ROI, **C: Cortical ROI

**Table 2** Comparison between parameters of DTPA and $MAG_3$

| | | | T max (min) | | T half (min) | | MTT (min) | | RCA | | Clearance (m*l*/min) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | H† | D‡ | H | D | H | D | H | D | H | D |
| Tc-99m DTPA | | | | | | | | | | | | |
| | WK* | Mean | 4.35 | 5.87 | 13.56 | 16.02 | 180.0 | 314.5 | 0.56 | 0.69 | 48.91 | 48.98 |
| | | S.D. | 1.57 | 3.30 | 6.55 | 6.73 | 54.9 | 171.3 | 0.16 | 0.22 | 14.48 | 13.06 |
| | | P value | 0.0386 | | 0.0437 | | <0.0001 | | 0.0019 | | 0.9764 | |
| | C** | Mean | 2.78 | 3.39 | 11.15 | 13.77 | 131.2 | 163.2 | 0.47 | 0.52 | | |
| | | S.D. | 0.66 | 0.84 | 5.99 | 7.59 | 24.3 | 70.96 | 0.08 | 0.11 | | |
| | | P value | 0.0106 | | 0.0696 | | 0.0428 | | 0.0205 | | | |
| Tc-99m $MAG_3$ | | | | | | | | | | | | |
| | WK | Mean | 3.78 | 4.60 | 6.17 | 7.44 | 210.9 | 290.7 | 0.193 | 0.278 | 135.3 | 137.3 |
| | | S.D. | 1.21 | 1.18 | 2.47 | 1.84 | 62.1 | 62.6 | 0.03 | 0.09 | 14.1 | 17.3 |
| | | P value | 0.0223 | | 0.0105 | | <0.0001 | | 0.0001 | | 0.3539 | |
| | C | Mean | 3.13 | 3.53 | 5.89 | 6.87 | 143.5 | 172.6 | 0.194 | 0.192 | | |
| | | S.D. | 1.33 | 1.05 | 1.14 | 1.49 | 29.7 | 41.0 | 0.03 | 0.03 | | |
| | | P value | 0.0530 | | <0.0001 | | 0.0078 | | 0.7147 | | | |

*WK = Whole kidney ROI, **C = Cortical ROI, †H = Hydration state, ‡D = Dehydration state

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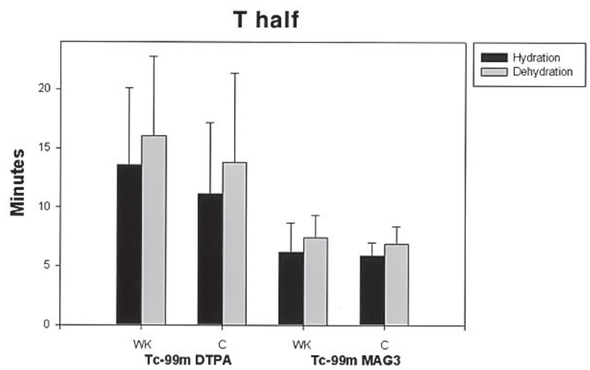


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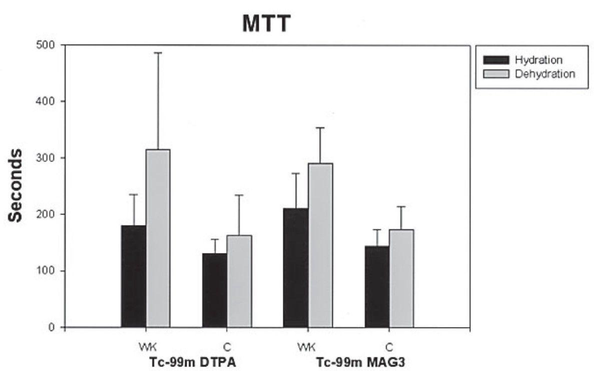


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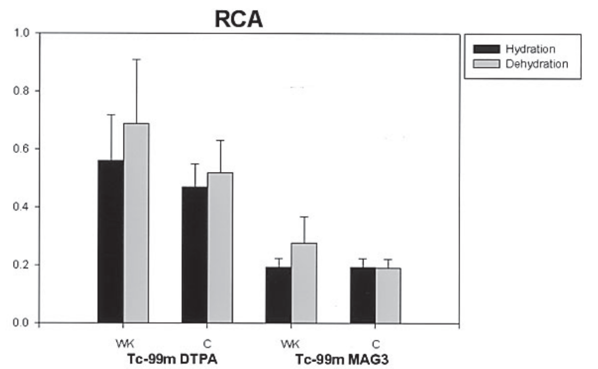


