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Original article

Spectrum of Disorders Diagnosed on 99mTc-MAG3 Radioisotope Renography: A Report of 260 Saudi Arabian Patients

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Abstract

Background: Diuretic renography using 99mTc-mercaptoacetyltriglycine (99mTc-MAG3) is a relatively non-invasive technique and has been increasingly used as a reliable technique for the evaluation of kidney function in a wide range of kidney disorders. ***Methods:*** In this retrospective study, we retrieved the medical records of patients referred to the Radiology Department of Radiology, King Abdulaziz Specialist Hospital, Taif, Saudi Arabia, with suspected kidney disease and underwent 99mTc-MAG3 diuretic renography during January 2020 to November 2021. ***Results:*** The medical records of 260 patients were retrieved. Most of the patients had either suspected obstructive (n = 80; 30.7 %) or non-obstructive hydronephrosis (n = 60; 23.1 %). The left kidney was affected in more than half of the patients (n = 155; 59.6 %). In terms of split kidney functions, the right kidney had a median function of 50.9 (38.5–75.5); overall, 39 patients (69.6%) had good right kidney function. The left kidney had a median function of 49.4 (24.5–61.5); overall, 33 patients (58.9%) had good left kidney function. ***Conclusion:*** Radioisotope renography is useful for assessing kidney functions in real-life settings. The present study's results indicate that radioisotope renography using 99mTc-MAG3 is helpful in the visual interpretation of kidney failure, obstructive uropathy and kidney stenosis.

Keywords: ***Radioisotope Renography, Kidney Function, Utility, MAG3, Nuclear Medicine, Urology Department.***

1. Introduction

Kidneys play a crucial role in maintaining the body's normal physiological function and homeostasis through excretory and hormonal properties. A proper assessment of kidney function remains a cornerstone during routine evaluation of several kidney disorders [1]. Historically, radiological evaluation has played a limited role in the assessment of kidney functions compared with biochemical measurements. Its use was mainly for assessing anatomic changes in kidney size and density and parenchymal alterations [2]. However, the past few decades have witnessed dramatic improvements in our understanding of kidney functions and radiological techniques, which have led to the emergence of novel imaging modalities to evaluate functional changes within the kidneys [3]. Advanced modalities, such as contrast-enhanced ultrasound (CEUS), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), have been widely studied to assess their utility in detecting kidney perfusion, oxygen delivery, and glomerular filtration [3-7]. Besides, imaging-assisted assessment of the adequacy of kidney excretion of electrolytes and metabolites has become possible with the introduction of sodium and hyperpolarized MRI [1]. Moreover, MRI sequences, CEUS, and CXCR4-targeted PET have gained popularity as reliable alternatives to kidney biopsy for the detection of kidney inflammation and fibrosis [8-10].

Nonetheless, despite the potential of these novel modalities in evaluating kidney functions, they face several challenges in their clinical applications due to high cost, limited availability in many centers, complexity, and risks of radiation exposure posed by some of these modalities [1]. Diuretic renography is a simple, non-invasive test for the dynamic assessment of kidney obstruction and functions initially described in the late 1950s. This modality is based on real-time scanning of an intravenously administrated radiopharmaceutical agent via dynamic kidney scintigraphy (DRS) to draw activity curves for kidney functions [11]. Diuretic renography provides both qualitative and quantitative measures of kidney functions, such as the relative function of each kidney and the time of the peak of the renographic curve (Tmax) [12]. Out of several radiopharmaceutical agents, such as 99mTc-mercaptoacetyltriglycine (99mTc-MAG3) and 123I-OIH, are available for diuretic renography, 99mTc-MAG3 remains the most widely utilized agent in the assessment of kidney functions due to its higher excretion rate than other agents [13].

