

Evaluation of Renal Function from ^{99m}Tc -MAG3 Renography Without Blood Sampling

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To develop a camera-based method for evaluating renal function with ^{99m}Tc -mercaptoacetyltriglycine (MAG3), we examined the relationship between various renogram parameters and ^{99m}Tc -MAG3 clearance. **Methods:** Twenty-one patients underwent renal scintigraphy with ^{99m}Tc -MAG3. Eighty 3-s frames were obtained after the bolus injection of 250 MBq tracer, followed by the collection of 52 30-s frames. Regions of interest were drawn for the kidneys, perirenal background areas and subrenal background areas, and background-subtracted renograms were generated. Renal accumulation at 0.5–1.5, 0.5–2, 1–2, 1–2.5 and 1.5–2.5 min after tracer arrival in the kidney was calculated as area under the background-subtracted renogram, and percent renal uptake was obtained after correction for soft-tissue attenuation and injected dose. The slope of the renogram was determined for the same segments used in calculating area under the renogram, and slope index was computed as slope corrected for attenuation and injected dose. Percent renal uptakes and slope indices were correlated by linear regression analysis with ^{99m}Tc -MAG3 clearance measured using a single blood sampling method. **Results:** Among the values of percent renal uptake, the value obtained at 1.5–2.5 min using the perirenal background correlated best with ^{99m}Tc -MAG3 clearance. The slope index at 0.5–1.5 or 0.5–2 min using the subrenal background provided better accuracy than percent renal uptake for predicting clearance. There were no substantial differences in the relative function of the right kidney between the methods using percent renal uptake and slope index. **Conclusion:** ^{99m}Tc -MAG3 clearance can be assessed with acceptable accuracy by a camera-based method. The method based on the slope of the renogram may replace the one based on the area under the renogram in evaluating renal function from ^{99m}Tc -MAG3 renograms.

Key Words: ^{99m}Tc -mercaptoacetyltriglycine; clearance; gamma camera

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Technetium-99m-mercaptoacetyltriglycine (MAG3) offers high-quality renal images and is widely accepted as an excellent renal radiopharmaceutical. The clearance of ^{99m}Tc -MAG3 is approximately proportional to effective renal plasma flow measured with ^{131}I -orthoiodohippurate (1–5) and can be used as an index of renal function. Camera-based

methods have been described to evaluate ^{99m}Tc -MAG3 clearance without blood sampling (6–11). Although less precise than techniques that require blood sampling, camera-based methods are convenient for both patients and nuclear medicine practitioners and are suitable for routine clinical use. Most camera-based methods determine ^{99m}Tc -MAG3 clearance from the area under the renogram (time-activity curve for the kidney) soon after the administration of tracer (6–10) and are classified as area methods. The slope method is another type of camera-based technique used to estimate renal function without blood sampling (12,13). It is based on the relationship between clearance and the slope of the early part of the renogram.

We performed renal scintigraphy with ^{99m}Tc -MAG3 and measured clearance by a method with single blood sampling. The area under the renogram and slope of the renogram were correlated with ^{99m}Tc -MAG3 clearance, and methods of estimating clearance without blood sampling were determined. The aim of this study was to examine the usefulness of various renogram parameters in assessing renal function with ^{99m}Tc -MAG3.

MATERIALS AND METHODS

Subjects

In this study, 21 patients (8 men, 13 women; age range 21–87 y, mean 58.0 ± 20.2 y) referred for renal scintigraphy to evaluate various renal disorders were examined. One patient had a single kidney; the others had two kidneys.

Imaging Procedures

Thirty minutes after the oral intake of 250 mL water, the patient was placed in the supine position on the imaging table. Immediately after the bolus injection of 250 MBq ^{99m}Tc -MAG3, posterior dynamic imaging was performed for 30 min. Eighty 3-s frames were acquired in a 128×128 matrix with a 20% energy window centered at 140 KeV, and then 52 frames were acquired at a rate of 30 s/frame. A gamma-camera system (Vertex; ADAC Laboratories, Milpitas, CA) equipped with a low-energy general-purpose collimator interfaced to a dedicated minicomputer was used.

