Original Article

Estimation of Absolute Renal Uptake of ^{99m}Tc DMSA in Potential Kidney Donors and its Accuracy in Determination of Split Function

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ABSTRACT:

Introduction: Calculation of 99mTc DMSA split renal function (SRF) is widely used in daily clinical practice; however it does not provide information regarding the functional status of each kidney separately. Absolute renal uptake (ARU) is a valuable quantitative parameter that is capable of assessing the kidneys' function independently. Discrepancies exist in ARU values due to various quantitative methods used and standardization of normal ARU values is probably required at different centers. **Objectives:** Establishment of normal ARU values derived from posterior view images. Methods: We retrospectively analyzed 80 healthy adults, potential kidney donors (64 males, mean age 29.8±8.7 years). All patients had 99mTc DMSA images. The SRF was calculated using geometric mean method.The depth of the kidneys for attenuation corrected ARU was derived Tonnensen method (Right kidney = 13.3 (W/H) + 0.7, Left kidney =13.2 (W/H) + 0.7) as well as from actual kidney depths on CT. Paired T-test, Pearson's correlationand Kappa test were used to compare different parameters. **Results:** The Tonnensen based ARU was lower compared to the CT based ARU for left (20.79 ± 4.01% & 24.08 ± 4.50%; p<0.001) and right kidney (18.79 ± 4.31% & 23.23±4.9%; p<0.001). Both methods were highly correlated for left and right kidneys (r=0.921, p<0.001 & r=0.905; p<0.001) respectively. The calculated kidney depths (cm) by the Tonnensen method compared to the CT were (6.24±1.03 vs.7.48 ± 1.27; p<0.001) for left kidney and (6.28±1.04 vs. 8.09±1.42; p<0.001) for right kidney. Agreement of posterior view based ARU regarding the kidney of higher uptake versus that of geometric mean based SRF, was better for ARU based on CT depth measurement compared to that using Tonnensen equation (Kappa =0.479; p<001 vs. Kappa= 0.162; p=0.83) respectively. **Conclusions:** The ARU calculated based on Tonnensen method althoughis underestimated compared to that based on CT measurement, both are highly correlated. The variability in normal ARU values reported in various studies is probably multifactorial however a key factor is the method used for kidneys depth assessment. Consequently it is recommended that local standardized reference ARU values be developed by every nuclear lab rather than using a predecided values from the literature.

Key words: Renal - ^{99m}Tc-DMSA - absolute uptake - split function – kidney depth - kidney donors.

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INTRODUCTION:

Calculation of ^{99m}Tc- Dimercapto-succinic acid (DMSA) split renal function (SRF) using geometric mean is commonly used to assess the relative kidneys function; however it does not provide information regarding the functional status of the individual kidneys. Absolute renal uptake (ARU) although less commonly used in routine DMSA studies is considered a valuable quantitative parameter capable of assessingthe absolutekidney function independently. The aim of our study was to establish a standardized reference value for ARU from posterior view only images, to assess the accuracy of Tonnensen equation(1) to estimate the kidneys depth compared to the actual kidney depth measured on CT.

MATERILAS AND MEHODS:

Patient Population:

We retrospectively analyzed 80 healthy adults, potential kidney donors of whom 64 (80%) were males and 16 (20%) were females with a mean age of 29.8±8.7 years (range 18-57 years). Serum creatinine and blood urea were measured for all individuals. The height in cm and the weight in kg were measured and reported in order to be used in estimation of kidneys depth according to Tonnensen equation. Contrast enhanced CT abdomen was performed for each potential kidney donor as a part of predonation workup.

^{99m}Tc DMSA Imaging:

All patients were imaged3 hours post IV injection of 150 MBq of ^{99m}Tc-DMSA. The pre and post injection syringe activities were reported. Both anterior and posterior static view images for 10 minutes were acquired in the supine position with the imaging field of view centered on the kidneys on a dual head gamma camera (Infinia, GE Healthcare or Nucline Spirit DH-V, Mediso Medical Systems) equipped by a low energy high resolution parallel hole collimator in a 256 x 256 matrix.

