Monitoring of renal function using $^{99m}$Tc-DMSA and $^{99m}$Tc-DTPA scintigraphy in patients with spinal cord injury

H. Tuna, T.F. Čermik, F. Tuna

Department of Nuclear Medicine, Hospital of the University of Trakya, Edirne, Turkey
Department of Physician Medicine and Rehabilitation, Hospital of the University of Trakya, Edirne, Turkey
Clinic of Nuclear Medicine, Istanbul Training and Research Hospital, Istanbul, Turkey
Edirne State Hospital, Edirne, Turkey

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A B S T R A C T

Aim: The aim of this study was to assess the degree of alterations of renal function by using $^{99m}$technetium dimercaptosuccinic acid ($^{99m}$Tc-DMSA) and $^{99m}$technetium diethylenetriaminepentaacetic acid ($^{99m}$Tc-DTPA) scintigraphy in spinal cord injury (SCI) patients.

Material and methods: Twenty-two consecutive SCI (15 paraplegic and 7 tetraplegic) patients (mean age: 49.1 ± 13.4 years) who had no urinary symptoms participated in this prospective study. The mean duration of injury was 45.6 ± 48.8 months before. Sixteen patients had at least one urinary tract infection history. Renal cortical scintigraphy with $^{99m}$Tc-DMSA, radionuclide renography with $^{99m}$Tc-DTPA and renal ultrasound were performed within 2-week period.

Results: Four (18%) patients had serious pathology on their kidneys such as unilateral or bilateral parenchymal scarring and increased background uptake in their renal cortical scintigraphy with $^{99m}$Tc-DMSA. Two of them had grade 3–4 pelvicaliceal ectasia on ultrasound. Additionally, 2 of 18 remaining patients had grade 2 pelvicaliceal ectasia on ultrasound. Sixteen (73%) patients had markedly delayed or delayed and decreased functions of one or both of kidneys on radionuclide renography. However, only four patients had grade 2–4 pelvicaliceal ectasia and none of them had a finding of loosening of renal parenchyma.

Conclusion: Combined use of renal cortical scintigraphy and radionuclide renography appears to be contributary to renal ultrasound in the long-term follow-up of patients with SCI. Patients with abnormal findings should be closely followed, and early therapeutic interventions may enable lower morbidity and mortality rates in these patients.

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Monitorización de la función renal mediante gammagrafía $^{99m}$Tc-DMSA y $^{99m}$Tc-DTPA en pacientes con lesión de la médula espinal

R E S U M E N

Objetivo: El objetivo de este estudio fue evaluar el grado de alteración funcional renal mediante el estudio gammagráfico con $^{99m}$Tc-ácido demercaptosuccínico ($^{99m}$Tc-DMSA) y $^{99m}$Tc-ácido dietilentriaminopentaácido ($^{99m}$Tc-DTPA) en pacientes con lesión de médula espinal (SCI).

Material y métodos: Estudio prospectivo que incluye a 22 pacientes consecutivos con SCI (15 parapléjicos y 7 tetrapléjicos) (media de edad: 49,1 ± 13,4 años) sin síntomas urinarios. La lesión medular se había producido hacía, 45,6 ± 48,8 meses. Diecisésis pacientes tenían al menos historia de infección del tracto urinario. La gammagrafía renal con $^{99m}$Tc-DMSA, el renograma con $^{99m}$Tc-DTPA y la ecografía renal se realizaron en un periodo de 2 semanas.

Resultados: En la gammagrafía cortical con $^{99m}$Tc-DMSA 4 pacientes (18%) presentaron alteraciones severas, unilaterales o bilaterales, en el parénquima renal y aumento de la captación de fondo. Dos de ellos tenían ectasia pielocalicial grado 3–4 en la ecografía. Además, 2 de los 18 pacientes restantes tenían ectasia pielocalicial grado 2 en la ecografía. En el renograma con $^{99m}$Tc-DTPA 16 pacientes (73%) presentaron retraso, o retraso y disminución de la función, en uno o en los 2 riñones. Sin embargo, solo 4 pacientes tenían ectasia pélvica grado 2 a 4 y ninguno de ellos, cicatrices corticales.

