Published in final edited form as:

Clin Nucl Med. 2013 January ; 38(1): 13–17. doi:10.1097/RLU.0b013e318270866f.

Reference Values for Renal Size Obtained From MAG3 Scintigraphy

Andrew T. Taylor, MD*, Neeta Shenvi, MS[†], Russell D. Folks, CNMT*, Ernest V. Garcia, PhD*, Bital Savir Baruch, MD*, and Amita Manatunga, PhD[†]

*Department of Radiology and Imaging Sciences, School of Medicine, Emory University, Atlanta, GA

[†]Department of Biostatistics and Bioinformatics, School of Public Health, Emory University, Atlanta, GA

Abstract

Purpose—The purposes of this study were to establish reference values for renal size determined from ^{99m}Tc-MAG3 renal scintigraphy and to derive regression equations to predict normal limits.

Methods—The study population consisted of 106 subjects evaluated for kidney donation who underwent ^{99m}Tc-MAG3 renal scintigraphy. Renal length, width, and area were determined from the pixel length and area of whole-kidney regions of interest and correlated with patient sex, height, weight, body mass index, and body surface area (BSA). Reference values were obtained based on estimation of the lower and upper percentiles via quantile regression.

Results—The mean (SD) left and right kidney lengths was 12.2 (1.0) and 12.1 (1.0) in male and 11.9 (0.9) and 11.8 (0.9) in female patients, respectively. Sex was not a significant factor in the quantile regression models. Regression equations defining the lower and upper limits of renal length (cm) and area (cm²) are as follows: left kidney length (5th percentile), $8.2 + 1.3 \times \text{BSA}$; left kidney length (95th percentile), $9.1 + 2.3 \times \text{BSA}$; right kidney length (5th percentile), $8.8 + 1.0 \times \text{BSA}$; right kidney length (95th percentile), $11.1 + 1.4 \times \text{BSA}$; left kidney area (5th percentile), $32.5 + 9.6 \times \text{BSA}$; left kidney area (95th percentile), $12.6 + 31.7 \times \text{BSA}$; right kidney area (5th percentile), $16.1 + 18.5 \times \text{BSA}$; right kidney area (95th percentile), $32.6 + 22.2 \times \text{BSA}$.

Conclusions—Regression equations have been developed, which define the upper and lower limits of renal size from ^{99m}Tc-MAG3 images and may assist in the detection of unsuspected bilateral increases or decreases in renal size.

Keywords

renal size; renal length; MAG3 scintigraphy; ^{99m}Tc-MAG3 scintigraphy; regression equations; quantile analysis; renal scintigraphy

Knowledge of renal size can assist in the interpretation of ^{99m}Tc-MAG3 renal scans. A number of chronic renal diseases will result in bilateral small kidneys, whereas the kidneys may be bilaterally enlarged in early diabetic renal disease, acute interstitial nephritis, HIV nephropathy, amyloidosis, and preeclampsia.^{1–5} A unilateral small kidney is obvious, but a

small kidney may not be obvious on a MAG3 renal scan when the contralateral kidney is similarly reduced in size; similarly, an abnormal increase in renal size may not be recognized if both kidneys are similarly enlarged and have a normal configuration. Correlative imaging studies may provide size information, but correlative imaging studies may not be available. Some software applications allow calculation of renal length or renal size in pixels with conversion to length and area, but normal values in adults have not been established for renal scintigraphy. Kidney length is often used as a measure of renal size; however, kidney length is known to correlate with body height^{6,7}; a renal length that is normal in a small adult may be abnormal in a larger individual. The purposes of this work were to establish reference values for renal length, width, and area determined from ^{99m}Tc-MAG3 renal scintigraphy; to correlate these values with sex, weight, age, height, and body surface area (BSA); and to use these relationships to derive regression equations to predict normal limits.