The injected dose was measured with the same gamma-camera system. A hollow paper box 20 cm in height was placed on the imaging table above the detector head. The syringe was placed on the paper box before and after injection, and data were acquired for 30 s at each time.

Venous blood samples were obtained from the arm contralateral to the injection site 40 min after the injection of ^{99m}Tc -MAG3. The

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sample was centrifuged, and plasma activity was measured with a well counter.

Standard Method

The single-sample method proposed by Bubeck et al. (14) and Bubeck (15) was used as a standard to measure the clearance of ^{99m}Tc -MAG3. The clearance of ^{99m}Tc -MAG3 (CLmag) normalized for body surface area (BSA) was calculated by the following equations:

$$\text{CLmag (mL/min/1.73 m}^2\text{)} = (A + B) \times \ln (\text{ID/C})$$

$$A = -517 \times e^{-0.011 \times t}$$

$$B = 295 \times e^{-0.016 \times t}$$

$$C = C_n \times \text{BSA}/1.73,$$

where ID is injected dose (cps), t is time of blood sampling postinjection (min) and C_n is plasma concentration at time t (cps/L). BSA was computed as follows (16):

$$\text{BSA} = 0.024265 \times \text{BW}^{0.5378} \times \text{BH}^{0.3964},$$

where BW is body weight (kg) and BH is body height (cm).

Data Analysis

Data obtained at 1–2 min after injection were added to produce a reference image on which regions of interest (ROIs) were manually drawn for the kidneys (Fig. 1). Perirenal background ROIs were determined by a method similar to that described by Taylor et al. (Fig. 1A) (17). An ellipse (inner ellipse) was drawn around each kidney, and another ellipse (outer ellipse) was drawn around the inner ellipse. The inner and outer ellipses shared the same center. The major and minor axes of the outer ellipse were each three pixels longer than the major and minor axes of the inner ellipse. The perirenal background ROI was determined as the area between the inner and outer ellipses. The counting rate (cps) per pixel in the background ROI was multiplied by the number of pixels in the corresponding kidney ROI and subtracted from the counting rate in the kidney ROI to produce a background-subtracted renogram. Background-subtracted renograms were also generated using subrenal background ROIs drawn manually (Fig. 1B).

Renal depth was calculated by the following equations (18):

$$\text{Dr} = 15.13 \times \text{BW}/\text{BH} + 0.022 \times A + 0.077$$

$$\text{Dl} = 16.17 \times \text{BW}/\text{BH} + 0.027 \times A - 0.94,$$

where Dr and Dl are depth of the right and left kidney (cm), respectively, and A is age (y). Attenuation factors for the right (AFr) and left kidney (AFl) were estimated assuming the attenuation coefficient of 0.12/cm:

$$\text{AFr} = e^{-0.12 \times \text{Dr}}$$

$$\text{AFl} = e^{-0.12 \times \text{Dl}}.$$

The counts in the entire field of view were determined for the preinjection and postinjection syringes and corrected for decay to the injection time. The injected count was assessed by subtracting the count for the postinjection syringe from that for the preinjection syringe and was expressed as counts per minute.

Renal accumulation at 0.5–1.5, 0.5–2, 1–2, 1–2.5 and 1.5–2.5 min after tracer arrival in the kidney was calculated as area under the background-subtracted renogram (Fig. 2A) and was expressed as counts per minute. The percent renal uptake at T1–T2 min ($\text{RU}_{\text{T1-T2}}$) was computed as follows:

$$\text{RU}_{\text{T1-T2}} = 100 \times (\text{rCa}_{\text{T1-T2}}/\text{AFr} + \text{lCa}_{\text{T1-T2}}/\text{AFl})/\text{Ci},$$

where $\text{rCa}_{\text{T1-T2}}$ and $\text{lCa}_{\text{T1-T2}}$ are renal accumulation at T1–T2 min for the right and left sides, respectively, and Ci is injected count.