Conclusión: El uso combinado de la gammagrafía cortical renal y el renograma con radiotrazadores puede contribuir, junto con la ecografía, en el seguimiento a largo plazo de pacientes con SCI. Los casos con alteraciones en la gammagrafía o en el renograma deben tener un seguimiento más estrecho; de este modo, un tratamiento adecuado precoz puede reducir la morbimidad y la mortalidad en este tipo de pacientes.

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* Corresponding author.
E-mail address: tfermik@yahoo.com (T.F. Čermik).

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Introduction

Traumatic spinal cord injury (SCI) is a neurological disorder where there is a complete or partial disconnection of efferent motor and afferent sensory tracts in the spinal cord. Depending on the level and the extent of disconnections, motor and sensory function deficits such as tetraplegia or paraplegia may ensue. Neurogenic bladder is a major cause of morbidity or mortality in patients with SCI.1,2 Some of patients with SCI may suffer upper urinary tract problems such as urinary tract infections, stone formation, and diagnosis of these renal problems may be difficult. For these reasons, periodic urological surveillance for SCI patients has provided a significant decline in morbidity and mortality rates.3 Annual tests recommended for screening of renal diseases in SCI patients include physical examination, renal ultrasound, abdominal radiograms and laboratory tests such as serum creatinine, electrolytes and creatinine clearance.

Renal cortical scintigraphy with 99mTc- dimercaptosuccinic acid (99mTc-DMSA) and radionuclide renography with 99mTc-diethylenetriaminepentaacetic acid (99mTc-DTPA) is commonly used in daily practice for assessment of functional morphology, perfusion and excretion of kidneys. These imaging techniques have a number of advantages over intravenous urography, such as no need for bowel preparation, much lower radiation doses, and no reported toxic reactions.99mTc-DMSA is an excellent renal cortical imaging method, because approximately 40–50% of the administered dose accumulates in the tubular cells after 6–7 h, providing excellent visualization of the renal cortex, after background activity has been cleared. Renal cortical scintigraphy with 99mTc-DMSA is used for both reliable diagnosis of acute pyelonephritis and detection of presence of renal cortical scarring.4–6 On the other hand, 99mTc-DTPA is excreted solely by glomerular filtration and it has a rapid clearance with a biological half-life of 1–2 h.7 99mTc-DTPA can be used to determine individual renal function and also any presence of obstruction of collecting system.

The aim of this study was to assess the degree of alterations of renal function as visualized by renal cortical scintigraphy by using 99mTc-DMSA and radionuclide renography by using 99mTc-DTPA, and also to compare the results of scintigraphic and ultrasonographic findings in SCI patients.

Material and methods

Patients

Twenty two consecutive SCI patients (18 males, 4 females) who had no urinary symptoms during ultrasound and scintigraphic studies, ranging in age 18–66 years (mean age: 49.1 ± 13.4 years) participated in this prospective study. The patients group consisted of 15 paraplegic and 7 tetraplegic patients. The mean duration of injury was 45.6 ± 48.8 months before (range 3–216 months). Six (86%) patients of tetraplegia and 10 (67%) patients of paraplegia had at least one urinary tract infection history. There was no history of urinary tract infections of remaining 6 (27%) patients in the study group (pts: T6, P10, P11, P16, P17, P19). The local ethics committee approved this investigation and each patient gave informed consent prior to participation in the study.

Clinical and sonographical assessments

The level and extent of motor and sensory deficits of patients were assessed according to the protocol of the American Spinal Injury Association (ASIA) (www.asia-spinalinjury.org; ASIA, 2002). The patients’ ASIA scale and clinical data are shown in Table 1. In all patients, serum urea and creatinine levels were normal. Renal ultrasound was performed with available gray-scale equipment by using a 3.5 MHz transducer. All patients underwent ultrasound study when their bladders were physiologically full. Kidney dimensions and parenchymal thickness were measured and parenchymal or pelvicaliceal abnormalities were noted in the sonographical evaluations. Renal ultrasound and both scintigraphic imaging were performed within 2-week period.