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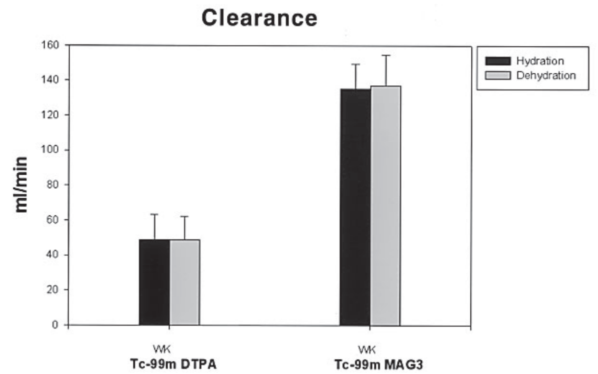


e

**Fig. 2** Differences of parameters according to the radiotracers and hydration status. a: T max, b: T half, c: MTT, d: RCA, e: Clearance

The T max, T half, MTT, RCA, and clearance that were acquired in the hydrated and dehydrated states, are summarized in Table 2. When Tc-99m DTPA was used and the ROI was placed over the whole kidney, parameters that increased statistically significantly were MTT and RCA, as compared with those in the hydrated state. When the ROI was placed over the cortex, the T max, MTT, RCA increased statistically significantly in the dehydrated state. The clearance did not show any change according to the degree of hydration (Table 2) (Fig. 2).

When Tc-99m $MAG_3$ was used and the ROI was placed over the whole kidney, the parameters that increased statistically significantly in the dehydrated state where T max, T half, MTT, and RCA. When the ROI was placed over the cortex, the parameters that increased statistically significantly in the dehydration state were T half and MTT. There was no significant difference in the clearance between the adequately hydrated and dehydrated states (Table 2) (Fig. 2).

The comparison between the parameters in the hydrated and dehydrated states, when the ROI was placed over the whole kidney and cortex, is shown in Table 3. The differences in the parameters in the dehydrated state, were more marked when the ROI was placed over the whole kidney than when placed over the cortex. The parameters that showed statistically significant differences between the whole kidney and cortical ROIs, were MTT and RCA when Tc-99m DTPA and Tc-99m $MAG_3$ were used (Fig. 3).

The comparison between the parameters in the hydrated and dehydrated states, when the Tc-99m DTPA and Tc-99m $MAG_3$ were used, is shown in Table 4. Statistical analysis with paired t-test and Wilcoxon signed rank test shows insignificant differences between most parameters of Tc-99m DTPA and Tc-99m $MAG_3$ with the whole kidney and cortical ROIs.

**Table 3** Comparison between parameters of the whole kidney and cortical ROIs

| | T max (min) | | | | T half (min) | | | | MTT (min) | | | | RCA | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | WK* | | C** | | WK | | C | | WK | | C | | WK | | C | |
| | H† | D‡ | H | D | H | D | H | D | H | D | H | D | H | D | H | D |
| Tc-99m DTPA | | | | | | | | | | | | | | | | |
| Mean | 4.35 | 5.87 | 2.78 | 3.39 | 13.5 | 16.0 | 11.1 | 13.7 | 175 | 316 | 131 | 163 | 0.56 | 0.69 | 0.47 | 0.52 |
| $\Delta$ (%)§ | 35 | | 22 | | 16 | | 23 | | 81 | | 24 | | 23 | | 11 | |
| P value | 0.2653 | | | | 0.4091 | | | | 0.0002 | | | | 0.0400 | | | |
| Tc-99m $MAG_3$ | | | | | | | | | | | | | | | | |
| Mean | 3.78 | 4.60 | 3.13 | 3.53 | 6.17 | 7.44 | 5.89 | 6.87 | 210 | 290 | 143 | 172 | 0.19 | 0.27 | 0.19 | 0.19 |
| $\Delta$ (%)§ | 22 | | 13 | | 21 | | 17 | | 38 | | 20 | | 42 | | 0 | |
| P value | 0.0811 | | | | 0.2128 | | | | 0.0007 | | | | <0.0001 | | | |

*WK = Whole kidney ROI, **C = Cortical ROI, †H = Hydration status, ‡D = Dehydration status

§$\Delta$ (%) = (D − H)/D × 100 (%)

