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Qualitative and quantitative evaluation of renal parenchymal damage by ^{99m}Tc-DMSA planar and SPECT scintigraphy

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The initial ^{99m}Tc-DMSA studies carried out over a four year period in 229 patients with various heterogenic causes of lower urinary tract abnormalities were reviewed. Anatomical damage to the renal parenchyma was graded by means of planar and SPECT studies into a six group classification proposed by Monsour et al.: grade 0 (normal), I (equivocal), II (single defect), III (more than 2 defects), IV (contracted or small) and V (no visualization). Parenchymal uptake of ^{99m}Tc-DMSA was quantitated from planar images at 2 hours postinjection by a computer assisted gamma camera method. SPECT studies could enhance the pick-up rate for parenchymal uptake defects by a factor of 1.5 in comparison with planar imaging. The incidence of anatomical damage to the renal parenchyma increased with a high radiological grade for VUR, and renal uptake per injection dose of ^{99m}Tc-DMSA by the individual kidney significantly decreased in grades III and IV of the anatomical classification.

These data revealed that ^{99m}Tc-DMSA planar is still useful for evaluating gross structural damage and for quantitative evaluation of the kidney with computer assistance. SPECT scintigraphy is more effective in disclosing anatomical damage to the renal parenchyma than planar, although it needs further discussion as to whether SPECT may increase sensitivity with minimal or no adverse affect on specificity.

Key words: ^{99m}Tc-dimercaptosuccinic acid (DMSA), scintigraphy, planar and SPECT, vesicoureteral reflux, upper urinary tract infection, renal scar

INTRODUCTION

RADIOLOGICAL CLASSIFICATION[1,2] by voiding cystography has been widely accepted for grading vesicoureteral reflux (VUR). This grading system is essential for assessment of the severity of VUR but is not always informative on the renal function of the diseased kidney. Anatomical and functional information is important for the management and longitudinal follow-up of patients with VUR and/or urinary tract infection (UTI). ^{99m}Tc-dimercaptosuccinic acid (DMSA) has been considered as a preferred scintigraphic method to evaluate renal parenchymal anatomy as well as an individual renal function.[3–6] Currently, ^{99m}Tc-DMSA scintigraphy is considered to be the first indicative study[7,8] as well as the "gold standard"[9] in the evaluation of renal scarring in VUR and acute or chronic renal infection.

In this study, we will describe qualitative and quantitative evaluation of renal cortical damage by means of ^{99m}Tc-DMSA planar and SPECT scintigraphy which was performed in patients with VUR and/or UTI.

MATERIALS AND METHODS

Materials

The initial DMSA studies which were carried out in 229 patients between August, 1988 and May, 1992 were reviewed retrospectively. All patients had a clinical history of VUR and/or UTI. These patients were placed in two groups (Table 1), those with known VUR and those without confirmed VUR. The first group included patients with neurogenic bladder, ureteral or urethral anomalies

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Table 1 Population studied

Clinical classification	No. of patients
Vesicoureteral reflux (VUR) Group	187
Primary VUR during follow-up with medication	66
Primary VUR after anti-reflux operation	54
Secondary VUR during follow-up with medication	40
Secondary VUR after operation of primary disease	27
No or Unknown Vesicoureteral Reflux Group	42
during follow-up with medication	35
after operation of primary disease	7
Total	229

such as ureteral duplication kidney, posterior urethral valve and anterior urethral stricture. The second group included patients with pyelonephritis, neurogenic bladder, ectopic ureter and bladder substitution with ureteral reimplantation. The age of the patients ranged from 2 months to 69 years (mean 14 years, median 8.5 years). The male to female ratio was 115 to 114.

