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RENAL CORTICAL VOLUME IN PATIENTS WITH CHRONIC KIDNEY DISEASE AT MUHIMBILI NATIONAL HOSPITAL, TANZANIA

Mboka Jacob (MD, MMED)[1], Joel J. Bwemelo (MD,MMED)[2], Ramadhan Kazema (MD,MMED)[3]

[1,3] Muhimbili University of Health and Allied Sciences, Department of Radiology
[2] Muhimbili Orthopedic Institute, Department of Radiology, Dar Es Salaam, Tanzania

Abstract: **Objective: Chronic kidney disease (CKD) is a general term for heterogeneous disorders affecting kidney structure and function. Many studies have been done on correlating sonographic renal changes with renal function by using serum creatinine as a functional mark of renal failure but less is reported on correlation of eGFR with sonographic findings. The aim of this study was to determine the role of renal biometry in predicting renal function among patients with chronic kidney disease (CKD). Method: This was a hospital based cross-sectional study which evaluated 145 patients with CKD at Muhimbili National Hospital. All patients underwent both kidney sonography and renal function test based on estimated glomerular filtration rate (eGFR). Renal volume was compared to eGFR by using correlation and Likelihood Ratio. Results: Almost half of the patients with CKD had renal cortical volume below the normal health adult average. About twelve percent (12.4%) of patients had above normal cortical volume average however this was among patients with HIV nephropathy. Pearson correlation coefficient revealed positive relationship as right and left renal cortical volume and eGFR of ($r \approx +0.49$ ($p < 0.001$); and $r \approx +0.43$ ($p < 0.001$). Despite significant p-values, Pearson coefficient ranged between +0.7 and +0.3 defining a weak linear association between eGFR and renal cortical volume. Conclusions: Renal cortical volume is a weak biomarker in predicting renal function in patients with CKD.**

Keywords: **CKD, Ultrasonography, renal biometry, cortical volume, eGFR.**

I. NTRODUCTION

Determination of renal parenchymal volume in healthy individuals is rarely carried out as it needs several calculations; it is therefore regarded as unpractical in daily clinical setting. However, in certain conditions it can be used to estimate nephron capacity as a representation of renal functional capacity. In abnormal condition such as renal failure, the measurement of renal parenchymal volume provides a more accurate parameter in estimating renal size and function than renal length only (1). Renal parenchymal volume depends largely on the difference between renal volume and renal sinus volume in the central echogenic area (2). In subjects with normal renal function, an important measurement of renal size is longitudinal length, however, the renal parenchymal volume is the more exact US parameter in end-stage renal failure(1).

The volumes of kidney, central echogenic area, and right and left renal parenchymal volume are measured using the following formulae (31):

1. Renal volume = length (L) x width (W) x thickness (T) x 0.523,
2. Central echogenic volume = (L x W x T) of central echogenic area x 0.523,
3. Renal parenchymal volume = renal volume - central echogenic volume.

The length of both kidneys in adults is considered normal when it is between 10cm and 13 cm being the longest distance from the upper edge of renal upper pole to the lower edge of renal lower pole at longitudinal section. The difference of right and left renal length should not exceed 2 cm, the left kidney being longer (2). It is generally agreed that normal renal parameters correspond to somatic parameters, normal values thus determined serve as a baseline to study renal growth and detect an abnormality with a greater degree of confidence(3). Despite the limited studies on renal parenchymal volume, the few available studies have shown the normal average value of renal parenchymal volume in health adults to be 88.04 cm^3 for the right kidney and 115.13 cm^3 for the left kidney (4). Another study showed an average value of healthy renal parenchymal volume of the right and left kidney to be 80.1 cm^3 and 85.2 cm^3 respectively (5). These two studies show a big variability of the left kidney cortical volume that has been explained by two reasons: first, as the spleen is smaller than liver, the left kidney has more space to develop and second, the left renal artery is shorter and straighter than the right renal artery, leading to larger amount of blood flowing to left kidney leading to more nutrition. Despite ultrasound having unlimited role in diagnosing intrinsic parenchymal renal disease but can assess size and shape precisely. It has been also shown to have a sensitivity of 62–77%, specificity of 58–73% and a positive predictive value of 92% for detecting microscopically proved renal parenchymal changes (6). In chronic kidney disease, there is increased fibrosis of the renal cortex, these fibrous tissues reflect sound waves, and causes increased echogenicity on renal ultrasound. Fibrosis causes kidney to shrink leading to less than 10 cm long, this suspects chronic scarring resulting in shrinking of the kidney (7). Renal biometric changes are on widespread use as the diagnostic yield of ultrasonography to detect early signs of reduced renal function. Renal parenchymal volume change in particular when shown by ultrasonography it can detect early reduced renal function, since reduced renal parenchymal volume may occur prior to elevation of serum creatinine. This biometrical renal change, if carefully noted on routine ultrasonographic examinations are suspicious indicator of renal compromise especially in elderly (8).

