Correlation of Differential Function and Glomerular Filtration Rate Estimated from Computed Tomography based Renal Volume and Diuretic Renogram in Living Renal Donor

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ABSTRACT

Introduction
In renal transplant, serum creatinine and isotope studies are used for determination of donor glomerular filtration rate (GFR). Studies have shown computed tomography measured renal volume can also be used. Our main objective was to assess the accuracy of volume based estimated GFR (vGFR) with diethylene triamine penta acetic acid (DTPA) measured GFR in living kidney donors.

Methods
An observational analytical study was conducted from July 2018 to June 2019 in Department of Urology and Kidney Transplant Surgery and Department of Radiodiagnosis in Tribhuvan University Teaching Hospital where a total of 38 eligible potential donors were evaluated and serum creatinine level, computed tomography with contrast and DTPA renogram were used to measure GFR and differential function.

Results
The mean age of the donors were 42.8±10.9 years with 70% of donors being females. Renal volume was not statistically different between male and female donors. There was moderate correlation between volume based and DTPA based GFR (r=0.76) and differential function (r=0.71). Compared to creatinine, volume based GFR estimate showed better correlation to DTPA renogram. There was no significant difference in differential function estimated by DTPA and volume based estimates (p = 0.96). The upper and lower limit of agreement between the volume based and DTPA based differential function was −4.7 and 4.6 respectively.

Conclusion
GFR measurement by CT volume overestimates total GFR compared to DTPA renogram but it has better correlation than creatinine based estimates. It can be used to estimate the differential function of the donor kidney.

Keywords
Computed tomography, DTPA, glomerular filtration rate, renal transplant, renal volume

INTRODUCTION

Chronic kidney disease (CKD) is a major global health concern.[1,2] Living donor renal transplantation for CKD has been shown to have excellent long-term results.[3,4] Assessment of donor's renal anatomy and glomerular function is very important for renal transplant.[5,6] Living donor must have a minimum glomerular function for kidney donation, in order to prevent them from acquiring End Stage Renal Disease (ESRD) during his or her lifetime.[7] Hence, guidelines recommend confirmation of predonation glomerular filtration rate (GFR) by atleast two different techniques before renal transplant.[7]

GFR is measured using radio-labeled exogenous filtration markers like diethylene triamine penta acetic acid (DTPA).[8] GFR can be also calculated by using Cockcroft-Gault formula (CG), Chronic Kidney Disease Epidemiology (CKD-EPI) collaborative equations, and Modification of Diet in Renal Disease (MDRD) from creatinine. Creatinine based estimates are however not very accurate.[9] It would therefore be beneficial to find additional techniques to estimate GFR which can be utilized in the assessment donor GFR.

In 2009, Hertz et al. reported the usefulness of renal volume measured from a renal Computed Tomographic (CT) to estimate renal function and others also have reported the same.[10] Radioisotope-based renography, while more reliable in assessing renal function, is not uniformly available in a developing nation like ours. As a result, other easily available and applicable methods of measuring GFR must be evaluated. So our goal was to assess the accuracy of CT volume based estimate GFR (vGFR) to isotope study and compare it with creatinine based GFR estimate in living donor transplant.

METHODS

After approval from the Institutional Review Committee of Institute of Medicine, an observational analytical study was conducted in the Department of Urology and Kidney transplant Surgery and Department of Radiodiagnosis at Tribhuvan University Teaching Hospital over a period of one year (July 2018 – June 2019). All prospective (eligible) donors fit for donation were evaluated with serum creatinine, Computed Tomography-Intravenous Urography and DTPA renogram.

Sample size (n) was calculated using 90% power and 95% significance level and assuming a correlation of 0.5 between volume based GFR (vGFR) and DTPA renogram (dGFR). The sample size was determined with the following formula,

$$N = \left\{ \frac{(Z_\alpha + Z_\beta)}{C} \right\}^2 + 3$$

where, N = sample size, Z_α = standard normal deviate for alpha, Z_β = standard normal deviate for beta, C = 0.5 * ln{(1+r)/(1-r)} and r = correlation.

Also, age, sex, weight, height and body mass index of the donors were recorded. Dual head gamma camera from Mediso Medical Imaging Systems (Nucline DH-V model) was used for DTPA renogram. Technetium-99m (99mTc) labeled diethylene triamine penta acetic acid used as an exogenous filtration agent. Total dose of 3-10 mCi of radioisotope labeled tracer was injected intravenously along with 40mg furosemide (F0 protocol) in the antecubital fossa. With patient in supine position using gamma camera behind the patient imaging was taken. In phase 1, 30 frames, each of 2 seconds was taken. In phase 2, 80 frames, each frame lasting 15 seconds each was taken. The delayed image was taken after 3 hours. Using pre and post injection images GFR (dGFR) was estimated using the Gate's Method. Total GFR was reported in ml/min/1.73m² and differential function (dDF) in percentage. Serum creatinine level was used to estimate GFR (eGFR) using Cockcroft-Gault formula (CG), Chronic Kidney Disease Epidemiology (CKD-EPI) collaborative equations and Modification of Diet in Renal Disease (MDRD) equations.