PATIENTS AND METHODS

Subjects

Review of patient records was approved by the institutional review board; the requirement for informed consent was waived because the study only involved a review of archived renal scans. The study population consisted of 106 subjects evaluated for kidney donation who underwent ^{99m}Tc-MAG3 renal scintigraphy. These 106 subjects included 44 male and 62 female subjects. The mean age (SD) of the subject population was 39.9 (10.8) years, with a mean (SD) age of 41.0 (11.9) years for male and 39.1 (9.9) years for female subjects. In addition to having no history of renal disease, most potential donors also had a normal imaging study result; of the 106 potential renal donors, 54 had normal magnetic resonance angiography result, 32 had normal percutaneous angiography result, and 5 had normal results; anatomic data were not obtained or not available in the remaining 15 subjects. A creatinine clearance was obtained in 99 of the 106 subjects; of these 99 subjects, all but 4 (2 male and 2 female subjects) had a normal 24-hour urinary creatinine clearance. The 4 subjects with a reduced creatinine clearance had normal serum creatinine levels ranging from 0.9 (79.6 mmol/L) to 1.1 mg/dL (97.2 mmol/L), normal laboratory range of 0.6 (53 mmol/L) to 1.4 mg/dL (123.8 mmol/L); in addition, 3 had a normal magnetic resonance angiogram, and the fourth had a normal CT result.

Data Acquisition, Regions of Interest, and Background Correction

The subjects were hydrated with approximately 500 mL of water 30 minutes before the study. Images were acquired in a 128 × 128 matrix with a 15-in. FOV General Electric gamma camera (Milwaukee, WI) fitted with a LEAP collimator. Each subject was imaged supine with the kidneys and bladder within the FOV. After the IV injection of ^{99m}Tc-MAG3, serial digital images of 2 seconds per frame were obtained for the first 48 seconds, followed by 16 images of 15 seconds per frame and 40 images of 30 seconds per frame for a total study duration of 24 minutes and 48 seconds. Time zero was defined as the 16-second interval that the dose reached the kidney.

Whole-kidney regions of interest (ROIs) were automatically assigned over each kidney using the 2- to 3-minute image. The algorithm to assign the whole-kidney ROI was written in Interactive Data Language (IDL, ITT Visual Information Solutions, Boulder, CO) and consisted of the following steps: (1) A thresholding technique was performed by finding the SD of the mean pixel counts and zeroing all pixels less than half this value. (2) This image was smoothed using a 3 × 3 convolution (in IDL terminology, a “boxcar average of width 3”). (3) The maximum pixel in the image was identified. (4) A contouring routine was applied that identified the pixels contiguous with the maximum pixel and 25% or greater of

its value. This became the mask for the first kidney region identified. (5) The mask was dilated by 1 pixel to smooth the edge and fine-tune the threshold. (6) The mask was then subtracted from the image, and the algorithm was repeated from step 3 to identify the second kidney. (7) Assuming a posterior orientation for acquisition, the minimum x coordinate values for the 2 masks were compared to determine which renal ROI represented the left kidney. The automated ROIs were modified by the operator if necessary.

Kidney area was determined by multiplying the area of a single pixel by the total number of pixels within the ROI, which included pixels that comprised the perimeter. The algorithm for finding the kidney long axis operated on the whole-kidney ROI. Axis lines were automatically drawn between all vertex points on the ROI perimeter; the longest of these lines is defined as the long axis and is expressed in pixels, which are converted to centimeter using the known pixel size, which is obtained from the image header. Width was calculated from the perimeter of the whole-kidney ROI as the maximum x coordinate minus the minimum x coordinate plus 1.

Statistical Analysis

Pearson and Spearman correlation coefficients were calculated relating renal length, renal width, and renal area to height, weight, body mass index (BMI) and BSA (Haycock equation⁸ for male and female subjects). Significance of the correlation was declared at 0.025 significance level after accounting for 2 multiple comparisons for male and female subjects. To establish reference values for kidney area, length, and width, we considered the estimation of the lower and upper percentiles via quantile regression because abnormal results are expected to be outside of the 5th and 95th quantile.⁹ Because BSA is related to kidney area and kidney length, we separately modeled the quantile of kidney area and length in BSA and estimated the quantile (5%, 95%) for kidney area and length and BSA. The effect of sex on the relationship between kidney area and BSA was examined. The corresponding confidence intervals for percentiles of kidney area and length are also reported.