A growing body of evidence has demonstrated the utility and reliability of 99mTc-MAG3 diuretic renography in a wide range of kidney disorders, such as identifying kidney obstruction, uropathy, hydronephrosis, and after chemotherapy [11-14]. The vast majority of the agent (95%) is excreted by the proximal kidney tubules, which permits real-time evaluation of the excretory functions of the kidney, as well as the assessment of any obstruction in the kidney flow through the pelvicalyceal system and bladder [12]. The 99mTc-

MAG3 agent has been proven for safe use in both children and adults [13]. In addition, 99mTc-MAG3 has shown higher binding affinity to protein, leading to slow plasma clearance, which in turn resulting in high-quality imaging regardless of kidney failure [11]. I It is usually preferred over the other agents (such as Tc-99m DTPA) due to its high plasma clearance value (40%) and a shorter half-life, making it more practical to evaluate kidney function. Recent consensuses have been published over the past two decades by international societies to standardize radioisotope renography procedures [15]. There are several indications for 99mTc-MAG3 diuretic renography, including suspected obstructive uropathy in both symptomatic and asymptomatic patients, as well as for assessing the degree of kidney function in patients with nephropathy. However, 99mTc-MAG3 diuretic renography should be performed only when there is sufficiently reliable serial imaging. In a 2013 report by Yousef et al., nearly 28% and 16% of patients who underwent radioisotope renography at Khartoum University Hospital had the abnormal right and left kidney function, respectively [16].

To date, there is a scarcity of real-world data regarding the utilization of 99mTc-MAG3 radioisotope renography for the evaluation of kidney function in clinical settings. Thus, we aimed to provide a single-center experience regarding the utility of 99mTc-MAG3 radioisotope renography in assessing kidney functions among patients presenting with kidney diseases.

3. Materials and Methods

The present study was conducted in the Department of Radiology, Kind Abdulaziz Specialist Hospital, Taif, Saudi Arabia. All the procedures in the study were conducted in accordance with the ethical standards of Institutional Ethical Committee [Directorate of Health Affairs, Taif, Health Committee no KACST, KSA: HAP-02-T-067] and Helsinki Declaration of 1975, as revised in 2008. The design of the study was retrospective so patient informed consent was waived. The preparation of the current manuscript complies with the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

3.1. Study Design

In this retrospective study, we retrieved the medical records of patients who were referred to the Radiology Department of Kind Abdulaziz Specialist Hospital, Taif, Saudi Arabia from a period of 01.01.2020 to 30.11.2021. There were no restrictions regarding the age of the patients or their nationality. We included only records with complete documentation of both kidneys' split-function results and anatomic findings. Patients were excluded in cases of poor quality of the obtained curves of the diuretic renography, documented interruption of imaging acquisition, and short imaging protocol. The referral suspected kidney disease patients were scheduled to undergo 99mTc-MAG3 diuretic renography. Only adult patients were enrolled in this study.

Inclusion Criteria

i) The patients with kidney disorder and complete history documentation.
ii) The patients with complete work of kidney function panel.

Exclusion Criteria

i) The patients with poor quality of the obtained curves of the diuretic renography.
ii) The patients with documented interruption of imaging acquisition.
iii) The patients with incomplete short imaging protocol.
iv) Pediatrics

3.2. Data Collection and Diuretic Renography Protocol

Clinico-Biological features including demographic characteristics, case history of kidney failure, complete kidney function tests, and the quantitative results of the diuretic renography, including split function in %, glomerular filtration rate (GFR), MAG3 clearance rate, and Tmax data was retrieved from the enrolled patients (n=260). All diuretic renography procedures were performed in concordance with the standardized in-house protocol followed in the Department of Radiology using GE Healthcare scintillation cameras equipped with low-energy general-purpose collimators (LEGP). Before the imaging acquisition procedure, the patients were instructed to follow the standard renography procedure (Drinking water and urination before 30 mins of image acquisition). Then, the patients were positioned supine and injected with an intravenous bolus dose (75 MBq) of 99mTc-MAG3, followed by the injection of furosemide 20 mg 10 min later. The imaging acquisition lasted for 10–20 min using 128 × 128 matrices in posterior view and was followed by post-micturition images in an upright position. The images were analyzed using Hermes Gold (Hermes Medical Solutions, Stockholm, Sweden) software.

3.3. Statistical Analysis

For the descriptive statistics, median with interquartile range (IQR) and frequencies with percentages were used in this study. The normality of the data was checked using Shapiro–Wilk test. Student's t-test and Mann–Whitney tests was performed for normally and non-normally distributed data respectively. The statistical significance level of $p<0.05$ and all the statistical tests were two-tailed tests. All statistical tests were performed on an SPSS ("Statistical Package for the Social Sciences") data analysis software system, version 28, IBM.