Linear regression analysis was performed by the least squares method for a segment of the background-subtracted renogram, and the slope was determined (Fig. 2B). The time periods used for analysis were 0.5–1.5, 0.5–2, 1–2, 1–2.5 and 1.5–2.5 min after tracer arrival in the kidney. Slope index at T1–T2 min ($\text{SI}_{\text{T1-T2}}$) was calculated by the following equation:

$$\text{SI}_{\text{T1-T2}} = 1,000,000 \times (\text{rS}_{\text{T1-T2}}/\text{AFr} + \text{lS}_{\text{T1-T2}}/\text{AFl})/\text{Ci},$$

where $\text{rS}_{\text{T1-T2}}$ and $\text{lS}_{\text{T1-T2}}$ are slopes calculated from the right and left renograms at T1–T2 min (cps/s), respectively.

The percent renal uptakes at various time periods were correlated by linear regression analysis with ^{99m}Tc -MAG3 clearance

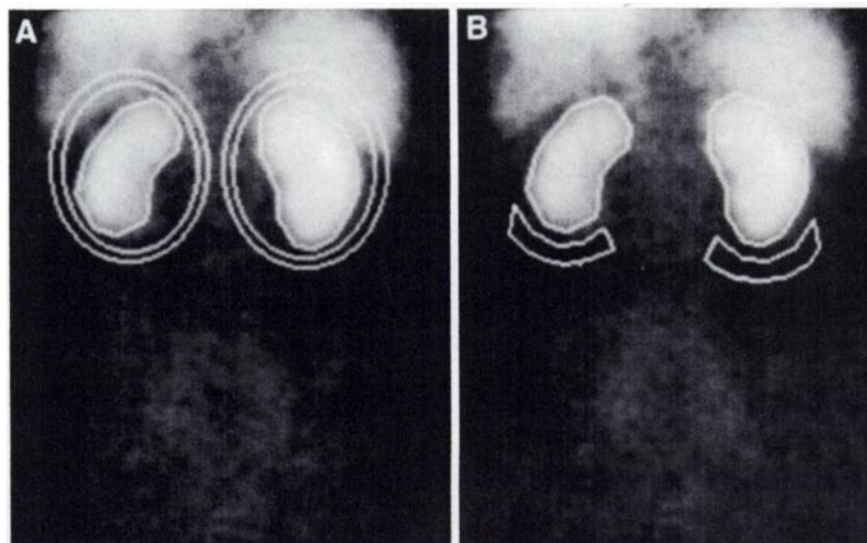


FIGURE 1. ROIs placed for kidneys, perirenal background areas (A) and subrenal background areas (B).

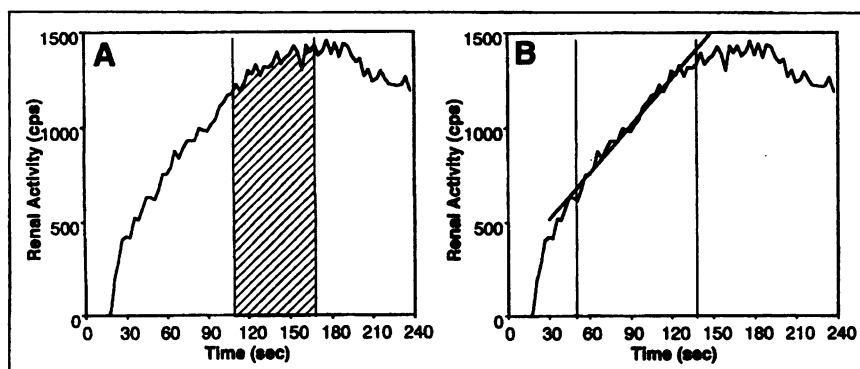


FIGURE 2. Determination of renogram parameters. (A) Renal accumulation at 1.5–2.5 min was calculated as area under renogram at 1.5–2.5 min after tracer arrival in kidney. (B) Slope of renogram at 0.5–2 min was determined as slope of regression line at 0.5–2 min.

measured by the single-sample method, and equations for calculating clearance based on the area method were obtained. Linear regression was also performed between the slope indices and measured ^{99m}Tc -MAG3 clearance, and equations for computing clearance based on the slope method were determined. Clearance was predicted using each regression line, and the residual, absolute difference between the measured and predicted clearances, was calculated as a marker of error in prediction.

