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The role of the geometric mean in DMSA scintigraphy for estimating the differential kidney function

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Abstract

Background: Renal scintigraphy was used to evaluate the relative renal function employing a specialized camera (Gamma camera), a computer, and variety of radiopharmaceuticals, including technetium-99m dimercaptosuccinic acid (99mTc-DMSA), technetium-99m diethylenetriaminepentaacetic acid (99mTc-DTPA), technetium-99m mercaptoacetyltriglycine (99mTc MAG3), iodine 131 orthoiodohippurate (OIH), and more recently, technetium-99m ethylenedicysteine (99mTc-EC), renal scintigraphy was utilized to assess the relative renal function. **Objective:** to determine if there were any significant differences between results from the geometric mean and posterior counts alone for measuring relative renal function. **Methods:** One hundred and fifty-eight DMSA scans performed from May 2022 to May 2023 were studied in This Randomized controlled clinical study (simple randomization) performed in the nuclear medicine unit of Sohag Oncology Institute. About twenty patients were excluded for having a single kidney. To assess the impact of the geometric mean calculation on patients of varying ages, patients were split into two age groups: group I, who were under 18, and group II, who were at least 18 years old. **Results:** The two methods were compared regarding age, gender, and presented renal pathologies. Regarding age and gender, our study reveals no statistically significant difference between the two methods, with P values of 0.364 and 0.971, respectively. **Conclusions:** Differential renal function (DRF) measurements using the geometric mean approach are as accurate as those using the posterior view method. There was a significant difference between the two methods regarding the criteria of >5% variance rate with different renal pathologies (P Value 0.004) our study concluded patients with ectopic and horse-shoe kidneys as well as other pathologies with normally located kidneys.

Keywords: scintigraphy, radiopharmaceuticals, geometric

Introduction:

Evaluation of the urinary system was one of the earliest experimental uses of radiology and contrast injection. After more than a century, enhanced ultrasonography, MRI, modern computed tomography, and renal scintigraphy have all become indispensable components of the assessment of patients with urology and nephrology disorders.[1].

For a very long time, renal scintigraphy was used to evaluate the relative renal function. This method employs a specialized camera, a computer, and various radiopharmaceuticals, which are minute quantities of radioactive substances [2]. Technetium-99m dimercaptosuccinic acid (99mTc-DMSA), technetium-99m diethylenetriamine penta-acetic acid (99mTc-DTPA), technetium-99m mercaptoacetyltriglycine (99mTc MAG3), iodine 131 orthoiodohippurate (OIH), and more recently technetium-99m ethylenedicysteine (99mTc-EC) are some of the radiopharmaceuticals that can be used with this medical imaging technique. In practice, using DMSA as a static renal agent may be the most highly anticipated method for evaluating relative renal function. [3].

All of these radiopharmaceuticals, with some exceptions, can be used to accurately estimate kidney function. The renal excretion route, radioactive material retention of the renal cell, plasma protein binding, and plasma clearance are all examples of radiopharmaceutical biological properties that contribute to these differences. When employed as a stationary renal agent, 99mTc-DMSA is regarded as the gold standard for renal cortical imaging and relative renal function quantification [4].

Lin et al. first presented dimercaptosuccinic acid (DMSA) in 1974, and it immediately became popular as a static agent. It has been known for quite some time that it is an excellent static renal imaging agent. Such research is carried out not only to provide accurate images of renal parenchyma but also to quantify the split renal function, which is of critical clinical value. The basic and important metric known as the left-to-right 99mTc-DMSA uptake ratio is frequently derived from planar scintigrams [5].

After being absorbed by the proximal renal tubule and the first segment of Henle's loop, the tracer preferentially accumulates in the renal cortex [6].

The level of renal absorption of 99mTc-DMSA can be used to quantify renal function and assess changes in renal performance over time. There are numerous methods for quantification: 1) Assessment using only the posterior view, with or without kidney depth adjustment; 2) Assessment using both the anterior and posterior views, with kidney depth adjusted using the geometric mean of the two views. The latter strategy is more commonly used and generally seen as more trustworthy [5].

This study's objective was to determine if there were any significant differences between results from the geometric mean and posterior counts alone for measuring relative renal function. Additionally, we assessed some variables, including gender, pathology, and the degree to which patient age affected these disparities [6].