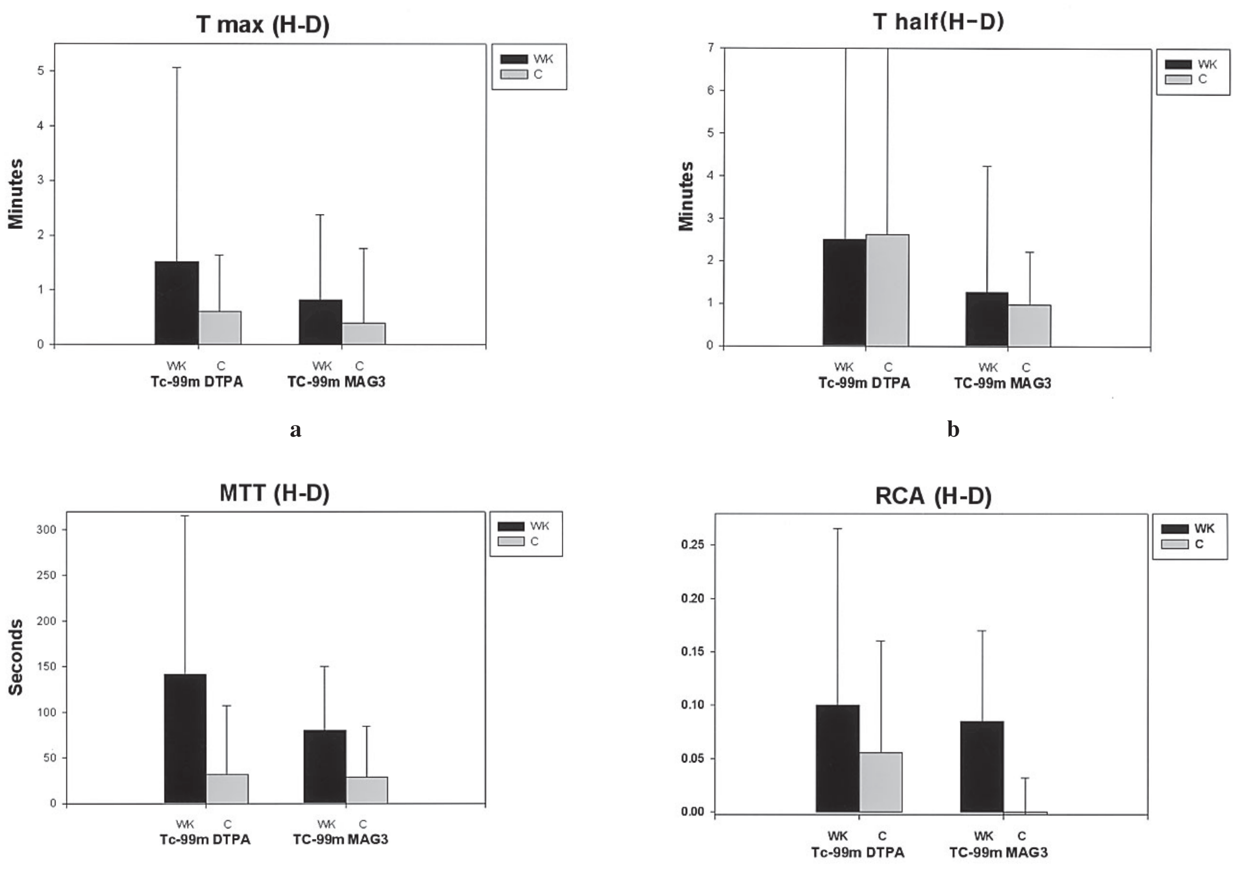


**Fig. 3** Differences of parameters according to the hydration status and definition of ROI. a: T max, b: T half, c: MTT, d: RCA

## DISCUSSION

Renal parameters can be affected by renal function, degree of hydration, distensible degree of urinary bladder, amino acid and protein intakes, kind of radiopharmaceutical used, acquisition method of imaging, measurement method of renal depth, drawing method of ROI and post-processing protocol.[1] One of these that is easy to overlook is hydration degree before the study. And dehydration can cause false positive results. Also in our study, hydration degree significantly affected renogram pattern and renal parameters. And some authors have performed studies in