Ageing is associated with a progressive loss of renal mass and kidney length and a decline in glomerular filtration rate (GFR) as it does in chronic renal parenchymal disease due to parenchymal fibrosis. Renal function and kidney size measured by ultrasonography significantly correlates with GFR ($r=0.46$; $p=0.02$), denoting the potential prediction of renal function by volume change (35). A significant relationship between renal parenchymal volume and kidney function measured by eGFR was also observed among 26 children with recurrent urinary tract infection (9). This study concluded that renal parenchymal volume is a reliable method for evaluating glomerular filtration rate.The most common measure used to assess overall kidney function is the serum creatinine concentration expressed as renal serum creatinine clearance (CLcr) (10;11). The use of serum creatinine concentration alone to assess kidney function results into false negative of 25% undiagnosed cases of CKD (12). GFR can be calculated from the results of blood creatinine, age, race, gender and other factors like BUN and serum albumin as it tells the stage of kidney disease and helps to plan management.

The possibility of determining the correlation between ultrasonographic kidney sizes and glomerular filtration rate (GFR) by ultrasonography employs an easy and less demanding type of investigation for renal function establishment. Kidney sizes, especially the kidney length, correlate with GFR (13). Glomerular filtration rate (GFR) is affected by the existing surface area in renal parenchyma where the filtration process takes place. The measurement of multi dimensional renal parenchymal area provides a more accurate estimation of renal function compared to one-dimensional renal measurement only for example length (14;15).

II. METHODS

Formal ethics approval was obtained from the Muhimbili university of Health and Allied Sciences Institutional Review Board (MUHAS-IRB). This was an observational cross-sectional descriptive study which was conducted from July to December, 2009 at Muhimbili National Hospital. One hundred and forty five (145) patients aged 20 – 60 years were include into the study as this age limits the extremes into which the kidneys grow to its maximum size (9-13cm) and gradually start to decrease in size from the age of 60years.

Data were collected through structured closed ended questionnaire gathering demographic factors, laboratory variables and Ultrasound variables. Blood samples were collected for Glomerular Filtration Rate (eGFR) on the same day of the patient sonography.

We used a Modified Diet for Renal Disease (MDRD) formula for estimation of GFR (eGFR).

The 6-variable MDRD study equation calculator for eGFR used in this research is:

6-Variables MDRD formulae:

170 ($Cr^{-0.999}$ **x** age $^{-0.176}$) x $BUN^{-0.170}$ **x** $alb^{-0.138}$ **x** (1.178 *if black*) **x** (0.822 *if female*)

Estimated GFR (eGFR) was grouped into stable renal function of more than or equal to 60 mL/min/1.73 m^2 and assigned a negative test (*normal*), less than or equal to 59 mL/min/1.73 m^2 to be on the positive test (*abnormal*). All patients attending Nephrology clinic at Muhimbili National Hospital with chronic kidney disease were eligible for the study after all exclusion criteria have been ruled out. Ultrasonography was done by using broadband curve-linear transducers of 2MHz to 5MHz range, HD 11 PHILLIPS. Parasaggital scan of the each kidney was done. The volumes of kidney, central echogenic area, and right and left renal parenchymal volume were measured using the following formulae (2):

1. Renal volume = length (L) x width (W) x thickness (T) x 0.523,
2. Central echogenic volume = (L x W x T) of central echogenic area x 0.523,

Renal parenchymal volume = renal volume - central echogenic volume. The statically package for social science (SPSS) version 13 was used for data analysis.Relationship between *Cortical volume and eGFR* was determined. Pearson and linear regression were used; sensitivity, specificity and likelihood ratio were computed accordingly. P-value of < 0.05 was considered significant.