Methods

Children who could not cooperate in the DMSA study were sedated prior to the procedure. No other pre-treatment was indicated for individuals. ^{99m}Tc-DMSA was prepared in our hospital by adding freshly eluted ^{99m}Tc-pertechnetate to a commercially available freeze-dried kit (Daiichi Radioisotopes Lab. Co., Tokyo). Before injection, the syringe containing ^{99m}Tc-DMSA was placed 30 cm from the collimator surface and counted for 10 sec in order to calibrate the device for renal uptake measurements. The patients were positioned supine on a bed beneath which the single-headed rotating gamma camera (Toshiba GCA-602A) was located, and it was equipped with a low-energy high-resolution parallel-hole collimator. An intravenous bolus injection of 185 MBq of ^{99m}Tc-DMSA for adults (scaled down to a minimum of 26 MBq for children) was given. Posterior planar images were obtained at precisely 2 hours after injection for a preset time of 5 minutes on a 512 by 512 matrix. Supplemental posterior oblique images were also obtained. SPECT was started after completion of the planar study. Each SPECT projection image was acquired on a 64 by 64 matrix until July 1991, and thereafter on a 128 by 128 matrix for 20 sec at each of 60 positions over 360 degree rotation.

For reconstruction of tomograms, a contiguous transaxial section image of each pixel (5.4 mm thickness in a 64 by 64 matrix and 2.7 mm thickness in a 128 by 128 matrix) was made by 3 point pre-smoothing and using a Shepp & Logan digital filter. Conventional transaxial and coronal images to the somatome axis and true coronal images (reoriented coronal images) to the visceral axis of the kidney after correction for renal axis rotation were generated. The three types of tomograms were displayed on a film for evaluation of the renal cortex.

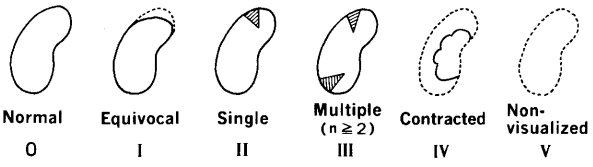


Fig. 1 Illustration of scintigraphic grading system for renal parenchymal uptake defect by ^{99m}Tc-DMSA planar and SPECT scintigraphy (modified from reference 15).

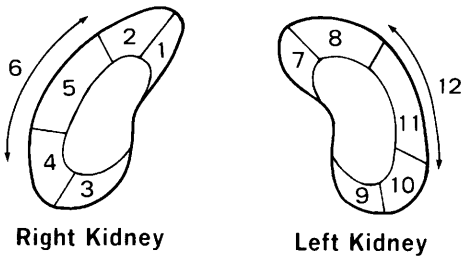


Fig. 2 Illustration of regional scar incidence (modified from the reference 15).

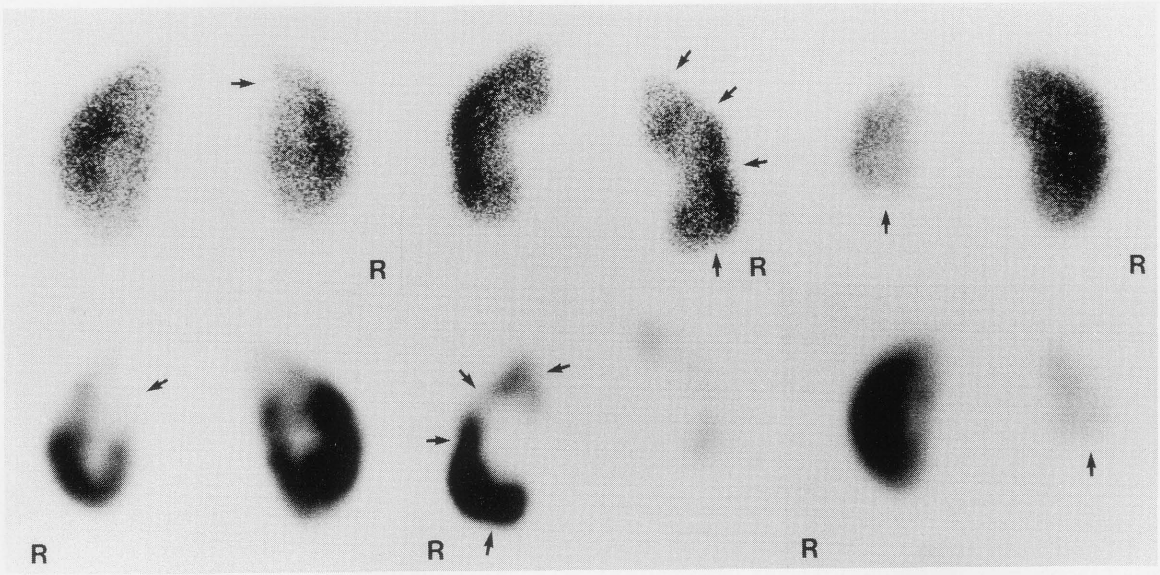
The anatomical damage to the renal parenchyma was classified by visual inspection of planar and SPECT images with a minor modification of the grading system proposed by Monsour et al.[10] into six types: normal (0), equivocal (I), single defect (II), more than two defects (III), small or contracted kidney in comparison with the opposite kidney (IV) and no visualization (V) (Fig. 1). Planar and SPECT images were read by one observer (K.I.) at the same session without knowledge of any clinical information. When the kidney was evaluated as contracted or non-visualized by visual inspection of the planar image, it was judged as the same grade on SPECT image. Location of the parenchymal defects was marked on the regional map as proposed by Monsour et al.[10] (Fig. 2).

