

Brief Report

Relationship of ultrasonographically determined kidney volume with measured GFR, calculated creatinine clearance and other parameters in chronic kidney disease (CKD)

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Abstract

Introduction. Kidney length has traditionally been used as a predictor of chronic kidney disease (CKD); however, kidney volume (KV) rather than length has been emphasized by researchers as a true predictor of kidney size in states of good health and disease. Since KV can be assumed to be a predictor of kidney mass or remaining surviving nephrons in CKD patients, we theorized that the KV should reflect the functional capacity of the kidneys, i.e. the glomerular filtration rate (GFR).

Methodology. Forty CKD patients were recruited and investigated. Measured GFR was determined by calculating the average of endogenous creatinine clearance (mCrCl) and urea clearance (mUrCl) while predicted GFR was determined using Cockcroft and Gault, Hull and Modification of Diet in Renal Disease (MDRD) equations. KV was assessed ultrasonographically using the formulae of Dinkel *et al.* and Solvig *et al.* for ellipsoid organ. The relationship between the KV and GFR was assessed using Spearman's correlation coefficient while Bland and Altman tests were used to assess intraobserver variation and agreement between measured and predicted GFR.

Results. The results showed a weak but positive correlation between KV and various indices of GFR, best with measured CrCl (correlation coefficient ranged between 0.408 and 0.503; $P < 0.05$), and which was not improved after normalization for body surface area (BSA). We also found a significant correlation between the measured CrCl and various values of estimated CrCl.

Conclusion. Ultrasonographically determined KV was found to correlate with GFR and hence can be used to predict it in established CKD, particularly in resource-poor settings.

Keywords: CKD; creatinine clearance; GFR; kidney volume; MDRD

Introduction

Kidney length has traditionally been taken and used as a predictor of chronic kidney disease (CKD). However, kidney length may not be an accurate predictor of kidney disease. Kidney volume (KV) rather than kidney length has been emphasized by several authors as a true predictor of kidney size in states of good health and disease [1,2]. Emamian *et al.* [1] called it the most exact measurement of renal size while Jones *et al.* [2] stated that kidney volume is a more sensitive means of detecting kidney abnormalities than any single linear measurement. Kidney volume is favoured because it correlates with body surface area (BSA) whereas kidney length correlates with height [1]. In addition, kidney length decreases with age as the kidney becomes thicker and wider whereas kidney volume is stable with relatively little change. Normal kidney length has been found to vary between 10 and 12.6 cm [3,4]. In support of these findings, Ninan *et al.* compared the methods of estimating renal size in normal adults and found that though the kidney length of some of the kidneys from donors was ≥ 10 cm, a substantial number of them were < 10 cm in length and several others were < 9 cm [5]. Hence, kidney length may not accurately determine the kidney volume even though it is widely used. In contrast, Griffiths [6] found the kidney length to be the best estimate of renal mass while Emamian *et al.* [1] argued that it was acceptable for routine clinical situations.

Since kidney volume can be assumed to be a predictor of kidney mass or remaining surviving nephrons in the CKD, we theorized that the kidney volume should reflect the functional capacity of the kidneys as determined by the average of endogenous creatinine clearance (mCrCl) and urea clearance (mUrCl) as well as estimated creatinine clearance using three formulae (i.e. Cockcroft and Gault, MDRD and Hull formulae).

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There have been a lot of criticisms on the use of endogenous creatinine clearance (mCrCl) as a measure of true glomerular filtration rate (GFR) in CKD patients because of tubular secretion of creatinine, which leads to overestimation of true GFR. Measured urea clearance (mUrCl) is also known to underestimate the true GFR in CKD, hence its unreliability; however, the mean value of mCrCl and mUrCl is assumed to closely approximate the true value of GFR in CKD [7]. The use of estimated CrCl using the Cockcroft and Gault equation has been found by our group and others to be a good predictor of true GFR in states of both good health and disease [8–11].

The purpose of this study was to find out whether the KV as determined ultrasonographically using Dinkel *et al.*'s formula [12] and its modification by Solvig *et al.* [13] reflects the functional capacity of the kidneys in established CKD.

Materials and methods

Patients' population

Forty individuals with established CKD referred to our clinic were prospectively recruited after a written informed consent. Those patients who required urgent dialysis and/or had unstable renal function were excluded. Also, patients on cimetidine, co-trimoxazole, salicylates, probenecid and trimethoprim were asked to stop the drugs at least 72 h before the study and patients with concomitant disease, e.g. liver disease, heart failure, etc., were excluded. Patients with diabetic nephropathy and polycystic kidney disease were also excluded.

