



ORIGINAL RESEARCH ARTICLE

Estimation of differential renal function in unilateral hydronephrotic kidneys with asymmetrical renal area ratio: Comparison of classical and unit area corrected methods

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ABSTRACT

Introduction: Differential renal function calculation plays an important role in surgical decisions in hydronephrotic kidneys, which may show false-positive or false-negative results owing to the asymmetrical renal area in hydronephrotic kidneys. The disparity between the visual and quantitative estimations of renal function can complicate decision making for renal interventions at the optimal time. This study was designed to evaluate whether correcting the differential renal function (DRF) estimation according to kidney unit area can be a more valuable predictor of the functional status of a hydronephrotic kidney than the classical geometric mean method.

Methods: Tc-99m Dimercaptosuccinic acid ([^{99m}Tc]Tc-DMSA) scans and ultrasonography finding of 524 patients with unilateral hydronephrosis due to urinary tract obstruction were reviewed. Differential renal function estimated by both classical geometric mean and unit area corrected method were compared. The correlations of the differential renal function values with the visual classification and the hydronephrosis grades were assessed.

Results: The mean Differential renal function by the classical geometric mean and the unit area corrected method of the hydronephrotic kidneys was $41.2\% \pm 12.3$ and $36.6\% \pm 9.9$ respectively, with mean difference of $4.6 \pm 7.7\%$ ($p < 0.001$). With increasing hydronephrosis grade, differential renal function decreased significantly by the unit area corrected method ($p < 0.001$).

Conclusion: Our results suggest that differential renal function estimation by the unit area corrected method is more reliable than by the classical geometric mean method in unilateral enlarged hydronephrotic kidney to avoid misinterpretation due to over-estimation of renal function.

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INTRODUCTION

Quantitative data on differential renal function (DRF) obtained by static renal scintigraphy with Tc-99m Dimercaptosuccinic acid (^{99m}Tc Tc-DMSA) scans has been accepted as the best method to evaluate renal function status due to its high-quality signal [1].

Initial differential renal function and its deterioration on follow up scans have been one of the important factors on which surgical decisions are based, to preserve renal function. In obstructed kidneys particularly in patients with asymptomatic hydronephrosis, it is the principal criterion for surgery and post-surgical assessment of the recovery of renal function and renal cortical damage. The classical geometric mean method has been used for the estimation of differential renal function, which has shown disparity between the visual and quantitative assessment of renal function in hydronephrotic kidneys, as increased, supranormal and overestimated renal function due to asymmetry in renal size compared to the contralateral normal renal unit [2, 3].

It has been recognized that altered scintillation detection due to the relative distribution of radioactivity in the renal parenchyma and the geometrical structure of the kidney especially in a hydronephrotic kidney may be the reason for renal function disparity. It could be due to compensatory glomerular and tubular hypertrophy or increased renal blood flow, which may increase renal function [4]. However, it remains unclear whether the overestimation of DRF on the affected side is physiological or just a quantification problem.

It has been noted that there is an influence of renal size on DRF estimation and the relatively high incidence of the paradoxical phenomenon due to kidney size raises the requirement for a more reliable method of DRF measurement. It has been suggested that a modified method of DRF calculation, taking renal unit area estimations into account, could reduce the false negative results of DRF measurements due to significant difference in renal size before and after surgical intervention [5, 6, 7].

This study was designed to assess whether correcting the radioactivity of each kidney according to its area could assess the renal function of a hydronephrotic kidney better than classical DRF calculation in large population and to determine their correlations with the degree of hydronephrosis and visual assessment.

METHODS

Patients with unilateral hydronephrosis with a normal contralateral kidney, who underwent

static renal scintigraphy using Dimercaptosuccinic acid ^{99m}Tc Tc-DMSA were retrospectively selected. The degree of hydronephrosis ranged from grade 1 to 3, classified as mild, moderate and severe urinary tract dilatation respectively based on the nearest ultrasound (US). Patients with ectopic kidneys, fused kidneys, bilateral hydronephrosis, duplex kidneys, solitary kidneys, renal masses, vesicoureteral reflux and other urologic anomalies were excluded.