Renal cortical scintigraphy

Patients were injected 150 ± 15 MBq 99mTc-DMSA via antecubital vein; 3 h after injection of the radiotracer, planar images were obtained in eight projections; including anterior, posterior, left lateral, left anterior and posterior oblique, right lateral, left anterior and posterior oblique, with 5 min images or 500,000 counts per image in a 128 × 128 matrix. A double-head gamma-camera with a low-energy high-resolution parallel-hole collimator and data analysis system (E-Cam, Siemens Inc., Erlangen, Germany) was used for imaging. Scintigraphic images were examined by the same nuclear medicine physician who was unaware of the clinical, laboratory data and US results. For semi-quantitative analysis, this static scintigraphic method allows relative measurements of kidney function without absolute quantitative information. This method allows the examination of split uptake, which is between 45 and 55% of the total function in healthy subjects. Irregular regions of interest were drawn manually around both kidneys and split renal functions (SF%) of each kidney were calculated using the following formula; for right kidney SF% = right kidney uptake/(right kidney uptake + left kidney uptake) × 100; for left kidney SF% = 100% – right kidney SF%.

Radionuclide renography

Within 1 week after the sonography, patients underwent renal scintigraphic imaging. The patients were given no special bowel preparation, and diuretics, ACE inhibitors, and other drugs that may alter renal functions were stopped at least 2 days before 99mTc-DTPA renal studies. Patients were well hydrated before the imaging to provide normal urine flow. For scintigraphic imaging, a double-head gamma-camera (E-Cam, Siemens Inc., Erlangen, Germany) with a low-energy high-resolution parallel hole collimator was used. After an intravenous bolus injection of 260 ± 20 MBq 99mTc-DTPA, perfusion images were obtained every 2 s for the first minute, every 15 s between 1 and 4 min and followed by acquisition dynamic images every 2 min for 30 min with the patients in a supine position and with detector placed in a posterior view. At 15th minute post-injection urine excretion was stimulated with 20 mg furosemide administered intravenously. Images were collected into a 64 × 64 matrix in word mode. The energy window around the 140 keV photon peak of 99mTc was 20%. After dynamic imaging, bladder catheterization was applied and 10 min later, single 5 min anterior view “late images” were obtained for both kidneys in supine position.

For semi-quantitative analysis, four regions of interest were drawn manually around the both kidneys and background areas on summation images. A time–activity curve of each kidney was constructed. On the basis of the time–activity curves, following functional parameters were calculated for each kidney. T_{max}: the time of peak (min.) renal parenchymal activity after the injection and T_{1/2}: the half-time (min.) of parenchyma activity after the peak. T_{max} was divided to in 4 categories; normal: ≥ 5 min, mildly delayed: between 5 and 8 min, moderately delayed: between 8 and 11 min and markedly delayed: over 11 min. T_{1/2} was divided to in 4 categories; normal: ≥ 10 min, mildly delayed: between 10 and 20 min, moderately delayed: between 20 and 30 min and markedly delayed: over 30 min.
Patients' characteristics are shown in Table 1. Twelve of 22 patients' renal ultrasound have been reported completely normal and 2 patients had only simple renal cysts. One patient had grade 1 pelvicaliceal ectasia in one kidney and 2 patients had grade 1 pelvicaliceal ectasia in both kidneys. Four patients had grade 2–4 pelvicaliceal ectasia. Detailed ultrasonographic findings of all patients are listed in Table 2. Remaining one patient had a calculus in one kidney. There were no ultrasonographic findings in 6 patients with no history of urinary tract infections.