The absolute individual renal parenchymal uptake of ^{99m}Tc-DMSA per injected dose was quantitated by a computer analysis of planar posterior image data at 2 hour-postinjection.[11,12] For quantitation, physical decay of ^{99m}Tc from the time of injection to planar image data acquisition and tissue attenuation of gamma ray from ^{99m}Tc-DMSA in the kidney were corrected mathematically. The renal depth (cm) was estimated from the equation of body weight (kg)/height (cm)[13] and the linear attenuation coefficient of ^{99m}Tc in the body was set at −0.153. The relative right and left renal uptake (%) was also calculated from the formula = (the absolute right or left renal uptake)/(absolute renal uptake of both kidneys) × 100.

RESULTS

Relationship between gradings by planar and SPECT studies

Examples of planar and SPECT images are shown in Figure 3. The anatomical gradings of each kidney in all



Grade II Grade III Grade IV

Fig. 3 Examples of the scintigrams of grade II, III and IV. Upper columns: planar images. Lower columns: SPECT images without renal axis correction.

Table 2 Distribution of scintigraphic grade for renal parenchymal uptake defects by ^{99m}Tc-DMSA planar and SPECT studies

	Scintigraphic Grades							
	0	I	II	III	IV	Total	V	No study
Planar	236 (53%)	47 (11%)	43 (10%)	60 (13%)	60 (13%)	446	12	0
SPECT	133 (36%)	34 (9%)	82 (22%)	73 (20%)	46 (13%)	368	12	78

patients by scintigraphy are summarized in Table 2. Twelve kidneys were not visualized on planar and SPECT images; 11 due to nephrectomy and one to congenital agenesis. One-hundred and sixty-three out of 446 kidneys (36.5%) showed grades II, III and IV on planar images. In SPECT studies, 201 out of 368 kidneys (54.6%) showed positive scintigrams of grades II, III and IV. SPECT scans were not performed in 39 patients most of whom were studied in 1988. Comparison of scintigraphic grades in kidneys examined by both planar and SPECT studies is shown in Table 3. Out of 368 kidneys 128 (35%) were graded as 0 in both studies, 11 (3%) grade I, 26 (7%) grade II, 46 (13%) grade III and 46 (13%) grade IV. Coincidence in the scintigraphic grades on both images was 70% (257/368 kidneys). SPECT images showed higher grades than planar images in 104 kidneys (28%). In contrast, the SPECT image was lower than the planar in the grading in only 7 kidneys. All parenchymal defects in this last group were located in the lateral border of the kidneys and were mostly equivocal or small in size. The anatomical evaluation by planar and SPECT images was significantly different in the chi-square test ($p < 0.001$).