^{99m}Tc Tc-DMSA scintigraphy images were obtained using a GE Infinia 2 model SPECT gamma camera (GE Medical Systems) equipped with a low energy general purpose parallel hole collimator. The imaging was performed in the supine position following intravenous administration of approximately 130 -185 MBq (1.85 MBq/kg pediatric dose) of ^{99m}Tc Tc-DMSA, 2-3 hours prior to imaging. Anterior, posterior, right and left oblique planar images were acquired with the energy setting photo peaked at 140 Kev with a 20% symmetric window. A total of 500K counts were acquired per view in a 256×256 matrix. The data were analyzed using GE Infinia Xeleris software. A bean-shaped region of interest (ROI) was drawn over the kidneys and a crescent shaped ROI was drawn inferolateral to the kidney for background subtraction. Differential renal function (DRF) was calculated using two methods. Initial calculations were performed using the classical geometric method (CM) by taking the square root of each kidney's background-subtracted ROI counts in the anterior and posterior views followed by a second calculation to correct the activity of each kidney according to its area, by dividing the counts of the kidneys by the number of pixels in each kidney's ROI. These corrected counts were used in the classical geometric mean calculation, as described in the equations a and b (Figure 1) [6, 7].

Values of DRF obtained were categorized into four groups. Kidneys with DRF between 40 to 55% were considered as good functioning, those with >55% were considered as supranormal functioning, < 40% were considered as reduced functioning and those with <25 % were considered as markedly reduced functioning. Visual assessments were performed by two experienced nuclear medicine physicians and the hydronephrotic kidneys were classified into three groups:

good, reduced, and markedly reduced functioning respectively. DRF values calculated by both methods were compared and their correlations with visual classification and

degree of hydronephrosis were evaluated. This retrospective study was approved by the Scientific Ethics Committee of the Sindh Institute of Urology and Transplantation.

$$\text{a) Classical Method (CM)} = \frac{\sqrt{AcH \times PcH}}{\sqrt{AcH \times PcH} + \sqrt{AcN \times PcN}} \times 100$$

$$\text{b) Unit Area Corrected Method (ACM)} = \frac{\sqrt{\frac{AcH}{ApH} \times \frac{PcH}{PpH}}}{\sqrt{\frac{AcH}{ApH} \times \frac{PcH}{PpH}} + \sqrt{\frac{AcN}{ApN} \times \frac{PcN}{PpN}}} \times 100$$

Figure 1. Equations for the calculation of DRF with the classical and Unit area corrected method. (DRF: Differential renal function of hydronephrotic kidney, AcH: Anterior counts of hydronephrotic kidney, AcN: Anterior counts of normal kidney, PcH: Posterior counts of hydronephrotic kidney, PcN: Posterior counts of normal kidney, ApH: Total pixels in anterior region of interest of hydronephrotic kidney, PpH: Total pixels in posterior region of interest of hydronephrotic kidney, ApN: Total pixels in anterior region of interest of normal kidney, PpN: Total pixels in posterior region of interest of normal kidney)

Statistical analysis

Differences in means of both methods of DRF calculations were tested using a paired T-test. Correlations between DRF, hydronephrosis grade and visual assessment were investigated using Spearman's rho. A p-value of ≤ 0.05 was set as statistically significant. Statistic evaluations of this study were conducted in collaboration with the Department of Biostatistics at SIUT.

RESULTS

524 [^{99m}Tc]Tc-DMSA scans of patient with unilateral hydronephrosis on ultrasound were retrospectively analyzed. There were 146 (28%) females and 378(72%) males, aged between 1 and 60 years (mean age 9.5 ± 8.5 years). 169 (32%) patients had grade 1, 150 (29%) had grade 2 and 205 (39%) had grade 3 hydronephrosis (Table 1). The mean DRF calculated by the Classical method and the Unit area corrected method were

$41.2\% \pm 12.3$ and $36.6\% \pm 9.9$, respectively with a mean difference of $4.6\% \pm 7.7$ (Figure 2), showing a statistically significant reduction in DRF calculation ($p < 0.001$). 42% of renal units showed a $\geq 5\%$ reduction in DRF (mean $11.9\% \pm 5.5\%$) which was considered a clinically significant change in %DRF values.

According to the classical method the %DRF of 261 (49.8%) renal units were classified as good functioning (group I), 139(26.5%) renal units as reduced functioning (group II), 72 (13.7%) as markedly reduced functioning (group III) and 52(9.9%) were supranormal (group IV). 30.3% of renal units showed a change in group category after the second calculations with ACM. Out of 261 renal units that initially belonged to group I, 80 (30.6%) were reclassified into group II and 8 (3%) into group III. 23 (16.5%) renal units from group II were reclassified into group III and only 4 (0.7%) renal units showed supra normal DRF with a mean DRF reduction of $14.4\% \pm 7.6\%$ (Figure 3).