4. Results

The medical records of 260 patients were retrieved. The median age of the cohort was 33 years (23–48) and included 145 (55.8%) female patients (M:F=1.2:1). The majority of the patients had either suspected obstructive hydronephrosis (n = 80; 30.7 %) or non-obstructive hydronephrosis (n = 60; 23.1%) (Table 1) and (**Figure 1**). The other abnormalities found in the decreasing order of frequency included atrophic kidney (n=25, 9.6%), Pelviureteric junction PUJ obstruction and pyeloplasty (n=15, 5.7% each), kidney failure (n=20, 7.7% each), hypoplastic kidney, renovascular hypertension, pelvic dilatation, kidney stone disease, (n=10, 3.8% each) and kidney transplant (n=5, 1.9%).

The left kidney was affected in more than half of the patients (n = 155; 59.6 %). Nearly 23 % of the patients (n = 60) underwent diuretic renography. In terms of split kidney functions, the right kidney had a median function of 50.9 (38.5–75.5); overall, 39 patients (69.6%) had good right kidney function. On the other hand, the left kidney had a median function of 49.4 (24.5–61.5); overall, 33 patients (58.9%) had good left kidney function (**Figure 2**).

The medical records largely lacked the findings of other parameters, such as GFR and Tmax. The data pertaining to the median GFR was available in 80 patients - [median GFR=81.7 (63.3–104)].

Table 1: Characteristics of the patients cohort (n=260).

Variables	Patients (n =260)
Age, median (IQR)	33 (23 – 48)
Female, N (%)	
145 (55.8 %)	
Male, N(%)	

115 (44.2 %)	
Suspected diagnosis, N (%)	
Obstructive hydronephrosis	80 (30.7 %)
Non-obstructive hydronephrosis	60 (23.1 %)
Atrophic kidney	25 (9.6 %)
PUJ Obustrction	15 (5.7 %)
Pyeloplasty	15 (5.7 %)
Kidney failure	20 (7.7 %)
Renovascular hypertentsioin	10 (3.8 %)
Hypoplastic kidney	10 (3.8 %)
Pelvic dilatation	10 (3.8 %)
Kidney stone disease	10 (3.8 %)
Kidney transplant	5 (1.9%)