Regional localization of the parenchymal uptake defects was evaluated in 72 kidneys which had the same scintigraphic grade (II and III) in planar and SPECT studies. More than 90% of defects were shown in both upper and lower poles of both kidneys (Fig. 4).

Table 3 Correlation of scintigraphic grade by ^{99m}Tc-DMSA planar and SPECT studies

		Planar Image					
		0	I	II	III	IV	Sum
	0	128	4	1	0	0	133
	I	23	11	0	0	0	34
SPECT	II	40	14	26	2	0	82
	III	13	7	7	46	0	73
	IV	0	0	0	0	46	46
	Sum	204	36	34	48	46	322

Parenchymal Uptake of ^{99m}Tc-DMSA

Because the renal function of the diseased kidney may be affected by the preserved renal function of the contralateral kidney, analysis was performed only in the kidneys which classified as the same grade bilaterally. Twenty-

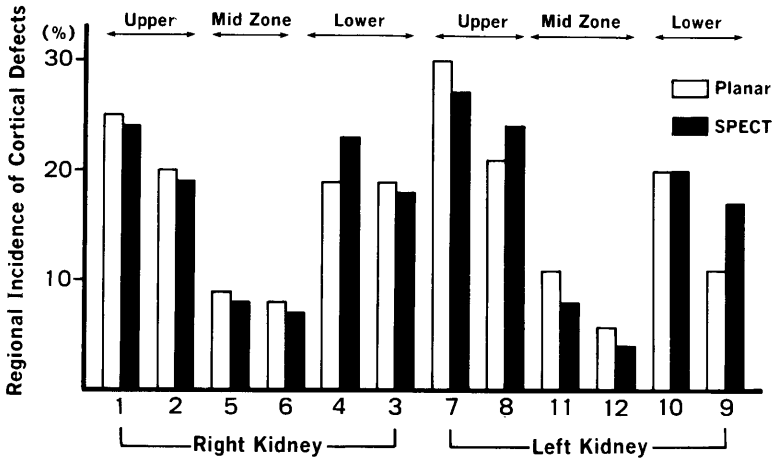


Fig. 4 Regional incidence of renal parenchymal uptake defects in planar and SPECT studies. The number of the renal segment is corresponding to that shown in Figure 2.

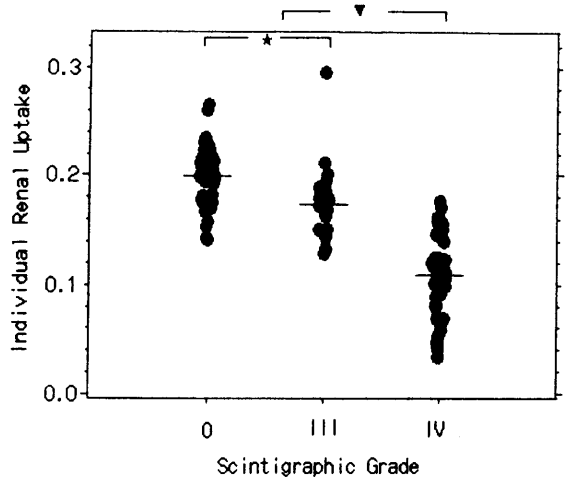


Fig. 5 Renal uptake per injected dose of ^{99m}Tc-DMSA by individual kidney at 2 hour-postinjection in scintigraphic grade 0, III and IV (★: $p < 0.004$, ▼: $p < 0.0001$).

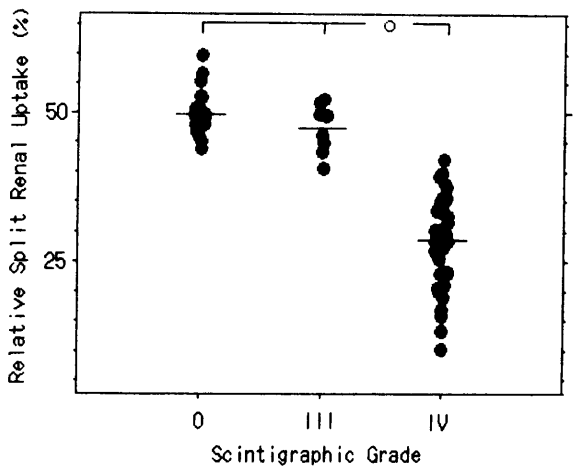


Fig. 6 Relative split renal uptake by the right kidney alone in grade 0 and III, and by the kidney of grade IV (○: $p < 0.001$).