Table 1. DRF distribution according to the degree of hydronephrosis

Hydronephrosis	Number	CM DRF% (mean \pm SD)	ACM DRF% (mean \pm SD)	Difference % (mean \pm SD)	p-value
Total # of patients	524	41.21 \pm 12.3	36.6 \pm 9.9	4.6 \pm 7.7	<0.001
Mild HN	169	43.2 \pm 10.5	42.0 \pm 8.1	1.15 \pm 5.39	<0.006
Moderate HN	150	41.04 \pm 11.42	37.6 \pm 8.6	3.34 \pm 6.12	<0.001
Gross HN	205	39.7 \pm 14.01	31.3 \pm 9.5	8.37 \pm 8.69	<0.001

CM: Classical method; ACM: Unit area corrected method; HN: Hydronephrosis; DRF: Differential renal function

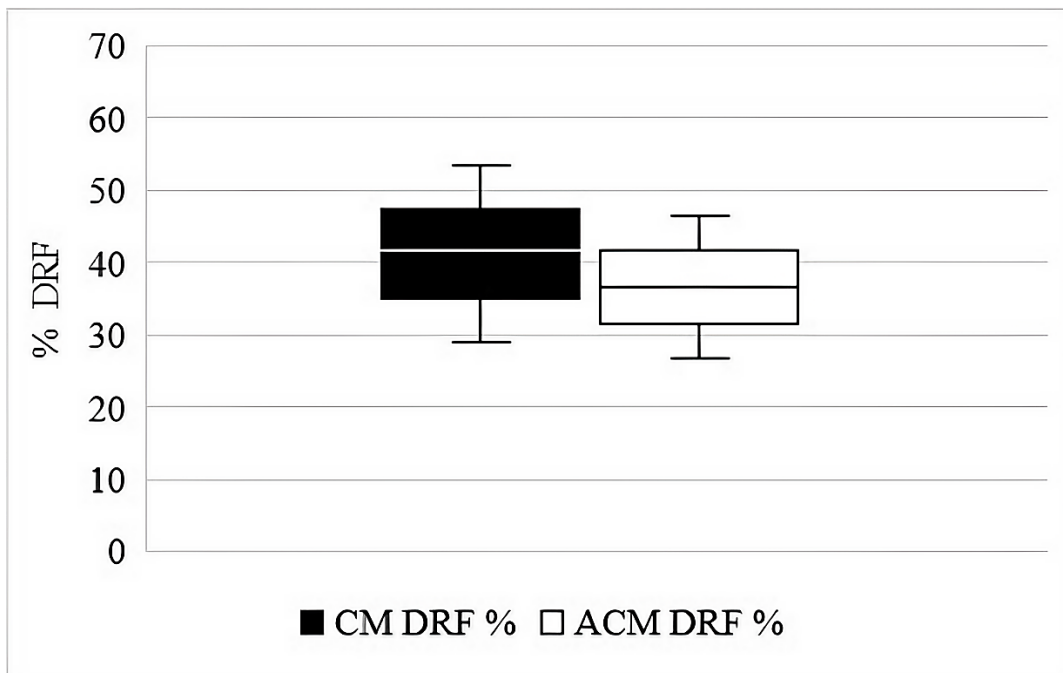


Figure 2. Differential renal function (DRF) distribution of the hydronephrotic kidneys by the Classical (CM) and the Unit area corrected method (ACM)

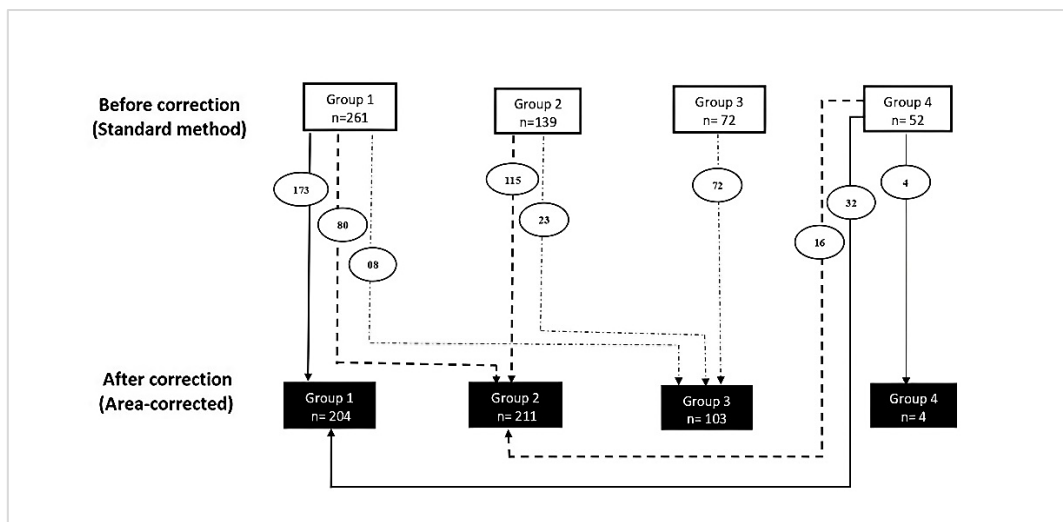


Figure 3. Functional distribution of the renal units according to the DRF estimation by standard method and corrected method