Calculation of DMSA Uptake: Regions of interest (ROI) were automatically drawn around each kidney in both anterior and posterior views with background correction performed using circumferential ROIs. Correction for radioactive decay was automatically performed. The SRF was calculated using the geometric mean counts of the anterior and posterior views. The depth of the kidneys were estimated either based on weight (W) in kg and height (H) in cm using Tonnensen equation[1]

(Right kidney = 13.3 (W/H) + 0.7, Left kidney =13.2 (W/H) + 0.7) or through direct CT measurement of individual kidney depths from the skin to kidney center at the level of the kidney hilum as seen on the transaxial slices (figure 3A).

The ARU was estimated based on the posterior view imagesonly.The ARU with no attenuation correction (NAC) was calculated based on the following equation:

$$ARU\ (NAC) = \frac{\left(\frac{\text{Renal Activity}}{\text{Detector Efficiency}}\right)}{\text{Net Activity injected}} \text{ x } 100$$

The attenuation corrected (AC) ARU was calculated for both CT measured kidney depth as well as for the estimated kidney depth based on Tonnesen equation, using tissue attenuation coefficient (μ) of -0.12 according to the following equation:

$$ARU\ (AC) = \frac{\text{ARU (NAC)}}{e^{(-0.12) \text{ x (Kidney Depth)}}}$$

Statistical Analysis:

Paired T-test was used to compare the difference in the mean values of ARU and kidney depth when using the Tonnensen equation compared to direct measurement from CT.T-test for independent samples was used to compare the mean differences between right and left kidney as regards depth or ARU. Pearson's correlations were performed between the ARU calculated by each method. Kappa test was used to assess the agreement between the SRF derived from the posterior view calculated ARU and SRF calculated based on both the anterior and posterior view geometric mean method.Linear regression was performed to estimate the regression equations that represent the relationship between ARU calculated based on each method while multiple regression was used to generate new equations for estimation of right and left renal depth based on models that included both height and weight as independent variables entered in a stepwise method. For statistical significance ap value of<0.05 was required. The statistics were performed using Statistical Package for Social Sciences (SPSS) *"SPSS Inc, Chicago, IL, USA"* version 13.0 and MedCalc® *"MedCalc Software, Ostend, Belgium"* version 10.2.0.0.

RESULTS:

The characteristics and clinical data of the study population are shown in Table 1.All individuals had normal urea and creatinine. The kidney depths and calculated ARU values for left and right kidney are shown in table 2.

Table 1: Demographic and clinical data of the study population

	Study group(n=80)
Mean age (years)	29.76 ± 8.65
Males	64 (80%)
Weight (kg)	71.04 ± 14.89
Height (cm)	168.66 ± 8.56
Urea (mmol/L)	4.04 ± 1.19
Creatinine (umol/L)	80.41 ± 17.19

The mean kidneys depth calculated using the Tonnensen equation was significantly less compared to the actual kidneys depth measured from CT scan for both left and right kidney (Table 2). The depths of the left and right kidney were not significantly different when estimated using the Tonnensen method, however the ARU derived based on these depths used for attenuation correction were significantly different being higher for the left kidney.On the other hand the actual depths measured from CT scans were significantly higher for the right kidney compared to the left kidney but there were no significant difference between the right and left kidneys when the ARU was calculated according to attenuation correction based on the skin to kidney center CT measured depths (Table 2). Prediction error for depth using Tonnensen equation was -1.16 ± 0.67 cm for the left kidney and -2.21 ± 0.87 cm for the right kidney. This consequently led to a prediction error in ARU calculation of -4.49 ± 1.92 % for left kidney and -5.61 ± 2.15 %.There was good correlation between kidney depths obtained by Tonnensen method and by CT measurement for both left and right kidneys with N=85 and R=78 respectively **(Fig. 1).**

Table 2: Comparison of depths and absolute DMSA uptake for both left and right kidney.