Relative renal function was estimated in 20 patients who had both kidneys and compared between methods. Relative function of the right kidney (%RK) was calculated by the following equation in the area method:

$$\%RK = 100 \times (rCa_{T1-T2}/AFr)/(rCa_{T1-T2}/AFr + 1Ca_{T1-T2}/AFI),$$

and by the following equation in the slope method:

$$\%RK = 100 \times (rS_{T1-T2}/AFr)/(rS_{T1-T2}/AFr + 1S_{T1-T2}/AFI).$$

RESULTS

^{99m}Tc -MAG3 clearance measured by the single-sample method ranged from 17.5 to 320.0 mL/min/1.73 m². The results of linear regression analysis between percent renal uptake and ^{99m}Tc -MAG3 clearance normalized for BSA are presented in Table 1. The correlation coefficient ranged from 0.911 to 0.939 and was higher when a later period was used for analysis. Use of the perirenal background provided a better correlation than that of the subrenal background, although the difference was small. The percent renal uptake at 1.5–2.5 min using perirenal background ROIs was the most closely correlated with ^{99m}Tc -MAG3 clearance among the area methods (Fig. 3A).

The slope index decreased as the time period used for analysis was delayed (Fig. 4). The results of linear regression of ^{99m}Tc -MAG3 clearance with slope index are presented in Table 2. The correlation coefficient between clearance and the slope index ranged from 0.887 to 0.972 and was higher when an earlier period was used for analysis. The dependence of the correlation on the period analyzed seemed to be greater for the slope method than for the area method. Slope indices at 0.5–1.5 and 0.5–2 min were closely correlated with ^{99m}Tc -MAG3 clearance (Fig. 3B). Although use of the subrenal background provided a closer correlation than that of the perirenal background, except at 1.5–2.5 min, the effect of background selection was limited. The residual

was significantly smaller for the slope index at 0.5–1.5 or 0.5–2 min using the subrenal background than for percent renal uptake at 1.5–2.5 min using the perirenal background ($P < 0.05$, Student paired t test).

The relative function of the right kidney determined from percent renal uptake at 1.5–2.5 min using perirenal background ROIs ranged from 22.7% to 95.2% (mean $56.1\% \pm 21.2\%$). Relative right kidney function ranged from 21.9% to 96.8% (mean $56.1\% \pm 22.1\%$), when estimated from the slope index at 0.5–2 min using subrenal background ROIs. The results were closely correlated (Fig. 5, $r = 0.994$), and the means were almost identical.

DISCUSSION

The area under the renogram represents the amount of renal accumulation. If the radiotracer taken up by the kidney does not leave the kidney during the early period of renal scintigraphy, renal accumulation at time t (R_t) is

$$R_t = CL \times \int p_t dt,$$

where CL is clearance and p_t is plasma concentration at time

TABLE 1
Relation Between ^{99m}Tc -MAG3 Clearance and Percent Renal Uptake

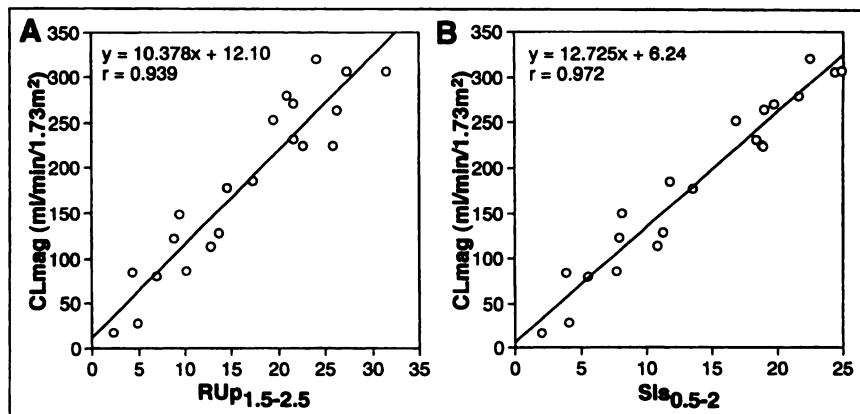
Time* (min)	Background	Regression equation†			Residual	
		Slope	Y-intercept	r	Mean	SD
0.5–1.5	P	14.339	21.63	0.925	30.5	17.5
0.5–2	P	13.041	18.00	0.931	29.3	16.6
1–2	P	11.875	15.17	0.936	28.3	16.0
1–2.5	P	11.100	13.72	0.937	28.1	15.8
1.5–2.5	P	10.378	12.10	0.939	27.7	15.6
0.5–1.5	S	12.846	4.88	0.911	33.4	18.3
0.5–2	S	11.918	3.13	0.920	31.8	17.2
1–2	S	11.045	2.18	0.928	30.2	16.3
1–2.5	S	10.417	2.05	0.930	30.0	16.1
1.5–2.5	S	9.835	1.48	0.932	29.4	15.8