RESULTS

The mean (SD) left kidney length (long axis) was 12.2 (1.0) cm for male subjects, 11.9 (0.9) cm for female subjects and 12.0 (1.0) cm for the combined group. Similarly, the mean (SD) right kidney length was 12.1 (1.0) cm for male subjects, 11.8 (0.9) cm for female subjects and 11.9 (0.9) cm for the combined group. The mean (SD) left kidney area was 63.8 (8.3) cm², 60.4 (7.1) cm², and 61.8 (7.8) cm² for male subjects, female subjects, and the combined group, respectively. The mean (SD) right kidney area was 63.4 (8.0) cm², 60.0 (7.9) cm², and 61.4 (8.1) cm² for male subjects, female subjects, and the combined group, respectively. The mean (SD) left and right kidney widths for the combined sexes was 7.9 (0.6) cm and 7.6 (0.6) cm, respectively.

Tables 1 and 2 show the Pearson correlation coefficients among BMI, BSA, patient height and age with the right and left kidney area, as well as length and width for male and female subjects; the Spearman correlation coefficients (not shown) were comparable. There was no significant correlation between age and any of the 3 kidney size variables. In males, BSA and height tended to show significant correlations with renal length, width, and area. In females, significant correlations were more consistent between BSA and BMI and renal width and area than with renal length.

Sex was not a significant factor in quantile regression models for kidney area, length, and width; consequently, the results for kidney length and area are expressed in a sex-independent overall model. Table 3 shows the 5th and 95th percentiles for kidney area and

long axis for selected values of BSA: 1.5, 1.7, 1.9, 2.1, and 2.3 m². For example, if a subject's BSA is 1.9 m², the abnormal values for his/her left kidney area are considered to be less than 50.8 cm² or greater than 72.9 cm².

Figure 1 shows the regression equation for the 5th and 95th percentiles for kidney area and length as a function of BSA. The corresponding regression equations are outlined in the footnote. The values that are outside the boundaries can be interpreted as abnormal. The plot can be used to determine the reference values of low and high kidney area and length for a given value of BSA, and the measurement of renal length is illustrated in Figure 2.

Figure 3 illustrates a ^{99m}Tc-MAG3 scan shown in a "Read with the Experts Session" at the 1997 Society of Nuclear Medicine national meeting. After being informed that the renal scan was obtained in a 56-year-old woman with a history of renal disease, members of the audience were asked to use their keypads to choose between 4 diagnostic options: normal, bilaterally impaired function, occult obstruction, and renovascular hypertension. Eighty percent of the respondents interpreted the kidneys as normal; 14% interpreted the kidneys as showing bilaterally impaired function, 3% as occult obstruction, and 3% as bilateral renovascular hypertension. Although not apparent from a qualitative review of the images and curves, both kidneys are abnormally small (Fig. 3). If this information had been available to the respondents, the number correctly identifying the diagnosis of bilaterally impaired function would likely have been substantially increased. Additional clinical history revealed that the patient had serum creatinine level of 2.4 mg/dL (212 mmol/L) and bilaterally small kidneys by ultrasonography.

DISCUSSION

Normal renal dimensions have been established based on excretory urography, sonography, and MRI, but reference ranges are influenced by the measurement technique as well as adjustments for body habitus and age.^{6,7,10,11} The mean long axis measurements of the left and right kidney in our study, 12.0 and 11.9 cm, respectively, are similar to the 11.6 and 11.4 cm values reported from ^{99m}Tc DMSA study in 195 adult kidneys¹² and are slightly higher than the 11.2 and 10.9 cm sonography measurements of renal length obtained in a study of 665 normal volunteers.⁶ In the sonography study, renal length (and volume) decreased with age, but this decrease became most apparent in older subjects greater than 60 to 70 years of age.⁶ In contrast, our study showed no correlation between renal length or area with age, but the lack of a significant correlation may have been due to the fact that our normal study population consisted of potential renal donors and only included 2 individuals older than 60 years. A recent MR study evaluated renal length in 150 patients undergoing abdominal MRI results for reasons other than suspected renal pathological diagnosis and excluded patients with renal abnormalities from analysis¹⁰; in this study, the mean renal length was 12.4 cm in men and 11.6 cm in women; these values are closer to those we obtained, and the authors noted that the renal length using MRI was greater than that reported by sonography. In summary, reference values for renal length using MAG3 are comparable with those reported in the literature using other modalities.