	Kidney Depth (cm) Mean ± SD		P-value	ARU (%) Mean ± SD		P-value
	Tonnensen	CT		Tonnensen	CT	
Left Kidney (n=80)	6.24±1.03	7.48±1.27	<0.001	20.79±4.01	24.08±4.50	<0.001
Right Kidney (n=80)	6.28±1.04	8.09±1.42	<0.001	18.79±4.31	23.23±4.9	<0.001
P-value	0.799	0.005		0.003	0.255	

Depth CT = 0.9048 + (1.0528 x Depth TN) **Depth CT = 1.3598 + 1.0710 x Depth TN)**

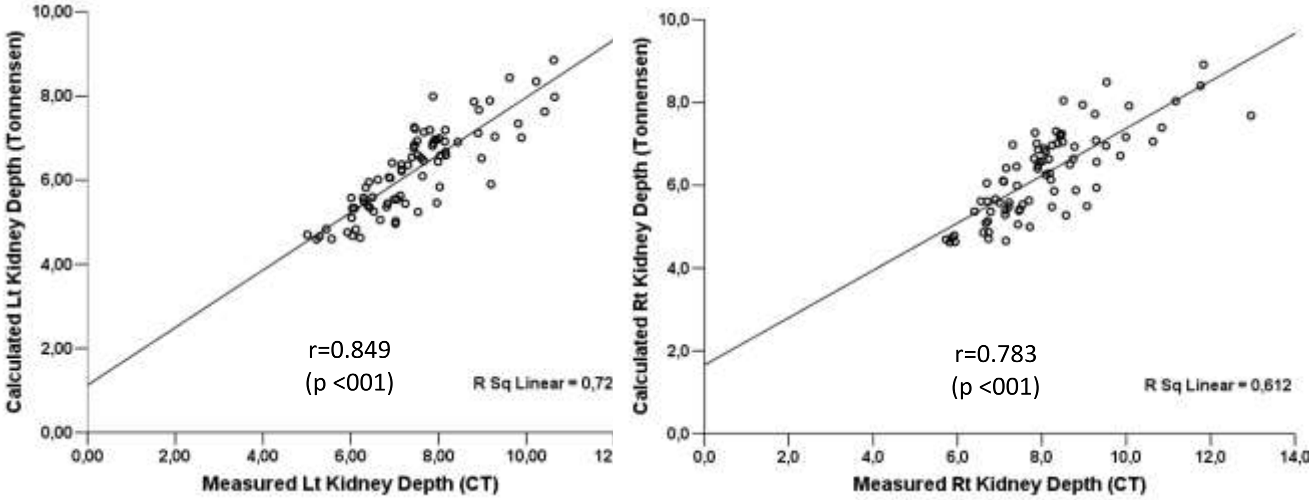

Figure 1: Correlation between Tonnensen (TN) equations estimated kidney depth and CT measured kidney depth in cm. linear regression equations generated for both left and right kidney are shown above.