There was no correlation between classical %DRF estimations and hydronephrosis grades. However, DRF estimations determined by the unit area corrected method (ACM) showed a moderately strong negative correlation with the degree of hydronephrosis ($p < 0.001$) (Table 2). With an increased hydronephrosis grade, %DRF decreased by the area corrected method. The difference in DRF calculated by two methods was $1.15 \pm 5.39\%$

in mild hydronephrosis, $3.34 \pm 6.12\%$ and $8.37 \pm 8.69\%$ in moderate and gross hydronephrosis, respectively (Figure 4). Visual evaluation showed that 195 (37.2%) hydronephrotic kidneys were good functioning 210 (40%) were reduced functioning and 119 (22.7%) were markedly reduced kidneys. There was a very strong negative correlation between visual interpretation and % DRF estimated by the

unit area corrected method (Table 2). The sensitivity of CM and ACM for evaluating renal function in relation visual interpretations were 63.8% and 88.8% and specificity were 96.9% and

93.8%, with a positive predictive value of 97% and 96%, a negative predictive value of 61% and 82%, respectively.

Table 2. Correlation between the DRF with degree of hydronephrosis and the visual interpretation

DRF	Hydronephrosis		Visual evaluation	
	ρ	p-value	ρ	p-value
CM	0.03	0.03	-0.682	<0.001
ACM	-0.465	<0.001	-0.850	<0.001

DRF: Differential renal function, CM: Classical method, ACM: Unit area corrected method

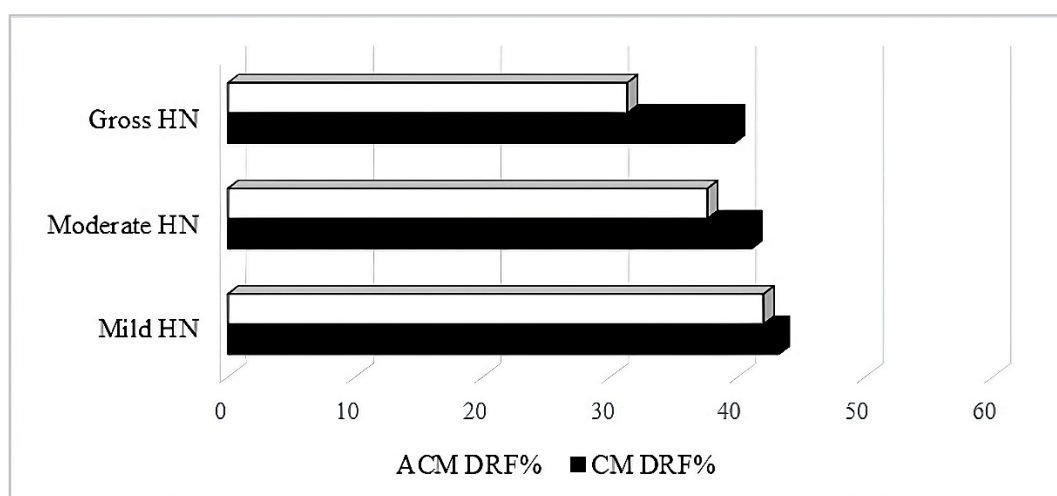


Figure 4. Differential renal function (DRF) distribution by the classical (CM) and Unit area corrected (ACM) method according to the grades of hydronephrosis

DISCUSSION

Overestimated differential renal function (DRF) is problematic in unilateral hydronephrotic kidneys and it is an important pitfall of the classical method of DRF estimation. Hydronephrotic kidneys can exhibit no significant functional loss, better function than the normal contralateral renal unit, or even supranormal function on renal scintigraphy, which can lead to missed opportunities for renal intervention to restore function and prevent early renal atrophy and permanent loss of renal function, particularly with false negative results [8, 9].

The hydronephrotic kidney seems to have decreased function in contrast to the contralateral healthy kidney. Studies have shown a correlation between the degree of hydronephrosis and DRF. Mild hydronephrosis has minimal impact while gross hydronephrosis has significant impact on DRF. However, this relationship is not always linear, and individual variations occur. Other factors, such as duration of obstruction, presence of infection, and

underlying a kidney disease, can influence the degree of kidney function impairment. Generally, a higher degree of hydronephrosis is associated with a greater decrease in differential renal function, indicating more significant impact on kidney function.