Patient and Methods:

This Randomized controlled clinical study (simple randomization) included One hundred and fifty-eight DMSA scans over the previous 12 months were examined. About twenty patients were excluded for having a single kidney. To assess the impact of the geometric mean calculation on patients of varying ages, patients were split into two age groups: group I, who were under the age of 18, and group II, who were at least 18 years old.

Inclusion criteria:

Patients between the ages of 2 and 70 who have been referred for renal DMSA scintigraphy are eligible to participate

Exclusion criteria:

Patients with unmanageable medical conditions or those with only one kidney are excluded.

Methods: Patient information and history will be recorded first, followed by information from any necessary investigations like ultrasound or computed tomography of the abdomen and pelvis, and finally, imaging will be performed using both the front and back detectors of a gamma camera.

Scintigraphy using 99mTc-DMSA: The patient was lying supine during the DMSA scintigraphy. Using a dual-head gamma camera (GE-Health care) with low energy, all-purpose collimator, static images were acquired in a 256_ 256 matrix 2 to 4 hours after the injection of 111 MBq (3 mCi) 99mTc-DMSA (proportionately lower in children).

Relative renal function was calculated using data processed by two skilled operators who had demonstrated strong agreement in a prior study conducted in our department. A background region in the inferolateral region of the kidneys was depicted as a crescent, and a region of interest was painted around each kidney on the anterior and posterior images.

Each kidney's background-corrected count was derived from the total number of counts in these zones. Different equations were used to manually determine the RRF of each kidney (RKF) based on the posterior numbers, such as: The right renal reserve fraction (RKF) was determined by utilizing the posterior count equation:

$$\mathrm{RKF}_{(\mathrm{POST})} = \frac{C_{R(POST)}}{C_{R(POST)} + C_{L(POST)}} \times 100\%$$

Where CR (POST) and CL (POST) are the right and left kidney background corrected counts, respectively, in the rear projection. Taking the geometric mean (GM) of the counts derived from the anterior and posterior images by the equation GM= √counts anterior x counts posterior

The relative renal function of the right kidney was calculated by

$$RKF_{(GM)} = \frac{\sqrt{C_{R(POST)} \times C_{R(ANT)}}}{\sqrt{C_{R(POST)} \times C_{R(ANT)}} + \sqrt{C_{L(POST)} \times C_{L(ANT)}}} \times 100\%$$

Where CR (ANT) and CL (ANT) are the background corrected counts of the right and the left kidneys in the anterior view, recently different types of cameras equipped to calculate differential function posteriorly and geometric mean automatically.

Statistical analysis:

When applicable, the data were statistically reported using frequencies and percentages, median and range, mean and standard deviation (SD). The Kolmogorov-Smirnov test was used to check numerical data for the normal assumption. The Paired t-test for matched samples was used to compare the numerical variables between DMSA and GM. Using the Chi-square, categorical data were compared. When the estimated frequency was less than five, the exact test was utilized instead. The Spearman rank correlation equation for non-normal variables/non-linear monotonic relations and the Pearson moment correlation equation for linear relations of normally distributed variables were used to correlate the different variables.

P values that were less than 0.05 on both sides were deemed statistically significant. SPSS (Statistical Package for the Social Science) program version 22 was used for statistical analysis

We looked at the DMSA scans where the difference between the two techniques was more than 5% to see if there was a clear anatomical explanation for the discrepancy.

Results:

One hundred and fifty-eight scans applied in the last year were examined in a cross-section study performed in the nuclear medicine unit of Sohag Oncology Institute. About twenty patients were excluded for having a single kidney. Patients were categorized into two groups based on their ages to test the effect of the geometric mean estimation on patients of different ages: group I, <18 years; 41 (29.7%) and group II, 18 years or more; 97 (90.3%). There were 45 (32.6%) females and 93 (67.4%) males. (Table 1).

Table 2: demonstrates that about one third of cases presented with hydronephrosis as well as one third presented with stones, with percent of 31% and 30% respectively, some cases presented with PUJO and pyelonephritis, each of them with percent of 11.6%, while the minority of cases like horseshoe and ectopic kidneys with percent of 5% for each of them, 0.7% for atrophy and 1.4 % for renal cyst

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Based on the geometric averages and posterior views, the mean and standard deviation of the RRF values for both kidneys were displayed in (Table 3). Mean and standard deviation of posterior to geometric mean methods in the left side was 0.134±5.045, the mean and standard deviation of posterior to geometric mean methods in the right side was 0.134±5.045, and these differences were not statistically significant with p values 0.755. The Mean and standard deviation of difference between posterior to geometric mean methods 1.01±8.99, with insignificant P. value: 0.189.