Demographic and anthropometric parameters such as age, weight and height were recorded, and then each patient undertook supervised 24-h urine collection from 7.00 A.M. on any particular day to 7.00 A.M. the following day.

Ten millilitres (10 ml) of venous blood was collected into EDTA plastic container in a fasting state, and sent for laboratory analysis. Also, after determining the total volume of the urine voided, 10 ml of aliquot was taken and sent to our laboratory along with the venous blood for the assay of creatinine, urea, protein, sodium and potassium in both blood and urine samples. Creatinine was assayed using the modified Jaffe's reaction method while the diacetyl monoxime method was used for urea assay. Urinary protein was determined by turbidimetry with trichloroacetic acid. Both mCrCl and mUrCl were calculated using standard formulae [14] and estimated CrCl was also determined from serum creatinine using Cockcroft and Gault, MDRD and Hull formulae. Also, body mass index (BMI) was determined from the weight and height of the patients, while BSA was determined using Mosteller's simplified equation [15].

Kidney volume determination

Ultrasound examinations were performed with SONOACE 3200 (Medison Co., Ltd, Korea) using a 3.5 MHz curvilinear array transducer. All the ultrasound examinations were carried out by one of the authors. Sonographic mea-

Table 1. Aetiology of CKD in studied patients

Diagnosis	Number of patients	Percentage
Chronic glomerulonephritis	25	67.6
Hypertensive nephrosclerosis	8	21.6
Lupus nephritis	3	8.1
Sickle cell nephropathy	1	2.7
Total	37	100

surements were taken in the maximum longitudinal and transverse kidney sections. Kidney volume was determined using the formulae of Dinkel *et al.* [12], $0.523 * L * W * (D_1 + D_2) / 2$, and Solvig *et al.* [13], $0.612 * L * W * (D_1 + D_2) / 2$. Here, L is the maximum bipolar diameter (BPD); W is the maximum width in the hilar region and D is the maximum depth in the longitudinal (D_1) and transverse section (D_2).

Statistics analysis

The statistical package used was SPSS for Windows (13th edition). Spearman's nonparametric bivariate correlation was used to assess the correlation between volume measurements and other parameters that included various measurements of GFR, BMI, weight and BSA. Multiple regression analysis was used to control for confounding variables while the paired *t*-test was used for comparison of data. The similarities between the various GFR indices and agreement with measured creatinine clearance were assessed using Bland and Altman plots [16]. The difference between the measured CrCl and estimated CrCl from the three formulae was plotted on the *y*-axis against the average value of the measured CrCl and estimated CrCl (from the three formulae), which was plotted on the *x*-axis (Figure 1a–c).

Results

Demographic parameters and aetiology of CKD in studied population

A total of 37 patients completed the study. There were 25 males and 12 females and their ages ranged between 17 and 72 years with a mean (\pm SD) of 37.32 (\pm 2.42) years. The aetiology of CKD in majority of the patients was chronic glomerulonephritis (67.6%) and hypertensive nephrosclerosis (21.6%); other diagnoses are as shown in Table 1. The serum creatinine ranged between 101 and 2796 μ mol with a mean (\pm SD) of 570.49 (\pm 98.04) μ mol/l while the serum urea ranged between 3.50 and 45.70 mmol/l with a mean (\pm SD) of 16.06 (\pm 1.52) mmol/l.

Kidney dimension and its relationship with measured and estimated CrCl

The right kidney length ranged between 7.86 and 12.18 cm with a mean (\pm SD) of 10.34 (\pm 1.28) cm and the left kidney length range was 7.00–13.00 cm with a mean (\pm SD) of 10.33 (\pm 1.50) cm. The mean (\pm SD) volumes of right kidney and left kidney calculated using the Dinkel formula were 123.60 (\pm 43.1) cm^3 and 136.01 (\pm 72.26) cm^3 ,