As illustrated in Figure 2, knowledge of normal renal dimensions may help in the diagnosis of kidney diseases because changes in renal dimensions occur in nephropathies due to hypertrophic processes and/or atrophy. Renal length and volume are important clinical parameters in the initial patient evaluation and can also be important parameters in follow-up of transplant recipients, patients with recurrent urinary infections, patients with hypertension, and patients with renal insufficiency; a change in kidney dimensions from one examination to the next may be an important indicator of the presence or progression of disease (2007).

Pediatric nomograms for renal length as a function of age, height, and weight have been developed for pediatric patients referred for DMSA scintigraphy.^{13–15} There are limited reports evaluating renal size in adults by planar nuclear medicine techniques.¹⁴ Mean renal length in adults was reported in a 1978 DMSA study¹⁴; however, radiopharmaceutical differences in target-to-background ratio as well as intervening differences in instrumentation and software could affect normal limits. Moreover, this DMSA study only evaluated renal length and did not relate renal size to sex, age, or body habitus.

Renal volume and renal area both correlate well with GFR and effective renal plasma flow.¹⁶ Using sonography, maximum kidney length correlates well with renal volume, but owing to the compounding nature of measurement errors in calculating volume using sonography, maximum renal length is preferred for assessment of renal size on sonograms; additional measurements in the transverse axes (renal width) are reported to be very inaccurate and of no utility.^{3,6,17} Similar to our results, an ultrasound study of normal adult patients found that kidney length did not vary between sexes in a multivariate regression analysis after correction for body height and age.⁷

Quantile regression has recently emerged as an important extension of linear regression. Compared with a traditional linear regression model that concerns the mean of a response, quantile regression directly models specified quantiles (ie, percentiles) of a response.⁹ The analysis by quantiles has allowed us to develop regression equations to predict the expected extremes of renal length and area as a function of BSA. We used BSA as a predictor of renal area and length because the BSA is the variable most highly correlated with area and length. Regression equations were developed for renal length because this measurement is commonly included in radiology reports and renal length is a routine descriptor of renal size in the CT, MRI, and sonography literature. Regression equations were also developed for renal area because area was significantly correlated with BSA, area may be a more robust measure of renal size than length, and area is partially dependent on renal width, which was also significantly correlated with BSA. We did not report regression equations relating BSA to renal width because sonography studies have reported renal width to be of no additional value in the measurement of renal size³ and variations of 1 to 2 pixels would have a greater impact on the measurement of renal width than on renal length.

There are several potential sources of error. Software programs that place a marker at the superior and inferior poles of the kidney and use the *y* distance between these markers will obtain values of renal length different from what we used in our study; our methodology used the longest axis to determine renal length. Anterior-to-posterior rotation can result in an underestimation of renal length, which cannot be corrected by supine planar imaging; this was an inherent limitation of our study. Our ROI was automatically defined; however, the operator was the final arbiter of the renal ROI, and the software gave the operator the option to modify the boundaries of the ROI if they seemed inappropriate. Different observers will draw slightly different ROIs; providing a computer generated renal ROI to the observer may minimize observer differences. Implementation of more robust software to automatically define the renal ROI will enhance reproducibility.¹⁸ Finally, GRF and effective renal plasma flow are known to decrease with age, and studies have reported a decrease in renal size in subjects older than 60 to 70 years.^{6,7,19} We did not have enough subjects in this age range to evaluate this group compared with younger adults, and our equations do not adjust for a decrease in renal area or renal length in patients older than 60 to 70 years.

CONCLUSIONS

In conclusion, this study has led to regression equations that define the upper and lower limits of renal size encountered in normal adults undergoing MAG3 scintigraphy. The use of

these equations has the potential to allow the reader to detect abnormally small or abnormally enlarged kidneys, particularly when both kidneys are similarly involved. This additional information may assist in the interpretation of the study and suggest other types of abnormality such as atrophy or early diabetes when bilaterally enlarged kidneys are encountered. The utility of these equations to assist clinicians in detecting symmetrically small or enlarged kidneys will need to be evaluated in a clinical study.