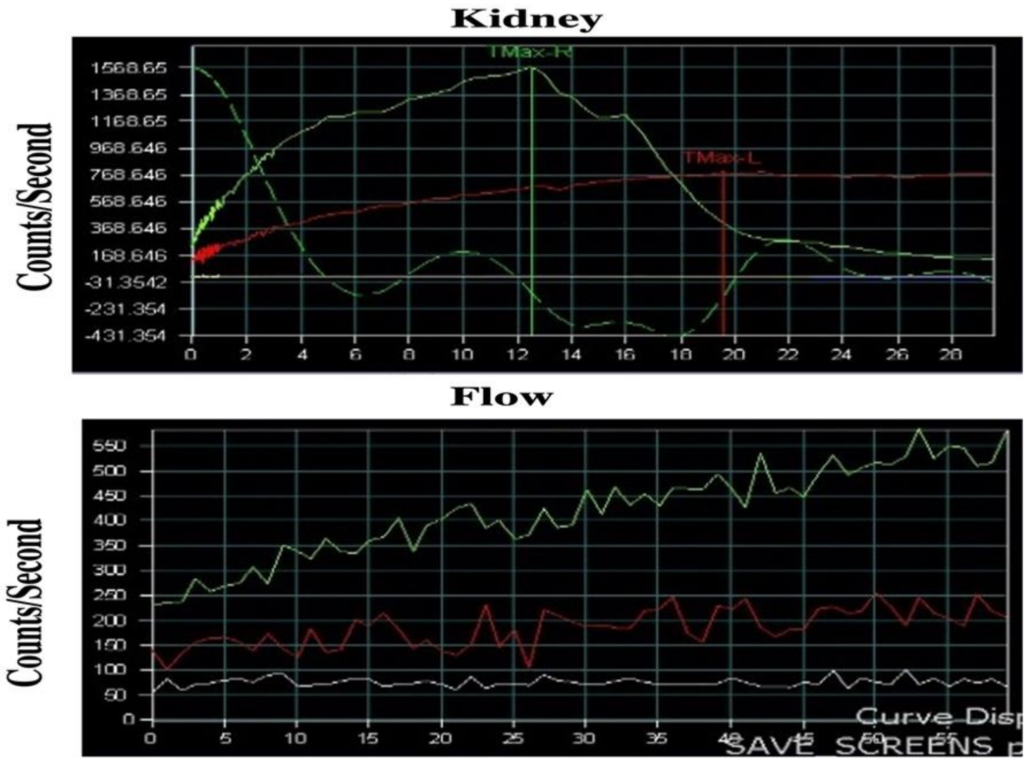

Figure 1: 99mTc-MAG3 dynamic kidney scan showing good functioning right kidney (Green Curve), enlarged diminished functioning left kidneys associated with significant non-obstructive hydronephrosis (Red Curve).

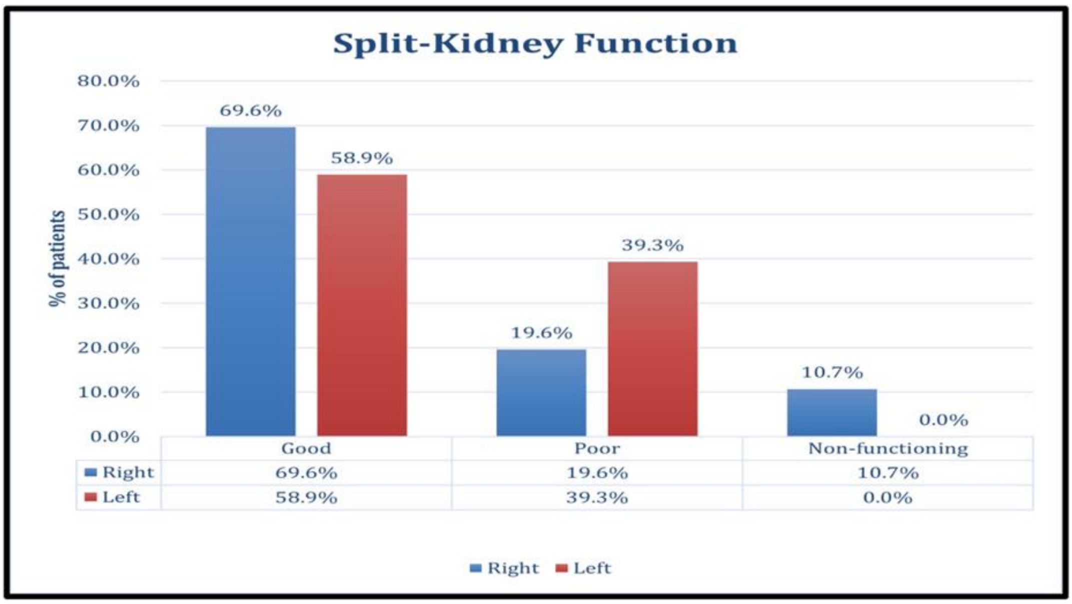

Figure 2: The findings of the Split kidney function (SRF), also known as differential kidney function, measuring each kidney's proportionate contribution to total kidney function.

5. Discussion

Since its first description in the late 1950s, radioisotope renography has gained popularity as a valid and reliable approach for the semi-quantitative evaluation of differential kidney function and detecting kidney hydronephrosis [17]. The concept of radioisotope renography depends on its ability to reflect the functional and drainage capacity of the kidney, thereby differentiating between obstructive and non-obstructive uropathy. In our study, using 99mTc-MAG3 radioisotope renography, we could find suspected obstructive hydronephrosis as a major cause of kidney failure (30.7%) followed by non-obstructive hydronephrosis (23.1%). While the utilization of radioisotope renography suffered from the lack of standardized procedures and interpretation, which limited its reproducibility, recent consensuses have been published over the past two decades by international societies to standardize radioisotope renography procedures [18]. However, real-world practice regarding the utilization of radioisotope renography is still lacking. Thus, we aimed to provide a single-center experience regarding the utility of radioisotope renography in the assessment of kidney functions among patients presenting with kidney diseases. Besides, we described the reference values obtained from the radioisotope renography and their interpretation.