ARU CT = 2.4185 + (1.1000 x ARU TN) **ARU CT = 4.2338 + (1.0733 x ARU TN)**

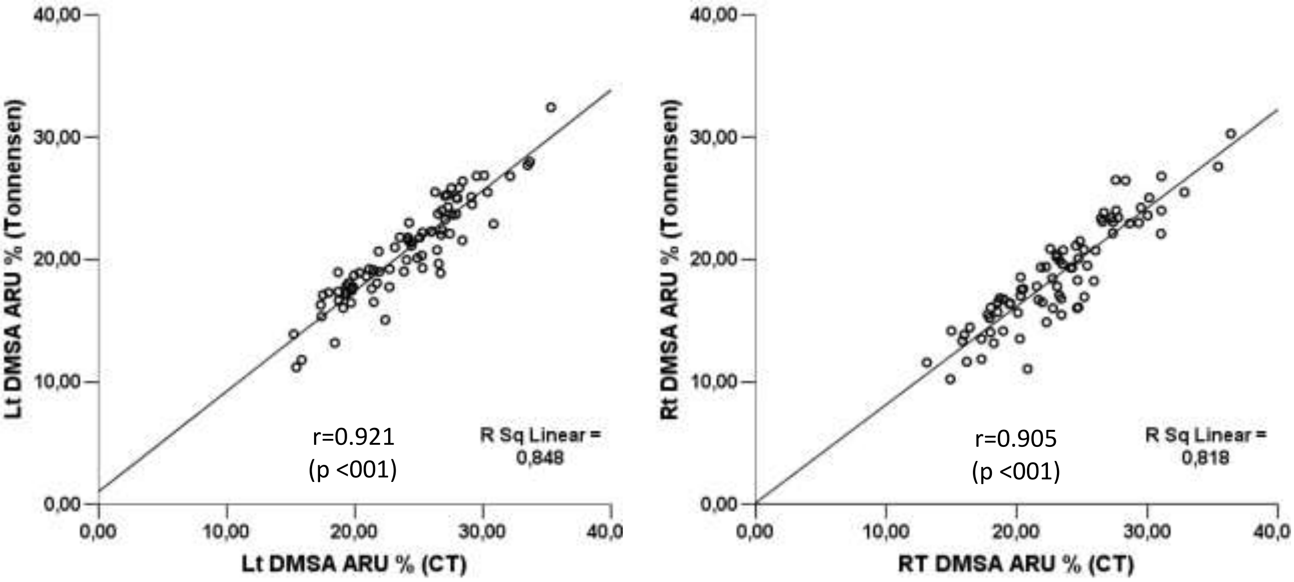

Figure 2: Correlation between calculated ARU with attenuation correction based on Tonnensen (TN) equation estimated kidney depth versus attenuation correction based on CT measured kidney depth. Linear regression equations generated for both left and right kidney are shown above.

This good correlation was maintained as well for the calculated ARU using the two methods with r=92 for LT kidney and R = 90.5 for RT kidney (Fig. 2). The correlations between the depth and ARU derived from Tonnensen method versus those derived from CT depth measurement were slightly better for the left kidney. Linear regression equations that reflect the relationship between Tonnensen equation estimated and CT measured kidney depths as well as between the ARU calculated according to attenuation correction using both sets of kidney depths, are displayed in figures 1 and 2.The multiple regression analysis for prediction of renal depth included weight (kg) and height (cm) revealed that weight (kg) is a powerful independent predictive variable in determination of renal depth while height was excluded from the regression model. The weight was significantly better correlated to kidney depth than height with correlation coefficient (r) of 0.862 versus 0.443 respectively for left kidney and 0.812 versus 0.473 respectively for right kidney.The regression equations generated for estimation of kidneys depth based on the body weight were:- Left kidney depth in cm = 2.2292 + (0.07384 xweight in kg)- Right kidney depth in cm =2.5935 + (0.07734 x weight in kg) .The agreement of the split renal function (SRF) derived from the ARU regarding the kidney of higher uptake versus the SRF calculated using the geometric mean of anterior and posterior view counts was better for SRF derived from ARU with attenuation correction based on CT renal depth measurement compared to that based on estimated renal depth by Tonnensen equation (Kappa = 0.479; p<0001 vs. Kappa = 0.162; p=0.832) respectively (Table 3) and (fig 3).

Table 3: Agreement between kidneys of higher uptake in SRF derived from calculated posterior view ARU versus SRF calculated based on geometric mean of anterior and posterior views.

		SRF (GM)		**Kappa**	
		Lt.	Rt.	K-value	P-value
SRF (TN)	Lt.	43	24	0.163	0.083
	Rt.	5	8		
SRF (CT)	Lt.	38	10	0.479	<0.001
	Rt.	10	22		

SRF (GM): SRF measured based on geometric mean; SRF (TN) & SRF (CT): SRF derived from ARU with attenuation correction using kidney depth from Tonnensen (TN) equation or CT measurement.