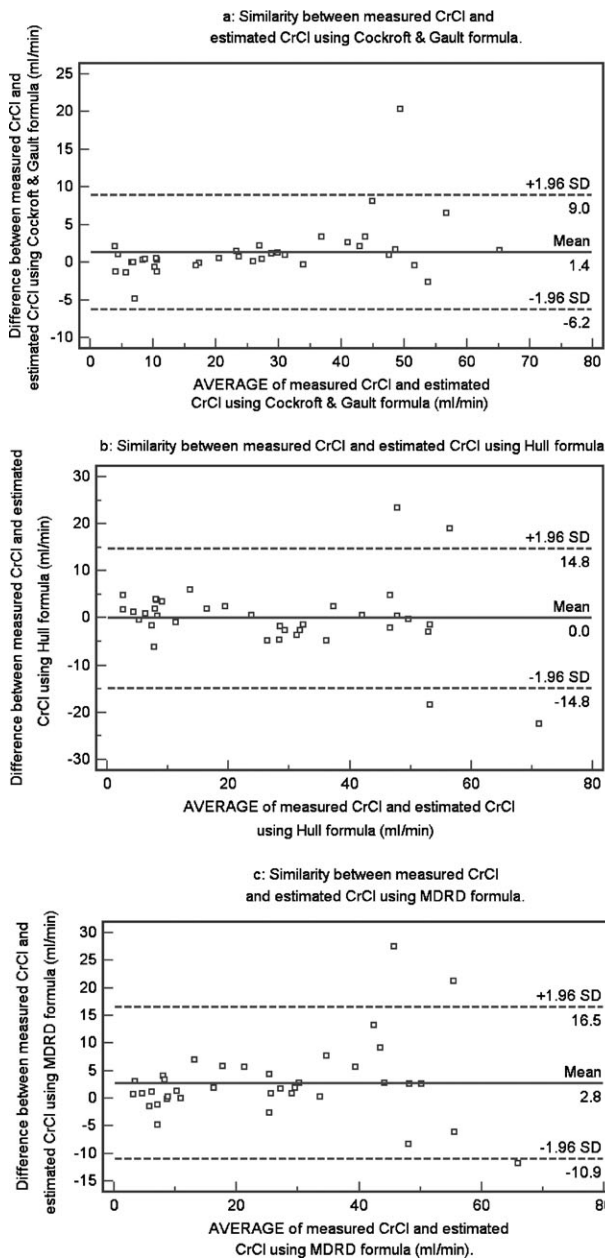


Fig. 1. Level of agreement between measured creatinine clearance and various GFR indices. (a) Similarity between measured CrCl and estimated CrCl using the Cockcroft and Gault formula. (b) Similarity between measured CrCl and estimated CrCl using the Hull formula. (c) Similarity between measured CrCl and estimated CrCl using the MDRD formula.

respectively, with a difference of 12.41 cm³ ($P = 0.128$), and the mean kidney volume (right and left) was 129.80 (± 54.36) cm³. When the Solvig formula was used, the mean volume of the right and left kidney was 151.89 (± 63.61) cm³. We found a significant difference in the volume determined by Dinkel *et al.* [12] and Solvig *et al.* [13]; the paired mean difference (PMD) was 28.09 and $P = 0.000$ (Table 2).

There was a positive correlation between the volumes determined sonographically using Dinkel *et al.*'s formula and Solvig's modified formula for ellipsoid organ and

Table 2. Comparison for various kidney dimensions

Parameter	Mean \pm SD	PMD	P-value
Kidney length (Rt) (cm)	10.34 \pm 1.28	0.01	0.957
Kidney length (Lt) (cm)	10.33 \pm 1.50		
Kidney width (Rt) (cm)	5.09 \pm 0.85	-0.10	0.485
Kidney width (Lt) (cm)	5.19 \pm 0.99		
Kidney diameter (Rt) (cm)	8.72 \pm 1.33	-0.45	0.033
Kidney diameter (Lt) (cm)	9.16 \pm 1.76		
Kidney volume by Dinkel (Rt) (cm ³)	123.60 \pm 43.1	-12.41	0.128
Kidney volume by Dinkel (Lt) (cm ³)	136.01 \pm 72.26		
Kidney volume by Solvig (Rt) (cm ³)	144.63 \pm 50.54	-14.52	0.128
Kidney volume by Solvig (Lt) (cm ³)	159.15 \pm 84.55		
Average kidney volume by Dinkel (cm ³)	129.80 \pm 54.36	-22.09	0.000
Average kidney volume by Solvig (cm ³)	151.89 \pm 63.61		
Average kidney volume by Dinkel corrected for BSA (cm ³)	75.81 \pm 31.89	-12.90	0.000
Average kidney volume by Solvig corrected for BSA (cm ³)	88.71 \pm 37.32		