Renal cortical uptakes of 8 of 16 patients with history of urinary tract infections have been accepted normal, but both of their kidneys had mild pelvicaliceal ectasia on the $^{99m}$Tc-DMSA scintigraphy. Three patients had a moderately diminished uptake in medial parts of both kidneys on the $^{99m}$Tc-DMSA scintigraphy, these findings were due to pelvicaliceal ectasia and urinary stasis. Same pathology was shown in 5 more patients, but these findings were limited to one kidney in these patients. Remaining 4 patients had serious pathology on their kidneys such as unilateral or bilateral parenchymal scarring and increased background uptake (pts: T5, P8, P9 and P18) (Table 3). All of these 4 patients had history of at least one urinary tract infection. On the other hand, $^{99m}$Tc-DMSA scintigraphy was demonstrated normal size and uptake in 6 patients who had no abnormal sonographic findings.

Twenty patients have normal blood flow in their $^{99m}$Tc-DTPA scintigraphy. Only 2 patients had a moderately or markedly decreased blood flow of both kidneys. However, all patients were demonstrated delayed or delayed and decreased renal functions (filtration and excretion) in visual and semi-quantitative assessments of images. Sixteen (73%) of these patients had markedly delayed or delayed and decreased functions of one or both of kidneys on radionuclide renography. However, after bladder catheterization none of these patients had stasis in the pelvicaliceal or parenchymal area in late images and none of our patients had obstructive uropathy. Detailed findings of $^{99m}$Tc-DTPA scintigraphy are presented in Table 4, Figs. 1 and 2.

### Discussion

Upper urinary tract abnormalities such as hydronephrosis, vesicoureteral reflux and pyelonephritis were reported in approximately 25% of patients with SCI.8 These problems can damage the kidney and ultimately lead to renal insufficiency.

Monitoring of kidneys and urinary tract can cause early intervention, decrease long-term morbidity and significantly increase life expectancy.9–12 There is no consensus for the follow-up imaging flow chart, but sonography, voiding cystoureography, intravenous urography, urinary tract radiography, and scintigraphic imaging techniques have got area of usage.12–14 Retrospective studies using renal ultrasound reported that there were renal abnormalities in 7%–8% of SCI patients.15,16 On the other hand, it has a relatively high sensitivity in detecting pelvicaliceal ectasia, but a low sensitivity in detecting renal scars,17,18 also renal ultrasound was found effective in SCI patients only who had genitourinary symptoms.18,19 Our study group was consisted of patients with no urinary symptoms during the study, and ultrasound was showed renal abnormalities in 27% (grade 2–4 pelvicaliceal ectasia in 4 patients, calculus in 1 patient and reduced kidney sizes in 1 patient). None of these abnormalities were required therapeutic interventions.

$^{99m}$Tc-DMSA scintigraphy is the most useful renal imaging procedure for detecting acute pyelonephritis and the presence of renal cortical scarring.5,6 It can distinguish acute pyelonephritis from extrarenal reasons of fever such as decubitus ulcers or osteomyetilis. Limited number of studies about the role of renal cortical scintigraphy in SCI patients has published in the literatures. Kao et al.20 reported that $^{99m}$Tc-DMSA scintigraphy is useful in distinguishing acute pyelonephritis from chronic bacteriuria in patients with SCI. There were established unilateral or bilateral...
multiple cortical scarring in kidneys of 4 (18.2%) patients. These findings had not been noted in sonographical assessment. Therefore, renal cortical scintigraphy has a complementary role not only in the evaluation of urosepsis secondary to acute pyelonephritis but also in detection of cortical scarring in SCI patients. However, sonography and \(^{99m}\)Tc-DMSA scintigraphy had normal findings in patients with no history of urinary infections in our study group. For this reason, we suggest that \(^{99m}\)Tc-DMSA scintigraphy is not necessary in SCI patients without urinary tract infection history.