Basically, radioisotope renography monitors the kidney uptake and washout of the radiopharmaceutical under the effect of an intravenous diuretic to assess kidney function. Differential kidney function is one of the six key parameters of radioisotope renography, which demonstrates the relative functional capacity of each kidney [19]. Previous reports demonstrated the existence of nearly 5% unilateral variations in the results of differential kidney function, which was found to be an insignificant difference. Nonetheless, a unilateral variation of 7-9% may reflect a considerable impairment in kidney function [20] Patients with >10% unilateral variation were found to be associated with an increased risk of kidney decline [19].

Nonetheless, it should be noted that the hydronephrotic kidney may present with a relatively higher function than the normal contralateral one, known as supernormal function phenomena; several theories have been proposed to explain such phenomena, including true compensatory hyperfunction or a technical artifact [21,22].

We also found that differential kidney function was universally reported in all medical records of the patient cohort. The right kidney had a median function of 50.9 (38.5–75.5); overall, 39 (69.6%) had good right kidney function. On the other hand, the left kidney had a median function of 49.4 (24.5–61.5); overall, 33 (58.9%) had good left kidney function. In a 2013 report by Yousef et al., reported abnormal right in 28% of the patients and abnormal left kidney function in 16% of patients who underwent radioisotope renography [16]. Notably, in a recent report by Cichocki et al., it was found that the accuracy of differential kidney function is affected by its parameters; their results indicated that the uptake constant had more diagnostic value than the mean transit time and parenchymal transit time [23]. Thus, future reports should investigate the contribution of mean transit time and parenchymal transit time to the potential errors of differential kidney function findings.

Measurement of the GFR is a commonly employed index for the assessing of kidney function. The 99mTc-MAG3 diuretic renography can reliably assess the GFR, with the advantages of being a fast modality that requires only one blood sample and has comparable accuracy to 24-hour creatinine clearance [24,25]. Another important parameter during the 99mTc-MAG3 diuretic renography procedure is the time to peak (Tmax), which can be impaired in the setting of kidney artery stenosis [26]. Despite the apparent benefits of such measures, we found that the GFR and Tmax were rarely reported within the patients' medical records. Thus, educational efforts should be directed toward the importance of documenting the key parameters of radioisotope renography and their interpretations.

In the present study, we used a dose of 75 MBq of 99mTc-MAG3for diuretic renography in our institution. This is in accordance with study by Taylor et al., who elaborated that the acceptable and safe dose for 99mTc-MAG3 was 37–185 MBq [27]. Other reports and expert opinions supported these findings [28,29]. According to Sachpekidis et al., this dose range is sufficient to ensure the reliability of 99mTc-MAG3 diuretic renography [28].

While the current study is one of a few reports that assessed the utility of radioisotope renography in the assessment of kidney function in routine clinical practice, it should be noted that it suffers from some limitations. First, the study was retrospective, with the inherited limitations of misclassification and selection bias. Besides, the medical records of the included patients were primarily confined to the results of differential kidney function, with limited reporting of other parameters of radioisotope renography. Thus, a comprehensive evaluation of the radioisotope renography findings and their correlation with the diagnosis of the affected patients was not possible.

Conclusion

Radioisotope renography is a valuable tool for assessing kidney functions in real-life settings. The technique provides a safe and easy-to-use tool that can guide the management approaches of patients presenting with kidney diseases. It can reduce the interval from presentation to definitive diagnosis and ensure the prompt initiation of therapy after diagnosis. The present study's results indicated that radioisotope renography was helpful in providing visual interpretation of kidney failure, obstructive uropathy and kidney stenosis. Nonetheless, as the current literature reveals a significant impact of operator experience on the reliability of radioisotope renography, it is encouraged to conduct training of the readers in a regular fashion. Besides, measures should be taken to increase the number of accredited operators in secondary and tertiary health centers.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Directorate of Health Affairs, Taif Health Committee no KACST, KSA: HAP-02-T-067

Informed Consent Statement

Owing to the retrospective nature of the study, the need for written informed consent was waived.

Data Availability Statement

The data of the research is available upon request from the corresponding author.

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Conflicts of Interest

The authors declare no conflict of interest.

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