five paired kidneys were normal bilaterally on both planar and SPECT studies. The renal uptake of ^{99m}Tc-DMSA per injected dose in these 50 kidneys was 0.199 ± 0.026 (mean ± sd) (Fig. 5). The paired kidneys which showed the same grade of I or II was only 2 (4 kidneys). These kidneys were excluded for analysis, because the number was not enough for statistical analysis. Of 46 kidneys in grade III, 18 kidneys in 9 patients were equal. The renal uptake of ^{99m}Tc-DMSA per injected dose in these 18 kidneys was 0.173 ± 0.039. The mean uptake between kidneys with grade 0 and III was significantly different in the Student's t-test ($p < 0.004$). Of 46 kidneys which were considered as grade IV, only 6 kidneys in 3 patients were of identical grade and 3 individual kidneys were very small in size and their split renal uptake was less than 10%. The renal uptake in all 43 grade IV kidneys, except 3 extremely contracted kidneys, was 0.106 ± 0.027. The uptake value was significantly lower than those in grade 0 and III ($p < 0.0001$). The relative split renal uptake of the kidneys in grades 0, III and IV was compared (Fig. 6). Relative split renal uptake of the right kidney in grades 0 and III ranged from 43.8 to 59.6% and 40.4 to 52.2%, respectively. The mean was $49.7 \pm 3.4\%$ in grade 0 and $47.5 \pm 4.1\%$ in grade III. In grade IV, it ranged between 10.3 and 42%, and the mean was $28.2 \pm 7.8\%$. The mean values for grade 0 or III and IV were significantly different in the Student's t-test ($p < 0.001$).

Grades of VUR vs. grades of parenchymal damage

VUR in each kidney was scored into five grades by voiding cystoureterography according to the Dwoskin-Perlmutter's classification.[1] When more than one study

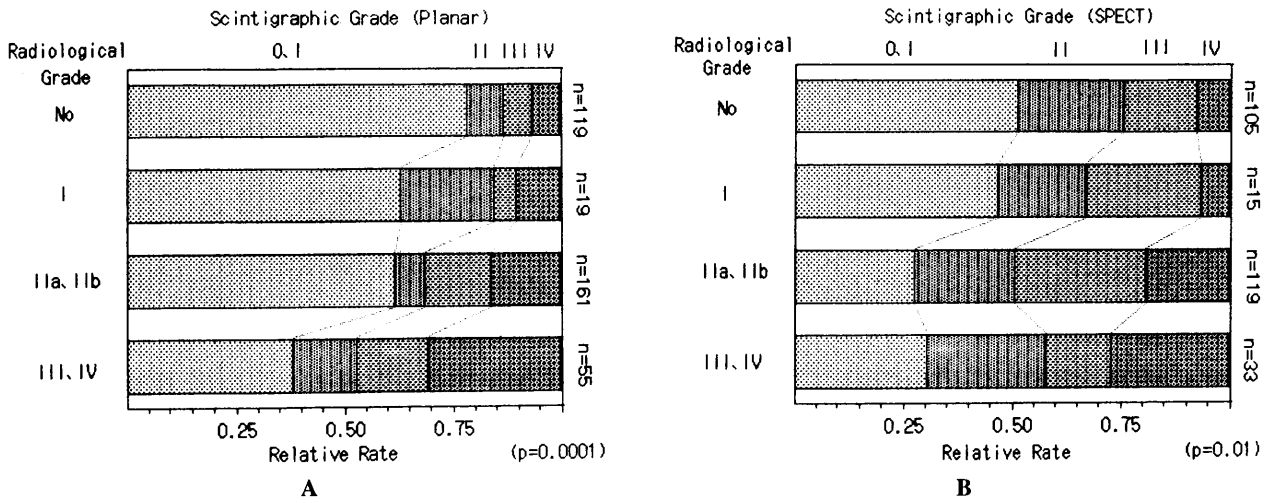


Fig. 7 Grade of VUR by cystourethrography vs. structural damage graded by scintigraphy. A: Planar study, B: SPECT study.