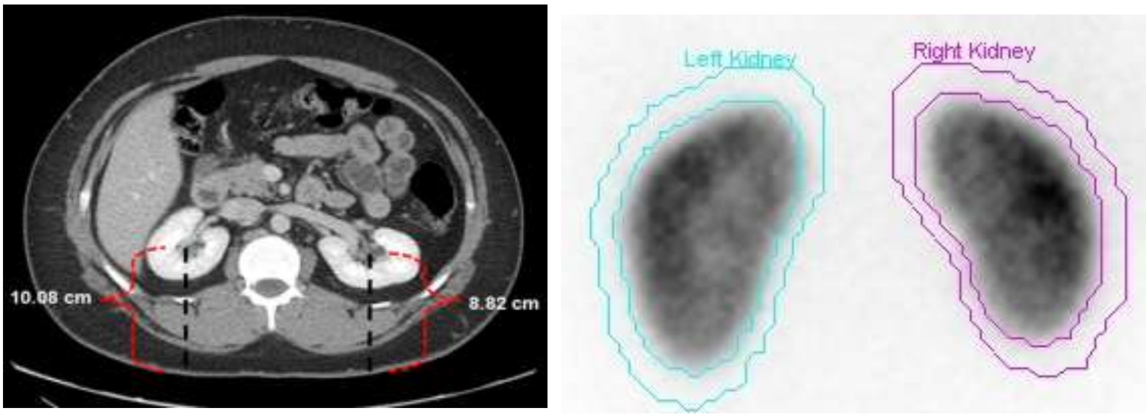

Figure 3: CT scan transaxial slice at kidneys hilum showing the measured kidneys depth from skin to kidney center (a) and a posterior view DMSA scan for the same patient (b) with a table showing calculated and measured kidneys depths and the ARU with no attenuation correction (NAC) and with attenuation correction according to the estimated depths.

Table 2: Comparison of depths and absolute DMSA uptake for both left and right kidney.

	LEFT KIDNEY	RIGHT KIDNEY
Kidney Depth (TN)	7.86 cm	7.91 cm
Kidney Depth (CT)	8.82 cm	10.06 cm
ARU % of Dose (AC/TN)	25.08%	24.01%
ARU % of Dose (AC/CT)	28.00%	31.07%
ARU % of Dose (NAC)	9.73%	9.28%
Height	165.00 cm	
Weight	89.50 kg	
Age	25 years	

DISCUSSION:

Absolute renal uptake (ARU) is a quantitative parameter capable of assessing the absolutekidney function for each kidney independently. Multiple previous studies had discussed various methods for calculation of ARU.[1-12] . The use of posterior view images is probably a practical and non-sophisticated method for ARU quantification and could be easily incorporated in routine processing of daily clinical DMSA studies. However the accuracy of ARU calculation using this method is dependent to a great extent on the knowledge of the kidneys depth in order to perform an accurate attenuation correction. We compared the famous and commonly used Tonnensen equation for estimation of kidneys depth to the measured depth from abdominal CT scan. The mean kidneys depth estimated using Tonnenesen equation was significantly less compared to the CT measured depth from skin to kidney center. This is consistent with previous findings by Manival et al. who reported an underestimation error of Tonnensen equation in prediction of left and right kidney depths of -0.91 cm and -1.19 cm respectively in a population of 53 pediatric patients.[8] In our study of adult population, the error was -1.16 ± 0.67 cm for the left kidney and -2.21 ± 0.87 cm for the right kidney showing again larger error for the right kidney depth estimation compared to the left kidney depth estimation. In a later study by Taylor et al. of 126 adult patients, again Tonnensen formula was found to underestimate renaldepth for both kidneys compared to CT measured depth and the error increased as renaldepth increased.[13] In our study, the CT measured mean kidney depths were comparable to that measured by Taylor et al.[13] reporting an average left kidney depth of 7.60 ± 1.97 and a right kidney depth of 7.70 ± 1.81 versus 7.48 ±1.27 and 8.09 ±1.42 respectively in the current study. The Tonnensen equation due to its simplicity had been widely used by multiple authors,[9-15] however it should be emphasized that Tonnensen equation was generated from a regression analysis for 55 adults with mean age of 46 years, based on ultrasound measured kidney depth in posterior oblique rather than direct posterior view and in sitting position rather than in the supine position during routinely used in DMSA scanning.[1]The ARU values we calculated are probably comparable to that previously reported by other authors using various methods. Using a geometric mean method, Zananiriet al.[2] reported a slightly higher ARU of 25.4 ± 8.9% for normal adults at 3 hours post DMSA injection. Lee et al. using a CT measured kidney depth reported a amean value of 21.8 ± 7.9% for normal young adult kidney transplantation donors,[5] which is significantly lower than our ARU value based on CT measured kidney depth but still slightly higher than our Tonnensen based ARU.This could simply be related to different technique in measuring kidneys depthon CT, however various other factors including the DMSA injected dose, time to imaging, the tissue attenuation coefficient used, body configuration and patient's age may be implicated. A decline in ARU with age in adults had been previously described[7] and hence patient age is to be considered for accurate interpretation of ARU values. We found no significant difference in ARU between the left and right kidney when the attenuation correction was performed based on the actual kidney depths measured from CT. This means that the difference between the left and right kidney in the ARU calculated based on attenuation correction using Tonnensen equation to estimate kidney depth, was due to failure of the Tonnensen equation to accurately estimate the difference in depth between the left and right kidney, leading to an attenuation correction that does not essentially reflect the actual attenuation correction for each kidney. Also this again reflects the above mentioned finding, concerning the larger underestimation error of Tennonsen equation in estimating the right kidney depth. This consequently led to an inaccurate SRF derived from the ARU when Tonnensen equation was used for attenuation correction and its poor agreement to the SRF derived from the geometric mean method as regards the kidney of higher uptake. Although significantly different, there was good correlation between the calculated ARU calculated using the two methods of kidney depth determination. In a study by Lopes de Lima et al., the author compared the ARU calculated from in vivo and ex vivo (post nephrectomy) images of 17 patients scheduled for nephrectomy, and reported an excellentcorrelation (r-squared = 0.95).[(9)] . The body weight was the most powerful and only independent predictor for kidneys depth, based on the multiple regression analysis we performed. This is consistent to what mentioned before by Samal et al., who reported that body weight is the best individual predictor of kidneys depth in a population of 765 patients including both children and adults.[(16)] Equations for prediction of kidney depth were previously postulated by multiple authors.[(12,13,16,17,18)] From those whom used equations based on body weight were Gordon et al.[12]and Shore et al.[(17)] The regression equations we generated for prediction of kidneys depth are very close to that mentioned by Gordon et al., who reported the following equation generated from a pediatric group of 21 patients: kidney depth = 0.0742wt(kg) + 2.3. On the other hand the equation mentioned by Shore et al. (1.37 + 0.349wt (kg)) was apparently different from both our equation and Gordon et al. equation. This is most probably due to the fact that Shore et al. measured kidney depth from skin to kidney surface and not to kidney center, ignoring the tissue attenuation effect of the kidney itself.

CONCLUSION:

The ARU calculated based on Tonnensen method although is underestimated compared to that based on CT measurement, both are highly correlated. The variability in normal ARU values reported in various studies is probably multifactorial however a key factor is the method used for kidneys depth assessment.A small change in the estimated or measured kidney depth will lead to a significant change in ARU calculated. Therefore we recommend that local center specific standardized reference ARU values be developed by every nuclear medicine department rather than using a predecided values from the literature. Alternatively ARU calculation with no need for kidney depth estimation had been accomplished based on SPECT imaging, [4, and 10] however is more sophisticated and less practical. We believe that the equations we generated for estimation of kidneys depth in adults, based only on body weight may serve as a simple alternative formula to the Tonnensen equation, however further validation may be required before its routine application in general population.

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