The study of Lloyd et al.\(^{21}\) in 1981 is one of the first studies using a radionuclide renographic method in SCI patients. Kuhlemeyer et al.\(^{22,23}\) reported that renal clearance of \(^{131}\)I-orthoiodohippurate was not significantly changed with duration of disease in SCI patients. Their data showed qualitatively effective renal plasma flow decreased in following period. Tempkin et al.\(^{24}\) concluded that radionuclide renography detected renogram abnormalities in 86% of the SCI patients. The most common abnormality was the delay of excretion from renal cortex and pelvis, and anticholinergic medications significantly reduced these excretion delays.
Table 4
Tc-99m DTPA scintigraphy findings of patients.

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Klingensmith et al.\textsuperscript{14} reported that significantly decreased $^{99m}$Tc-MAG3 effective renal plasma flow occurred in tetraplegic patients more than paraplegic patients after 2 years of SCI. $T_{\text{max}}$ was calculated significantly delayed for SCI patients compared to normal subjects. In our study, all of the patients have delayed and 73% of them have markedly delayed $T_{1/2}$ and or delayed $T_{\text{max}}$ of one or both of kidneys on radionuclide renography. These abnormalities can be sensitive indicators of SCI patients with early renal deterioration.\textsuperscript{24,25} However, we could not demonstrate any adverse effect of delayed $T_{1/2}$ and $T_{\text{max}}$ on the renal parenchyma in our patients group.

The design of the present study had some limitations. Some of them are patients’ number and wide range of injury period. We believe that analysis of higher numbers of patients can provide more detailed information about the effect of duration after injury. Another limitation is absence of voiding cysto-ureterogram or vesicoureteral reflux scintigraphy studies. Thus, urinary bladder abnormalities and presence of reflux could not be evaluated. These two imaging techniques are invasive methods compared to renal cortical scintigraphy and radionuclide renography. For this reason, we did not prefer to add these imaging techniques in our study protocols.

Fig. 1. A 48-year-old male paraplegic patient (pt. 9 in Tables 1–4) having level L1 incomplete lesion. In renal sonography, there was no parenchymal abnormality on kidneys but he has a 14 mm calculus in the left kidney pelvis. Images of $^{99m}$Tc-DMSA scintigraphy showed loss of normal renal outline and scarring in the middle part of left kidney (arrows) (A: anterior, P: posterior, RPO: right posterior oblique, LPO: left posterior oblique, RL: right lateral, LL: left lateral, RAO: right anterior oblique, LAO: left anterior oblique).
Tables 1–4) having level L2 complete lesion without parenchymal abnormality in renal sonography. Images of 99mTc-DTPA scintigraphy showed normal perfusions of kidneys. But right kidney demonstrated delayed filtration and mildly delayed excretion; left kidney functions demonstrated markedly delayed filtration and moderately delayed excretion. There was no finding of obstructive uropathy.

**References**


**Conflict of interests**

The authors have no conflict of interests to declare.

**Conclusion**

This study described the renal cortical pathology and impaired parameters of renal function using scintigraphic methods in SCI patients who had no evidence of renal diseases. Renal cortical scintigraphy appears to be contributive to ultrasound in long-term follow-up of patients with SCI who had history of urinary tract infections. Patients with abnormal findings on corticograms should be closely followed, and therefore early therapeutic interventions may enable lower morbidity and mortality rates in these patients. However, clinical importance of impaired parameters of renal functions on radiouclide renograms is not clear yet. We think that using repetitive radionuclide renograms in studies of large series of SCI patients may be useful to reveal impaired $T_{1/2}$ and $T_{max}$ values.

**Fig. 2.** A 46-year-old male paraplegic patient (pt. 11 in Tables 1–4) having level L2 complete lesion without parenchymal abnormality in renal sonography. Images of 99mTc-DTPA scintigraphy showed normal perfusions of kidneys. But right kidney demonstrated delayed filtration and mildly delayed excretion; left kidney functions demonstrated markedly delayed filtration and moderately delayed excretion. There was no finding of obstructive uropathy.