*Time period used for analysis.

†Linear regression was performed for ^{99m}Tc -mercaptoacetyltriglycine (MAG3) clearance plotted against percent renal uptake.

P = perirenal background area; S = subrenal background area.

FIGURE 3. (A) Relation between ^{99m}Tc -MAG3 clearance (CLmag) and percent renal uptake at 1.5–2.5 min using perirenal background ROIs (RUP_{1.5–2.5}). (B) Relation between CLmag and slope index at 0.5–2 min using subrenal background ROIs (SIs_{0.5–2.0}).



t. This relationship forms the basis of the area method used to assess renal function. In the area method, percent renal uptake is determined from gamma-camera renography and is converted to clearance by a given equation. A large number of camera-based techniques can be categorized as the area method (6–10,19–23).

In this study, percent renal uptake was well correlated with ^{99m}Tc -MAG3 clearance normalized for BSA. The correlation was higher when a later period was used for analysis. Increased renal accumulation at a later period depresses the contribution of the background count to the count in the kidney ROI, and calculation of true renal accumulation becomes less vulnerable to inappropriate background subtraction. Although underestimation of the radiotracer taken up by the kidney may occur as a result of early escape from the kidney, the beneficial effects of using a later period appear to outweigh the drawbacks in the range examined in this study. However, the accuracy of the

area method showed only mild dependence on the period analyzed, and percent renal uptakes at 1–2, 1–2.5 and 1.5–2.5 min provided almost the same ^{99m}Tc -MAG3 clearance.

The slope of the renogram represents the rate of renal accumulation. If the tracer picked up by the kidney remains in the kidney, the rate of renal accumulation at time t (dR_t/dt) is expressed by the following equation:

$$dR_t/dt = CL \times p_t$$

and the slope of the renogram depends on clearance and plasma concentration. Clearance can be evaluated from the slope, and slope methods without blood sampling have been proposed to assess glomerular filtration rate (GFR) from renography with ^{99m}Tc -diethylenetriamine pentaacetic acid (DTPA) (12,13).

The finding that slope index gradually decreased in ^{99m}Tc -MAG3 renography appears to be caused by a reduction in plasma concentration and early escape of the radiotracer from the kidney. The plasma clearance of ^{99m}Tc -MAG3 is more rapid than that of ^{99m}Tc -DTPA (24),

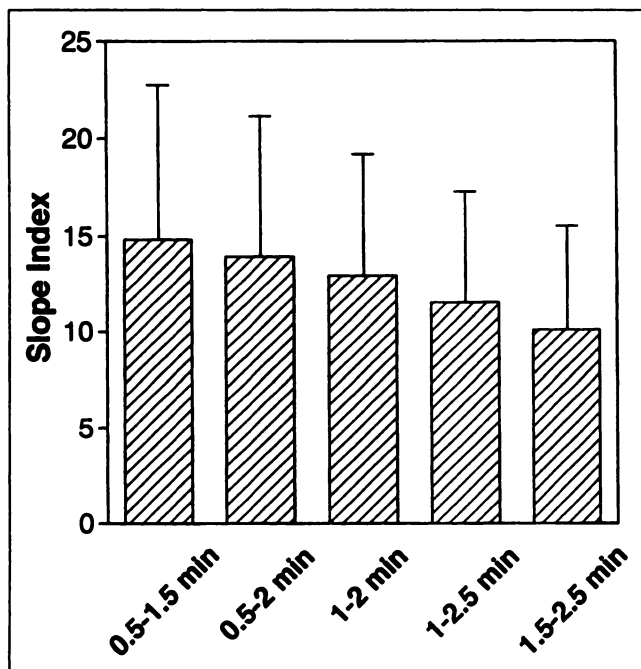


FIGURE 4. Slope indices at various time periods.