III. RESULTS

A total of 145 patients participated in this study, 83 (57.2%) males and 62 (42.8%) females. The age ranged from 20 years to 60 years with a mean age of 40 years.

This research results intended shows the relationship(s) *renal cortical volume* on eGFR in patients with CKD. Almost half of the patients had renal cortical volume below the normal health adult average. On the right kidney 75 (51.7%) patients had cortical volumes less than 80cc,; more than and 13 (9.0%) patients had larger cortical volumes of 110cc, [*table: 1] while on the left kidney* From the left kidney 67 (46.2%) patients had cortical volumes less than 80cc and 18 (12.4%) had larger volumes of more than 110cc, *[table: 2]*. These cortical volume categorizations were based on the normal median cortical volume from the normal population which is 88.04 cm^3 for the right kidney and 115.13 cm^3 for the left kidney (4). This study found 12.4% above normal cortical volume average among CKD patients, this observation can probably have more than one explanation that was not taken care of by this study. However, the noted sonographic finding was larger renal volume among HIV nephropathy individuals which is inversely proportional to CKD renal change caused by other causes. Table 3&4 shows almost 60% of right and left cortical volumes to be below the normal cortical median volume. Pearson correlation coefficient reveals positive relationship as right and left renal cortical volume and eGFR of ($r \approx +0.49$ ($p < 0.001$); and $r \approx +0.43$ ($p < 0.001$)). Despite significant p-values, Pearson coefficient ranges between +0.7 and +0.3 defining a weak linear association between eGFR and renal cortical volume. Linearity was interrupted at different points along the renal function, this visual interpretation corresponds with Pearson correlation coefficient (*$r \approx +0.49$ right kidney and $r \approx +0.43$ for the left kidney*). It concludes that right and left renal cortical volume relates to estimated GFR within the weak coefficient range (*$r = +0.7$ and $+0.3$*) [Fig 1].

Cortical volume as a predictor of renal function shows the best-fit linear regression line along which the data do not show linearity. The right cortical volume has shown a weak predictive value for its corresponding renal function as estimated by GFR (r^2=0.184; p<0.001). Regression line slope confidence interval 95% CI: 0.50-1.04 shows big range of variability if the same study is to be repeated. Hence, requires a bigger sample size [Fig 2].The left renal cortical volume as independent to renal function shows the best-fit linear regression line presenting poor relationship between these two variables. The left cortical volume has revealed a weak correlation to renal function as estimated by GFR. It is showing a slope **b (**95%CI: 0.16-0.59) and r^2=0.075; p<0.01. These results do not show credible confirmation to reject the null hypothesis despite its low p-value. The slope confidence interval on other hand shows big variability [Fig 3].

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Table.1: Right kidney cortical volume (n=145)

Cortical Volume		Frequency	Percent %
	<80	75	51.7
	81-110	57	39.3
	>110	13	9.0
	Total	145	100.0

Table.2: Left kidney cortical volume (n=145)

Cortical Volume	Frequency	Percent %	Valid Percent
<80	67	46.2	46.2
81-110	60	41.4	41.4
>110	18	12.4	12.4
Total	145	100.0	100.0

Table.3: Estimated GFR with right kidney cortical volume change (n=145)

Estimated GFR	Right kidney cortical volume (CC)			Total
ml/min/1.73 m^2	<80cc	81-110cc	>110cc	
>90	8	28	8	44
60-89	4	14	0	18
30-59	14	6	2	22
15-29	13	1	1	15
<15	36	8	2	46
Total	75	57	13	145