Table 4, shows the difference of both calculation methods versus pathology in the estimation of DRF, 34 cases; (24.6% within pathology that demonstrates a difference of 5% or more), the highest percent of patients with 5%or more was among ectopic pelvic kidney with percent of 85.7%, followed by mass and cyst with percent of 50%, then patients with horse-shoe kidneys with percent of 42.9%, other pathologies like stones: 23.8%, hydronephrosis: 20.9%, pyelonephritis:12.5% and 2.9% for PUJO with the accepted percent of 5% difference in RF. while among 104 patients with a difference <5%, 32 were with stones, 34 with hydronephrosis, 14 with pyelonephritis, 15 with PUJO, one cyst, and one atrophy. The table demonstrates that there is a significant P value (0.004) between the two calculation methods of DRF regarding the clinically valuable 5% difference or more versus pathology.

There is no significant difference (P value 0.364) between the two calculation methods regarding the clinically variable difference "5% or more" in calculation of DRF versus age (Table 5).

Table 1: Characteristics of the studied population

Variables		Frequency	Percent
Age groups	< 18y	41	29.7
	18y or more	97	70.3
	Total	138	100.0
Sex	Female	45	32.6
	Male	93	67.4

Table 2: The presented renal pathologies and different complains of the patients in this study

Pathology	Frequency	Percent
Atrophy	1	0.7
Cyst	2	1.4
ectopic pelvic	7	5.1
horse-shoe kidney	7	5.1
Hydronephrosis	43	31.2
Mass	4	2.9
PUJO	16	11.6
Pyelonephritis	16	11.6
Stone	42	30.4
Total	138	100.0

Table 3: Mean difference of both methods of calculation of differential RF

	Mean difference ± Std. Deviation	p. value
Left sided DMSA-GM	-0.13428 ± 5.04577	0.755
Right sided DMSA-GM	0.13428± 5.04577	0.755
DMSA-Diff. - GM-Diff.	1.01000± 8.99007	0.189

Table 4: Comparison between 5%differences between the two calculation methods of differential renal function versus pathology

Pathology	DMSA-GM diff-Rt state		P value
	< 5%	≥ 5%	
Atrophy	1 (100%)	0 (0%)	0.004
Cyst	1 (50%)	1 (50%)	
ectopic pelvic	1 (14.3%)	6 (85.7%)	
horse-shoe kidney	4 (57.1%)	3 (42.9%)	
Hydronephrosis	34 (79.1%)	9 (20.9%)	
Mass	2 (50%)	2 (50%)	
PUJO	15 (93.8%)	1 (6.3%)	
Pyelonephritis	14 (87.5%)	2 (12.5%)	
Stone	32 (75.4%)	10 (23.8%)	
Total	104 (75.4%)	34 (24.6%)	

Table 5: comparison of 5%differences between both calculations' methods on right kidney versus age

Age group	DMSA-GM diff-Rt state		P value
	< 5%	≥ 5%	
< 18 years	33 (31.7%)	8 (23.5%)	0.364
≥ 18 years	71 (68.3%)	26 (76.5%)	
Total	104 (100%)	34 (100%)	

Discussion:

It is feasible to use the patient's differential renal uptake of 99mTc-DMSA as an index of split renal function and to assess the change in renal function over time. Physicians specializing in nuclear medicine, as well as nephrologists and urologists, have long been interested in developing more precise methods for evaluating split renal function.

If the relative renal uptake is measured while there is a significant disparity in the renal depth between the left and right kidneys, it may be incorrect to calculate relative kidney function from the posterior image without modification. Therefore, a variety of mathematical methods can be used to quantify split renal function. The most common method is to use planar images with kidney depth adjusted using the geometric mean, which can be calculated using anterior and posterior views. The geometric mean of the counts could correct errors caused by depth variations.

Although some authors contend that calculating the geometric mean is more time-consuming and labor-intensive than calculating the corrected counts solely from the posterior view, manual geometric mean calculation is no longer acceptable due to the advancement of dual-head gamma cameras and automatic processing software.