TABLE 2
Relation Between ^{99m}Tc -MAG3 Clearance and Slope Index

Time* (min)	Background	Regression equation†			Residual	
		Slope	Y-intercept	r	Mean	SD
0.5–1.5	P	10.711	–1.89	0.962	21.0	14.1
0.5–2	P	11.798	–5.23	0.962	21.7	13.0
1–2	P	13.003	–6.12	0.948	25.3	14.9
1–2.5	P	14.320	–2.53	0.940	27.8	15.2
1.5–2.5	P	15.290	9.56	0.905	31.9	23.3
0.5–1.5	S	11.531	12.37	0.972	19.1	10.1
0.5–2	S	12.725	6.24	0.972	19.0	10.7
1–2	S	14.154	0.69	0.952	23.5	15.6
1–2.5	S	15.578	3.25	0.943	27.3	14.3
1.5–2.5	S	15.675	24.27	0.887	35.3	24.2

*Time period used for analysis.

†Linear regression was performed for ^{99m}Tc -mercaptoacetyltryglycine (MAG3) clearance plotted against slope index.

P = perirenal background area; S = subrenal background area.

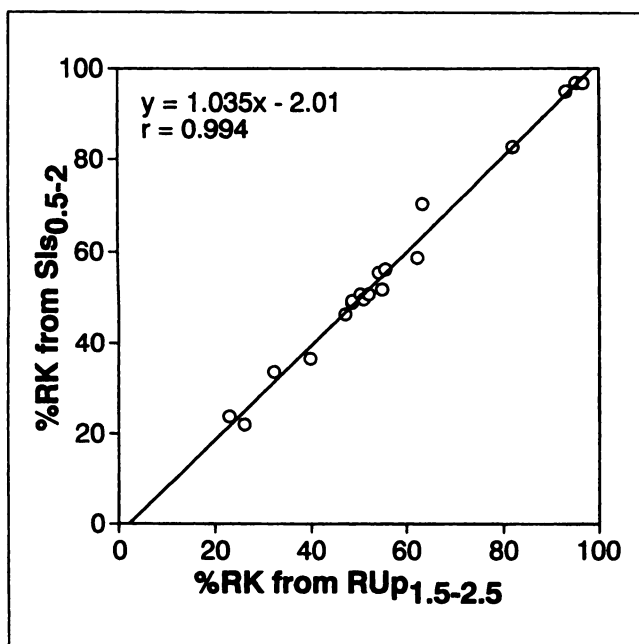


FIGURE 5. Relative function of right kidney (%RK) calculated from percent renal uptake and slope index. Percent renal uptake was calculated at 1.5–2.5 min using perirenal background ROIs (RUP_{1.5-2.5}), and slope index was obtained at 0.5–2 min using subrenal background ROIs (SIs_{0.5-2.0}).

and the slope of the renogram appears to be more dependent on the time period analyzed by ^{99m}Tc -MAG3 renography than by ^{99m}Tc -DTPA renography. In the slope methods using ^{99m}Tc -DTPA, the linear portion of the uptake phase of the renogram is determined visually by the operator, and the slope is calculated for this portion (12,13). It is indicated that the time period used for analysis should be fixed in the slope method with ^{99m}Tc -MAG3 because of the substantial temporal change in the slope.