Table 3. Correlation between kidney volume (using Dinkel's and Solvig's formulae) and various parameters

Parameters	Correlation coefficient (CC)	P-value
Kidney volume (cm ³) versus measured CrCl (ml/min)	0.510	0.001
Kidney volume (cm ³) versus Cockcroft and Gault estimated CrCl (ml/min)	0.471	0.003
Kidney volume (cm ³) versus MDRD-estimated CrCl (ml/min)	0.462	0.004
Kidney volume (cm ³) versus Hull-estimated CrCl (ml/min)	0.453	0.005
Kidney volume (cm ³) versus average kidney length (cm)	0.772	0.000
Average kidney length (cm) versus measured CrCl (ml/min)	0.426	0.009
Average kidney length (cm) versus Cockcroft and Gault estimated CrCl (ml/min)	0.371	0.024
Kidney volume (cm ³) versus urinary protein (g/day)	0.408	0.012 ^a

^aMultiple regression analysis revealed ($\beta = 0.192$ and $P = 0.238$).

measured and estimated CrCl generated by Cockcroft and Gault, Hull and MDRD equations. The correlation coefficients (CC) ranged between 0.453 and 0.510 and the P -value was < 0.05 (Table 3). When the kidney volumes were corrected for BSA we still found significant correlation (Correlation Coefficients ranged between 0.439–0.471 and P -value < 0.05) (Table 4), though the correlation coefficient was lower after normalization. The range of measured GFR using the mean of mCrCl and mUrCl was 3.50–66.00 ml/min while the mean (\pm SD) was 27.85 (± 3.11) ml/min. The mean (\pm SD) of estimated CrCl for Cockcroft and

Table 4. Correlation coefficients (CC) and their *P*-values between kidney volumes (KV) corrected for BSA and various parameters

Parameters	Correlation coefficient (CC)	<i>P</i> -value
KV corrected for BSA versus measured CrCl (ml/min)	0.471	0.003
KV corrected for BSA versus Cockcroft and Gault (ml/min)	0.439	0.007
KV corrected for BSA versus MDRD (ml/min)	0.458	0.004
KV corrected for BSA versus Hull (ml/min)	0.463	0.004
KV corrected for BSA versus body mass index (kg/m ²)	-0.073	0.670*
KV corrected for BSA versus height (cm)	-0.326	0.049
KV corrected for BSA versus urinary protein (g/l)	0.396	0.015

Gault, MDRD and Hull equations was 26.29 (± 2.82) ml/min, 27.87 (± 3.32) ml/min and 25.15 (± 2.93) ml/min, respectively. There was a positive correlation between kidney volumes and urinary protein (CC = 408, and *P* = 0.012) (Table 2), but this was not sustained on multiple regression analysis (β = 0.192 and *P* = 0.238).

Relationship between measured CrCl and estimated CrCl using the three formulae

There was a strong correlation between the measured CrCl and various values of estimated CrCl as evidenced by correlation coefficient (CC ranging between 0.953 and 0.978; *P*-value = 0.000). The similarities or otherwise of the three predictive formulae were tested against measured creatinine clearance using Bland and Altman plots (Figure 1a–c). The results again showed the superiority of the Cockcroft and Gault formula over MDRD and Hull formulae in predicting CrCl in CKD. The Bland & Altman plot revealed that the difference between mean (± 1.96 SD) was smallest with the Cockcroft and Gault equation followed by the Hull and then the MDRD equation.

Relationship between anthropometric parameters, kidney dimensions and CrCl

The BMI ranged between 13.05 and 31.21 kg/m² with a mean (\pm SD) of 23.01 (± 0.69) kg/m² while the BSA ranged between 1.25 and 2.19 m² with a mean (\pm SD) of 1.73 (± 0.03) m². BSA and height were not found to correlate with bipolar diameters of the kidney (BPD) and kidney volumes (*P* > 0.5). The average bipolar diameter (average kidney length) was, however, found to significantly correlate with average kidney volume (*r* = 0.772, *P* = 0.000), measured creatinine clearance (*r* = 0.426, *P* = 0.009), urinary protein estimation (*r* = 0.416, *P* = 0.010) and estimated CrCl by the Cockcroft and Gault equation (*r* = 0.371, *P* = 0.024). No correlation was, however, observed between average kidney length and estimated CrCl using the Hull and MDRD equations.