**Table 4** Comparison between parameters of DTPA and $MAG_3$: hydration effect

| | T max (min) | | | | T half (min) | | | | MTT (min) | | | | RCA | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tc-99m DTPA | | Tc-99m $MAG_3$ | | Tc-99m DTPA | | Tc-99m $MAG_3$ | | Tc-99m DTPA | | Tc-99m $MAG_3$ | | Tc-99m DTPA | | Tc-99m $MAG_3$ | |
| | H† | D‡ | H | D | H | D | H | D | H | D | H | D | H | D | H | D |
| WK* | | | | | | | | | | | | | | | | |
| Mean | 4.35 | 5.87 | 3.78 | 4.60 | 13.5 | 16.0 | 6.17 | 7.44 | 175 | 316 | 210 | 290 | 0.56 | 0.69 | 0.19 | 0.27 |
| $\Delta$ (%)§ | 26 | | 18 | | 16 | | 17 | | 45 | | 28 | | 19 | | 30 | |
| P value | 0.8140 | | | | 0.2112 | | | | 0.6261 | | | | 0.2150 | | | |
| C** | | | | | | | | | | | | | | | | |
| Mean | 2.78 | 3.39 | 3.13 | 3.53 | 11.1 | 13.7 | 5.89 | 6.87 | 131 | 163 | 143 | 172 | 0.47 | 0.52 | 0.19 | 0.19 |
| $\Delta$ (%)§ | 18 | | 11 | | 19 | | 14 | | 20 | | 17 | | 10 | | 0 | |
| P value | 0.5473 | | | | 0.4022 | | | | 0.6486 | | | | 0.0187 | | | |

*WK = Whole kidney ROI, **C = Cortical ROI, †H = Hydration status, ‡D = Dehydration status
§$\Delta$ (%) = (D − H)/D × 100 (%)

subjects both in the hydrated and dehydrated states to evaluate the effect of hydration on the renogram.[2,3]

The effect of the rate of urine flow on the renogram pattern has been well investigated.[5,12] If the rate of urine flow decreased by dehydration, the secretory and excretory phases of the renogram are prolonged. Furthermore the renogram of normal kidneys may show a fluctuating pattern. These fluctuating patterns occur when the radiotracers are highly accumulated in the intrarenal collecting system and then move to the distal portion because of peristalsis of the collecting system. These fluctuating renogram curves are not seen in the adequately hydrated state. It is because urine is abundantly made, and diluted radiotracers continually move to the distal portion.

In the results of our study, 12 of 13 cases that showed fluctuating pattern on the renogram in the dehydrated state when the ROI was placed over the whole kidney, did not show the fluctuating pattern on the renogram when the ROI was placed over the cortex. This is probably because the renal collecting system containing a high concentration of radiotracers could be excluded from the ROI.

Wedeen et al.[13] reported that the renogram frequently showed a step-like pattern in the case of decreased urine volume following the dehydrated state. However, following 600 m*l* water intake, T max is significantly shortened, and the step-like pattern disappeared. On the renogram, the secretory and excretory phases were the phases influenced by the dehydration state.

In the results of our study, when Tc-99m DTPA was used and the ROI was placed over the whole kidney, the T max was delayed 35%, the T half 16%, and the MTT 81%. Also the residual cortical activity increased 23% in the dehydration state as compared to the adequately hydrated state. But the clearance showed little change. And when the ROI was placed over the cortex, the T max was delayed 22%, the T half 23%, and the MTT 24%. Also the residual cortical activity increased 11%, and the clearance showed little change. As noted above, there was less change in most renal parameters on the renogram between the two states when the ROI was placed over the cortex than when placed over the whole kidney. Also, when Tc-99m $MAG_3$ was used, it showed similar features. These findings are in accord with Taylor's results that the hydration-dependent changes of renal parameters can be minimized by placing the ROI over the cortex.[14] As mentioned above, also in our study, changes in the renal parameters between the hydrated and dehydrated states were minimized when the ROI was placed over the cortex.

Some authors reported that dehydration decreases the hydrostatic pressure across the glomerular capillaries and causes consequent decrease in clearance.[5] But, we found that the degree of hydration had only a small effect on the value of the clearance.

In conclusion, routine renal radionuclide study should be performed with adequate hydration. But if adequate hydration is impossible or the renal radionuclide study has been already done in the dehydrated state, the false positive curve pattern on the renogram by the dehydration effect can be prevented or minimized by placing the ROI over the cortex. Also, there were insignificant differences between most parameters of Tc-99m DTPA and Tc-99m $MAG_3$ with the whole kidney and cortical ROIs.

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