This study compares the validity and efficacy geometric mean with the default method considering almost all age groups as well as different renal pathologies. Our study included 158 patients randomly assigned into 2 age groups:

Below 18 years and 18 years-or more, excluding about 20 patients were found after imaging to have one functioning kidney, using dual head (GE) Gamma camera and automated calculation of geometric mean.

In this study, about 70% of cases were 18years or more, and only 30 % below 18 years. Similarly, regarding gender, 67% were males and the rest were females, the conducted finding revealed that there is no significant difference between the forementioned calculation methods as regard gender or age.

In a study that was comparable to ours, Lythgoe et al. [8] used the geometric mean method to evaluate a pediatric population. They looked at a group of 19 kids and used the geometric mean and posterior projection to determine the relative renal function. They discovered that when evaluating differential renal function for well positioned kidneys in children using the geometric mean method or any other method, it doesn't seem necessary to take individual renal depth into account. Children's lesser renal depth explains why geometric mean correction has less of an impact on their measurements than it does on adults.

Collectively, the mean and standard deviation of posterior view and geometric mean method were measured for all patients as followed: - Mean and standard deviation of posterior to geometric mean methods in the left side 0.134±5.045, with insignificant P. value: 0.755. the mean and standard deviation of posterior to geometric mean methods in the right side 0.134±5.045, with insignificant P. value: 0.755. Mean and standard deviation of difference between posterior to geometric mean methods 1.01±8.99, with insignificant P. value: 0.189.

Many other previous studies supported these findings, in view of normally located kidneys and pediatric population in concern.

Several studies examined the DMSA scans where the difference between the two methods was greater than 5% to determine whether there was a clear anatomical reason for any significant changes observed. Similar criteria were used in our study to categorize patients based on the clinically relevant variation rate (>5% difference) between the two techniques used to calculate relative renal function. According to earlier research, a difference of up to 5% was deemed clinically inconsequential [6].

Comparison between the two methods calculation was made regarding age, gender and presented renal pathologies. In view of age and gender, our study reveals no significant difference between the two methods, with P. value 0.364 and 0.971 respectively.

The agreement of our study with Yapara et al. [7], In age group less than10 years with major malformations and position anomalies, a significant difference was found between the two calculation methods; a clinically meaningful RRF variance (>5%) rate was significantly higher in the groups with pathological or asymmetrically low (40% RRF) functioning kidneys than in the groups without pathological or asymmetrically low functioning kidneys (P 0.05).

Our results showed a significant difference between the two methods regarding the criteria of >5% variance rate with different renal pathologies (P. value 0.004) compared to (P. value: 0.005) in Yapara et al et al. (2005). However, our study concluded patients with ectopic and horse-shoe kidneys as well as other pathologies with normally located kidneys.

The same study; Yapara. et. al., and Hervás et al. [6,7] conducted a correlation of difference with age, the former added the criteria of the clinically meaningful difference (>5%), both revealed a positive relation between increasing age with presence of significant difference between the two methods.

Similarly, we correlated the difference with age in view of (>5% criteria) for the right kidney in all 138 cases, however and may be due to reduced number of total cases compared another study [7], our finding revealed no correlation.

On discussing a more detailed point of renal pathology regarding hydronephrosis, Wehbi et al [9], concluded that severe hydronephrosis is increasingly validates the geometric mean method for getting a more accurate estimation of DRF.

Conclusions:

Differential renal function (DRF) measurements using the geometric mean approach are as accurate as those using the posterior view method, and they are more accurate in improperly placed and diseased kidneys. Despite this, DRF is typically evaluated using the posterior method. The geometric mean of anatomical pictures taken from the front and back may provide a more reliable estimation of DRF because it is less susceptible to variations in renal depth. Using the geometric mean method yields the same results in terms of exam duration, cost, and radiation exposure as other methods.

Only a tiny percentage of patients, such as those being assessed for donor nephrectomy and those with renal abnormalities, may benefit from the depth correction that the geometric mean gives, even in the adult population. Most validity of the geometric mean in our study regarding pathology is found mainly to be attributed to ectopic, horseshoe, renal cyst mass, and hydronephrosis, thus detailed studies of different renal presentations would be an index of geometric mean specificity.

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