Discussion

The burden of CRF has increased exponentially and is consuming the resources of both developed and developing economies, and efforts to reduce the cost of managing this dreadful disease are always welcomed. This study was geared towards looking for a simpler method of determining the functional capacity of kidneys in CKD and eliminating (if possible) the need for double determination of GFR using serum chemistry, particularly in resource-poor settings. We attempted to find out the usefulness of ultrasonographically determined kidney volume as a measure of kidney function (GFR). The ultrasound machine is quite cheap and widely available and provides real-time information on the renal parenchymal mass or volume particularly in resource-poor settings. This study found a correlation between the kidney volume measured by these existing formulae and GFR determined by average values of endogenous CrCl and UrCl, and also that determined by predictive formulae namely Cockcroft and Gault, MDRD and Hull equations. The correlation was maintained even when the kidney volume was corrected for BSA. The similarities or otherwise of the three predictive formulae were tested against measured creatinine clearance using Bland and Altman plots (Figure 1a–c), and the results showed the superiority of the Cockcroft and Gault formula over the MDRD and Hull formulae in predicting CrCl in CKD in agreement with previous studies [8,17].

However, our study did not observe a distinctive association between the body's anthropometric parameters such as BSA, height, BMI, and body weight and kidney volume. This is in contrast with the study of Emamian *et al.* [1], Rasmussen *et al.* [18] and Burkhardt *et al.* [19] who observed that kidney volume correlated with body weight and BSA, while kidney length correlated with height [1,18,19]. The differences observed between the findings in these studies and ours are not surprising as healthy volunteers were used in all of them while ours was on the CKD population. Mancini *et al.* [20] evaluated renal dysfunction in allograft recipients, using ultrasonographically determined kidney volume and found it to be quite useful, hence his suggestion that this can be applied to native kidney in diseased state. It was argued by Bakker J *et al.* [21] that ultrasound determination of kidney volume has an inherent defect, due to the ellipsoid formula being applied to the kidney, which is not actually ellipsoid, and therefore he suggested that MRI technique could be better. Unfortunately, they found that the MRI technique also had a similar defect, underestimating the true kidney volume, though not to the same degree. They therefore concluded that in view of the higher cost and increased processing time of MR imaging-based volumetry, ultrasound will probably remain the modality of choice. In a recent publication, Cheong *et al.* [22] applied the ellipsoid formula to MRI data generated by multiplanar reformation and compared it with the water displacement method (standard). They found that this also underestimated the kidney volume by as much as 21–29%. This difference in volume determination was quite similar to the percentage error seen in ultrasound kidney volume determinations with the ellipsoid formula. It could be argued that the margin of error

using ultrasound is probably due to the ellipsoid formula when in fact not all kidneys have this shape. Our finding of a good correlation between kidney length and volume on one hand, and both measured and predicted GFR on the other, further strengthens the usability of kidney length in roughly predicting the GFR. Burkhardt *et al.*'s study [19] examined an elderly population without evidence of kidney disease and therefore differed from this study because all our subjects had established CKD. This study found no superiority between Dinkel [12] and Solvig formulae [13] because the two correlated to the same degree with measured CrCl, though the Solvig *et al.* formula gave higher kidney volume measurements. This is not surprising as both were derived from similar equations and only differed in the value of the constant used. However, in evaluating kidney volume sonographically either of the two could be applied. It must, however, be noted that Solvig *et al.*'s formula was derived using perfused kidneys, compared with Dinkel's that used non-perfused kidneys.

It is now increasingly recognized that MRI-determined kidney length and volume are superior to ultrasonographically determined kidney length and volume, but the drawbacks are that the processing time is longer for routine clinical decisions, the cost is prohibitive and it is not freely available; hence its use cannot be justified, particularly in a resource-poor economy like ours. On the other hand, ultrasound is widely available, significantly cheaper and free of radiation exposure, but has a drawback of operator dependence. We believe, however, that this study is reproducible and can provide a cheaper source of determining kidney function in patients with CKD on a routine basis. The MRI method may, however, be reserved for research purposes. Ultrasound predictions of renal volume can be improved on by eliminating the ellipsoid formula and adopting a cross-sectional area and parenchymal thickness [23].

There is, however, the need to increase the sample size to further assess the relationship between kidney volumes determined ultrasonographically using either or both formulae and GFR (kidney function).

Conclusion

Sonographically determined KV can be used to predict kidney function and GFR estimation in established CKD. A larger sample size is, however, needed to further evaluate this method.

Conflict of interest statement. None declared.

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