Shore et al. (13) reported that the slope method is better than the area method for predicting ^{99m}Tc -DTPA clearance in children. In this study, the slope method using the slope obtained at 0.5–1.5 or 0.5–2 min provided better accuracy in calculating ^{99m}Tc -MAG3 clearance than the area method. In addition, high concordance in estimating the relative function of the right kidney was shown between the slope method and area method. Although evaluation of relative renal function is difficult to validate, the slope method provides estimates of relative function approximately equal to those by the area method and is better than the area method in predicting total renal function. These results suggest that the slope method presented in this article can replace the area method in evaluating renal function with ^{99m}Tc -MAG3. No substantial differences were indicated between results using slopes at 0.5–1.5 and 0.5–2 min in calculating ^{99m}Tc -MAG3 clearance. The injected dose was 250 MBq in this study. Renography may be performed with a smaller dose, and use of the slope at 0.5–2 min is recommended to reduce the effects of statistical noise.

Counts in the kidney ROI contain background counts in

addition to true renal counts, and background correction is usually required to estimate renal function by a camera-based method. In this study, background counts were assessed as counts in the perirenal ROI or subrenal ROI and subtracted from counts in the kidney ROI. Use of the perirenal ROI was superior in the area method, whereas use of the subrenal ROI was better in the slope method. However, the effect of background selection on the accuracy of prediction was limited for both methods. Although the perirenal area has been found to better represent the actual background in the kidney ROI (17,25,26), background selection has less effect in renal scintigraphy with ^{99m}Tc -MAG3 than with ^{99m}Tc -DTPA because of the high kidney-to-background contrast in ^{99m}Tc -MAG3 renography (27). A subrenal ROI is easier to draw than a perirenal ROI. The findings in this study appear to justify the use of subrenal ROIs in calculating ^{99m}Tc -MAG3 clearance by the slope method.

Temporal changes in the slope of the renogram appear to be a potential source of error in evaluating renal function by the slope method. The gradual decrease in the plasma concentration should in part be responsible for the decrease in slope. Correction for plasma disappearance may be attained using the time-activity curve for the heart as a representative of the plasma curve (28–32) and may be assumed to improve the accuracy of the slope method. We assess the urinary tract in addition to the kidneys in routine renal scintigraphy. The bladder and ureters are included in the field of view, and sometimes the heart is not adequately visualized. An appropriate heart ROI cannot always be drawn, and correction using the heart curve was not attempted in this study. Piepsz et al. (33) performed the Patlak plot using the heart curve in ^{99m}Tc -MAG3 renography and found a decrease in the Patlak slope, an index of the uptake rate in the kidney corrected for plasma concentration, in the first few minutes postinjection. They pointed out early escape of the tracer from the kidney and the discrepancy between the heart curve and plasma curve (34) as the causes of the observed decrease. Correction using the heart curve is unlikely to offer a major advantage to the slope method.

The standard value of ^{99m}Tc -MAG3 clearance was measured by a single-sample method in this study. The single-sample method is less accurate than a continuous infusion technique or a single-injection multiple-sample technique. The close correlation between single-sample clearance and the slope index at 0.5–2 min indicates the usefulness of the slope method. Validation of the technique using a more accurate standard method and larger population is encouraged.

Only adults were examined in this study. Evaluation of renal function also plays a major role in pediatric practice, and the application of the slope method to children remains to be investigated. The effect of distribution volume on renal accumulation needs to be considered in camera-based techniques, and special attention should be given in children because of the large variations in distribution volume. We

demonstrated a close correlation between percent renal uptake of ^{99m}Tc -DTPA and GFR normalized for BSA in subjects including children and adults and described a method to evaluate renal function in both groups (35). Itoh et al. (9) reported the correlation of ^{99m}Tc -MAG3 clearance normalized for BSA with percent renal uptake in children. A single equation may be applicable in children and adults to convert the slope index with ^{99m}Tc -MAG3 to clearance normalized for BSA. It is also possible that the segment of the renogram analyzed in children should be earlier than that in adults because of the early escape of tracer from the pediatric kidney.

CONCLUSION

We presented the relationship among various renogram parameters and ^{99m}Tc -MAG3 clearance measured by a single-sample method. The slope index at 0.5–2 min after tracer arrival in the kidney was closely correlated with clearance. The slope method using an early fixed segment of the renogram is suggested to provide better accuracy than the area method in evaluating renal function with ^{99m}Tc -MAG3.

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