Acknowledgments

Sources of funding: Three of the authors, Andrew T. Taylor, Russell Folks, and Ernest V. Garcia, are entitled to a share of the royalties for the use of QuantEM software for processing MAG3 renal scans, which was licensed by Emory University to GE Healthcare in the mid-1990s. These investigators have subsequently developed in-house software in Interactive Data Language, which was used in this study and could affect their financial status.

This research was funded by a United States National Institutes of Health (NIH) grant RO1-EB008838; specifically, the research was supported by the National Institute of Biomedical Imaging and Bioengineering and the National Institute of Diabetes and Digestive and Kidney Diseases.

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FIGURE 1.
Predictive 5th and 95th percentiles of renal length and area as a function of BSA with the corresponding regression equations.

FIGURE 2.
Posterior image of the kidneys showing the long axis of each kidney.

FIGURE 3.

A 56-year-old woman with a history of renal disease was referred for renal scintigraphy. Sequential 2-minute images and a postvoid image are displayed after an IV injection of 185 mBq (5.0 mCi) of ^{99m}Tc -MAG3. Renogram curves were generated using whole-kidney and parenchymal ROIs. The patient's BSA was 1.765 m², and the relative uptake was 52% in the left kidney and 48% in the right kidney. There is prompt uptake and excretion, but both kidneys are small. The long axis of the left kidney was 8.85 cm (reference range, 10.49–13.16 cm), and the long axis of the right kidney was 9.06 cm (reference range, 10.5–13.57 cm). The left kidney area is 36 cm² (reference range, 49.4–65.6 cm²), and the right kidney area is 38.7 cm² (reference range, 48.8–71.8 cm²). Without the quantitative information that both kidneys are abnormally small, the study might have been interpreted as normal (see text).

TABLE 1
Correlation of BMI, BSA, Height, and Age With Kidney Area, Length, and Width in Male Subjects (n = 44)

	Right Kidney Area	Left Kidney Area	Right Kidney Long Axis	Left Kidney Long Axis	Right Kidney Width	Left Kidney Width
BMI	0.32	0.32	0.24	0.22	0.27	0.34 *
BSA	0.62 *	0.54 *	0.42 *	0.51 *	0.54 *	0.58 *
Height	0.42 *	0.34 *	0.26	0.38 *	0.36 *	0.36 *
Age	0.14	0.24	0.23	0.14	-0.11	-0.02

* *P* 0.025 is considered to be significant while accounting for multiple comparisons for male and female subjects.

TABLE 2
Correlation of BMI, BSA, Height, and Age With Kidney Area, Length, and Width in Female Subjects (n = 62)

	Right Kidney Area	Left Kidney Area	Right Kidney Long Axis	Left Kidney Long Axis	Right Kidney Width	Left Kidney Width
BMI	0.40 *	0.35 *	0.04	0.07	0.50 *	0.47 *
BSA	0.38 *	0.45 *	0.14	0.27	0.51 *	0.44 *
Height	0.09	0.28	0.18	0.35 *	0.14	0.10
Age	-0.04	-0.09	0.03	0.02	0.07	-0.23

* *P* 0.025 is considered to be significant while accounting for multiple comparisons for male and female subjects.

TABLE 3
Estimates for 5th/95th Percentile Kidney Area (cm²) and Kidney Long Axis (cm) for Male and Female Subjects (n = 106)

BSA *	Left Kidney Area Percentile, cm ²		Right Kidney Area Percentile, cm ²		Left Kidney Long Axis Percentile, cm		Right Kidney Long Axis Percentile, cm	
	5th	95th	5th	95th	5th	95th	5th	95th
1.5	46.9	60.2	43.8	66.0	10.2	12.6	10.3	13.2
1.7	48.9	66.5	47.5	70.4	10.4	13.1	10.5	13.5
1.9	50.8	72.9	51.2	74.8	10.7	13.5	10.7	13.7
2.1	52.7	79.2	54.9	79.3	10.9	14.0	11.0	14.0
2.3	54.6	85.6	58.6	83.7	11.2	14.5	11.3	14.3

* BSA values were selected from the total population of 106 subjects based on the 5th, 25th, 50th, 75th, and 95th percentile values.