was performed, the maximum grade for VUR during the follow-up of the patient was employed here. Cases where the grade of VUR was unknown were excluded from analysis. The relative incidence of parenchymal uptake defects increased with higher grades of VUR (Fig. 7), but the grades of VUR by voiding cystoureterography were significantly different from the grades of parenchymal anatomical damage by planar ($p < 0.0001$) and SPECT studies ($p < 0.01$).

DISCUSSION

The planar image was abnormal in 163 out of 446 kidneys (36.5%), showing higher scintigraphic grades than I. SPECT was abnormal in 201 out of 368 kidneys (54.6%). SPECT studies were therefore about 1.5 times more successful in the pick-up rate for regional parenchymal damage than planar studies. This is comparable to our previous results.[12] Joseph et al.[14] reported that the identification of renal parenchymal defects with ^{99m}Tc-glucoheptonate was 59% by planar, 83% by SPECT and pin-hole imaging.[14] SPECT studies compared with planar images increased the detection of parenchymal abnormalities by approximately 1.4 fold, although all 3 combined studies were required to obtain 100% sensitivity.

Most of the regional parenchymal damage detected by scintigraphy was localized in both the upper and lower poles of the kidney. This suggests that the parenchymal damage in VUR may be primarily related to the reflux of infected or sterile urine in compound or refluxing papillae shown in upper and lower regions of the pelvis.[15-18] The knowledge of localization of regional parenchymal damage is helpful when reading the ^{99m}Tc-DMSA scintigram.

Comparison of renal parenchymal damage by scintigraphic imaging and histopathology in removed kidneys of acute pyelonephritis in piglets showed no false positive results.[19,20] A SPECT study may be helpful in the detection of renal parenchymal damage when small in size and which cannot be revealed by a planar study. Several factors, however, may limit the clinical application of SPECT for identifying renal parenchymal damage. In general, the SPECT technique is a sophisticated method for enhancing contrast resolution (or increasing sensitivity) but it may cause false positive results (or decrease specificity).[21] The false positive results have been reported as 10% in the literature on renal space occupying lesions.[22] Hydronephrosis alone also produces appearances resembling renal scars on a planar image.[23] In our experience, DMSA uptake in a thin cortex due to hydronephrosis was so prone to being affected by the partial volume effects in SPECT that it appeared as decreased uptake areas mimicking renal scars. In this context, regional uptake defects which are demonstrated by DMSA scintigraphy may include not only renal scars but also some false positives and other abnormalities as cited above, particularly in heterogeneity of the population studied here. Therefore, it will be further discussed whether ^{99m}Tc-DMSA SPECT scintigraphy can enhance sensitivity for the diagnosis of parenchymal damage with minimal or no effect on specificity.

The incidence of parenchymal damage increased with the high grade of VUR on voiding cystoureterography, but the grading systems for VUR and parenchymal damage were significantly different. This means that scintigraphy is complementary to the grading of VUR on evaluating parenchymal damage in a patient with UTI and/or VUR.

In conclusion, the grading system proposed by Monsour et al.[10] for ^{99m}Tc-DMSA planar scintigraphy is feasible for use in SPECT studies. A SPECT study is a more sensitive and sophisticated technique for the detection of structural renal parenchymal damage than a planar study, although somewhat complicated image processing and expertise are required for identification of the structural abnormali-

ties in the diseased kidney. ^{99m}Tc-DMSA planar and SPECT scintigraphy complement the grading system by voiding cystourethrography and are helpful for qualitative and quantitative evaluation of the diseased kidney.

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