Table.4: Estimated GFR with left kidney cortical volume change (n=145)

Estimated GFR	Left kidney cortical volume (CC)			Total
ml/min/1.73 m^2	<80cc	81-110cc	>110cc	
>90	7	33	4	44
60-89	2	10	6	18
30-59	11	9	2	22
15-29	12	1	2	15
<15	35	7	4	46
Total	67	60	18	145

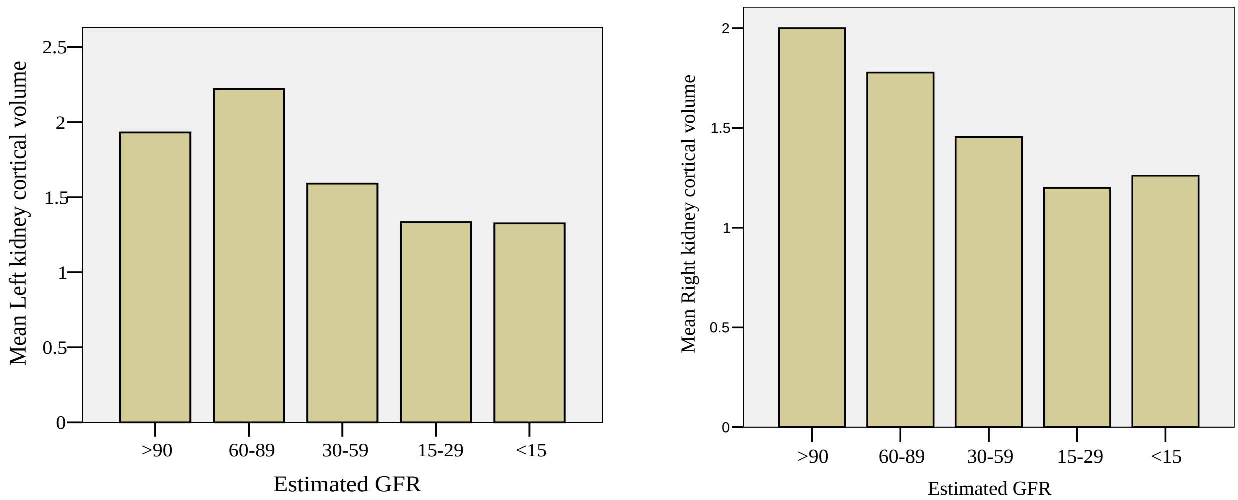

Fig.1: Right and Left cortical volume with eGFR (n=145)

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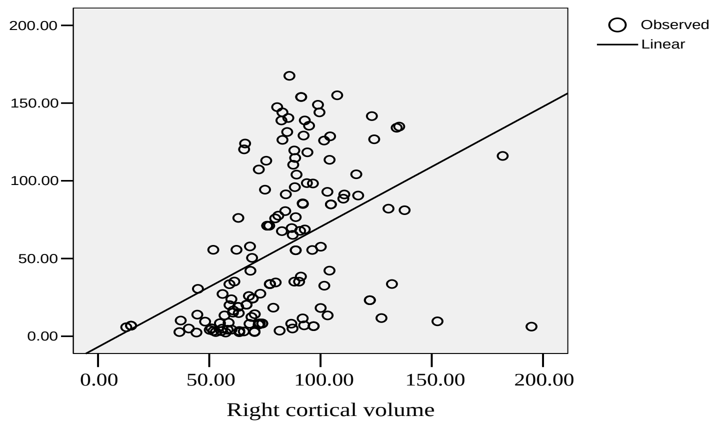