Supranormal and overestimated functions with both higher and lower grades of hydronephrosis have been reported previously are in concordance with our findings. It has been experimentally shown that overestimated function is due to parenchymal thinning caused by significant hydronephrosis and altered detection of scintillations due to the geometrical configuration of the kidney [10, 11]. It has been suggested that higher intrarenal vascular background activity and a higher renal area ratio are related to overestimated DRF in high grade hydronephrosis using the classical method [12, 13]. It remains unclear whether overestimated DRF is due to artifact, pathophysiology or a fault in quantification due to increased renal size in hydronephrotic kidneys. Preoperative DRF is most

significant predictor of postoperative renal function improvement. Decrease in the differential renal function (DRF) <40% in unilateral hydronephrosis due to suspected ureteropelvic junction obstruction, is usually considered an indication for surgery [14, 15]. If renal function is severely impaired <20% the management becomes more controversial. It has been reported that lower renal function preoperatively is unlikely to improve post operatively. Pre-operative differential renal function between 35% and 40% has greater probability of post-surgical functional improvement. DRF increase >5% is considered as surgical success. These findings contribute to understand and evaluate effective treatment options for unilateral renal obstruction to preserve renal function and reducing symptoms [16, 17]. In contrast to studies analyzing pediatric patients, whose renal function had a greater chance of improving postoperatively [18, 19].

Therefore, a more reliable assessment method is required to help determine the optimal surgical time. Nam et al. retrospectively compared pre and post-surgical differential renal function (DRF) measured by taking renal areas into account from different imaging modalities in the pediatric population, which exhibited a lower false-negative rate [5].

Aktaş et al. determined that over estimation of DRF occurs in kidneys with higher renal area ratio than the contralateral normal kidney [6]. Correcting DRF by dividing the counts of the kidneys by the number of pixels in each kidney's region of interest (ROI) showed a significant reduction in DRF of hydronephrotic kidneys [6]. Kepenek et al. also found a significant difference in DRF when corrected with unit area in low-grade hydronephrotic kidneys [7]. In our study 41.6% of kidneys showed a >5% reduction in DRF by the corrected method and the difference was higher as the degree of hydronephrosis increased which is concordant with the results of previous studies. Supranormal differential renal function (snDRF) is considered to exist when the differential renal function in the affected kidney is >55% of the total renal function. The reported prevalence of snDRF, ranges from 4 to 28%. It is also debated whether the snDRF represent a true supranormal function or simply an artifact of the examination. Renal parenchymal hypertrophy, contralateral hypofunction, and hyperfiltration in the hydronephrotic kidney as well as insufficient sub renal background, have been considered as reasons for the unusual elevation in differential

renal function [20, 21, 22]. It has been reported that supranormal function may be related to significantly larger renal size and obstructive hydronephrosis [23, 24]. It was suggested to administer a diuretic during [^{99m}Tc]Tc-DMSA studies to overcome this problem which has been proven to be unnecessary [25]. In our study 52 (9.9%) kidneys showed supra normal renal function, out of which 67% were moderate to grossly hydronephrotic kidneys. Only four renal units showed supra normal renal function after corrected calculations. The limitation of the study is that it is retrospective; we did not correlate the renal sizes with the second calculation. However, it was observed that enlarged renal units showed more reduction in DRF. This study might be more informative if it is repeated with inclusion of renal size quantification and APPD and correlating it with DRF determined by the two methods and to validate the usefulness of area corrected method. Secondly, we did not include the pre- and post-surgical data due to non-uniformity in management plans and follow-up protocol.

There was a discrepancy between visual and quantitative DRF estimations by the classical method resulting in an overestimation of renal function, which were consistent with the observations by Cho et al. Renal parenchymal thinning related to the extent of hydronephrosis increases the total renal surface area, showing normal DRF signifying the reliability of visual evaluation for renal interventions [26]. There was a strong correlation between the visual evaluations of [^{99m}Tc]Tc-DMSA scans and the corrected DRF. As visual interpretation is subjective, ACM can be a reliable method for renal function evaluation in cases of overestimated DRFs.

CONCLUSION

Our results suggest that [^{99m}Tc]Tc-DMSA uptake uncorrected for renal size can overestimate renal function in larger kidneys. Area corrected quantification seems to be more reliable method in the estimation of relative renal function in unilateral hydronephrotic kidneys to reduce the discrepancy between visual and quantitative interpretation, which may influence decisions for surgical interventions to preserve renal function due to over estimation of renal function.

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