Fig.2: The eGFR and right cortical volume regression correlation

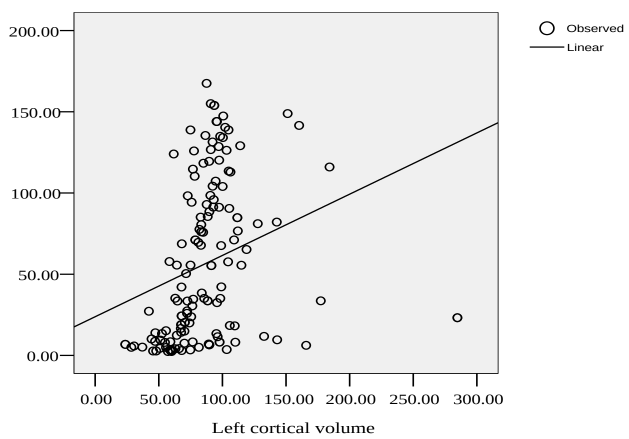

Fig.3: The eGFR and left cortical volume regression correlation

IV. DISCUSSION

The pathology of chronic kidney disease usually involves structural and functional changes and often interconnected. Regardless of observed renal cortical volume change, this study did not statistically qualify hyperfiltration theorem by Brenner (59). Renal cortical volume change prediction of renal function in our study revealed a likelihood ratio (LR) of less than 4.8 with 95% CI: 0.16-0.59, regression coefficient of $r^2 = 0.075$; in spite of significant p value ($p<0.01$).

Mazzotta *et al* (1).examined healthy adult subjects and nephropathic patients to detect relations between kidney's sonographic dimensions and renal function expressed by creatinine clearance. They concluded that renal parenchymal volume is the more exact sonographic parameter among end-stage renal failure (1). However, the present study did not study the end stage kidney failure but the wide spectrum of renal insufficiency from stable renal function to end stage renal insufficiency. Differences in study design could have shown this inconsistence, end stage kidney disease can be easily appreciated by signs and symptoms of the patient. This research investigated benefits of sonographic picked renal cortical volume to detect renal function across the whole spectrum of CKD patients advocating on early intervention.

Burkhardt *et al* (8) observed that Ultrasonography cannot replace or complement eGFR in order to detect early reduced renal function in the elderly age. The aim of Burkhardt research was to prove a new method to a routine sonography for renal cortical volume assessment to demonstrate renal function. The current study has indicated the similar findings as that of Burkhardt *et al(8)*; however, these two studies differ in the type of population studied and renal function stage considered. With these reasons we can conclude our findings based on Burkhardt research with precaution. Troell *et al*(9) looked into the relationship that might exist between ultrasonographically calculated renal parenchymal volume and kidney function. They found a high correlation between renal parenchymal volume and GFR and concluded that ultrasonographic determination of renal parenchymal volume is a reliable method to evaluate glomerular filtration rate in children with recurrent urinary tract infections (9).

These findings differ to current study which showed a weak correlation between cortical volume and renal function $r \approx +0.49$. These differences could be explained by different situations that, Troell observation based only in children with enlarged kidneys different from ours that recruited adult with expected shrunken kidneys. On the other hand, differences from the current study could have been contributed from different diseases being studded and negative volume change caused by CKD rather than positive volume change caused by recurrent ascending urinary tract infection. There could be a strong correlation on positive cortical volume change (renal expansion) rather than negative cortical volume change (renal shrinkage) as shown by these studies if patients' age is standardized. Vergesslich *et al* (16) studied acute renal failure patients who showed a positive renal cortical volume change and concluded that changes in renal function are parallel with rapid positive changes in renal size (16).

The current study compared biometrical sonographic cortical volume change as a predictor of renal function estimated by GFR, lacks supporting similar literature to verify its importance. This has been observed from literature search which showed the relationship between cortical volume and creatinine in children and other diseases rather than CKD. This observation therefore, creates an opportunity for more researchers to work more on this area, bearing in mind that metabolic diseases are on the alarming increase which predispose patients to chronic kidney disease especially CKD.

V. CONCLUSION

Renal cortical volume is a weak biomarker in predicting renal function in patients with CKD .If the recommended gold standard for estimating renal function is eGFR and practitioners look at it as a time consuming task, a dedicated research to validate renal cortical volume as predictor of eGFR can be of urgency.

VI. ACKNOWLEDGMENT

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