All the prospective donors underwent contrast enhanced CT scan with 128 slice Siemens SOMATOM AS. After taking a plain CT scan of the abdomen, Iohexol, low osmolar non ionic contrast, was used for conducting the scans. A total dose of 1 ml/kg was infused at the rate of 8 ml/min over 24 seconds and various phases of scan were taken. Using bolus tracking technique (scan acquisition after renal parenchymal attenuation reaches 100 HU) arterial phase was taken. Venous phase was taken 60-75 seconds after injection of contrast. Similarly excretory phase was taken 5-7 minutes after injection. Then using 5 mm axial sections in arterio-venous phase the region of interest (ROI) marked manually in each 5mm slice including the renal parenchyma but excluding the renal sinus and pelvi-calyceal system. Renal cyst if present was marked and the volume of the cyst was subtracted from total renal volume. CT automatically calculates the area of ROI in centimeter square and all the area of the axial sections are added and multiplied by the thickness of the slice (5 mm) to get the volume of each kidney. Total renal volume was obtained by adding the volume of both the kidneys. Calculation of unadjusted volume based GFR was done using equation by Hertz et al.[13]

Unadjusted GFR =

$$70.77 - 0.444A + 0.366W + 0.200V_R - 37.317Cr$$

Where, A = age in years, W = weight in kilogram, VR = total volume of the kidneys (ml) and Cr = creatinine (mg/dl). The calculated unadjusted GFR is then adjusted for 1.73 m² body surface area to

estimate the volume based total GFR (vGFR).

The volume estimated percentage differential function (vDF) of left kidney was calculated as:[14]

$$vDF = \frac{\text{vol. of left kidney}}{\text{vol. of left kidney} + \text{vol. of right kidney}} \times 100\%$$

All the data was entered in SPSS version 21 and analyzed using the software. Single sample t test was used to assess the significance of mean difference between vGFR and dGFR. Independent sample t test was used for comparison of means. Pearson's correlation coefficient was used to evaluate correlation between volumes estimated GFR (vGFR), differential function (vDF) and creatinine based estimated GFR (eGFR) with DTPA renogram. Bland-Altman plot was used to evaluate the level of agreement between vDF and dDF. P value < 0.05 was considered statistically significant.

RESULTS

The mean age of the donors was 42.8±10.9 years. The age of the donor ranged from 25 to 65 years of age. In an average male prospective donor were older in comparison to female donors. In the current study, females made up 70% of the donors. The prospective donors' average body mass index (BMI) was 26.5±3.9 kg/ m², with no significant differences in BMI between males and females. The mean serum creatinine level in the current study was 65 ± 32 μmol/dl, ranging from 56 to 122 μmol/dl. Mean creatinine level was higher in males compared to females (84±32 μmol/dl vs 56±28 μmol/dl).[Table 1]

The right kidney was larger than the left in both males and females, but the difference was not statistically significant. When compared to DTPA renogram based GFR (dGFR), the mean vGFR estimated by CT volumetry was greater. Mean GFR measured from DTPA was 86.9 ± 9.4 ml/min/1.73 m² whereas it was 91.9 ± 11.4 ml/min/1.73 m² when calculated from CT volumetry. [Table 2] The mean difference between the two GFR was 2.51± 3.7 ml/min/1.73 m² (CI 95%: 3.59, - 10.76) with CT significantly overestimating GFR incomparision to DTPA. vGFR accuracy was within 10% of dGFR in 68.4% of donors in the current study. [Table 2]

CT volume-based GFR had only a moderate correlation with dGFR (0.76), but it correlated better than creatinine-based estimates (0.44-0.54). [Table 3]

Table 1. Demographic profile

Characteristics	Total (mean±SD)	Male	Female	P-value
Age (yrs)	42.8 ± 10.9	46.8±12	40.8±10.2	0.13
Sex (male:female)	11 : 27	30%	70%	n.a
BMI (kg/m²)	26.5±3.9	27± 5	26 ±3	0.42
Serum creatinine (μmol/dl)	65 ± 32	84±32	56±28	0.02
Renal volume (ml) - (total)	200.0 ± 42.4	203.4± 49.4	198.6± 40.4	0.21
Right kidney	-	102.5± 25.6	100.0± 21.6	-
Left kidney	-	101.2± 27	98.1± 20.7	-

Table 2. Comparison of mean GFR

Technique of estimation of GFR	Mean total GFR±SD (ml/min/1.73 m²)	P-value
DTPA (dGFR)	86.9 ± 9.4	0.04
CT volumetry (vGFR)	91.9 ± 11.4	
Mean difference in GFR estimate (dGFR – vGFR)	–2.51± 3.7	<0.001

Table 3. Correlation of dGFR with vGFR and eGFR

eGFR estimation tool	Correlation coefficient (r)
CT Volume (Hertz equation)	0.76
Cockcroft Gault (CG)	0.44
Modification of Diet in Renal Disease (MDRD)	0.44
Chronic Kidney Disease Epidemiology collaboration (CKD-EPI)	0.54

Table 4. Correlation between the mean differential function based on renal volume (vDF) and DTPA(dDF)

Differential function	Left	Right	Correlation	p-value
DTPA renogram based (dDF)	49.4 ± 2.9	50.6 ± 2.9	0.71	0.96
Renal volume based (vDF)	49.5 ± 2.2	50.5 ± 2.2		

There was no significant difference in mean split renal function calculated from renal volume and DTPA renogram in the current study while showing a moderate degree of correlation. [Table 4]

The concordance analysis of dDF and vDF showed that the average difference of the two measurements was - 0.1 ± 2.3 % (CI 95%: -0.7, 0.8) and the lower limit of agreement being -4.7% (CI 95%: -5.9, 3.2) and upper limit of agreement being 4.6% (CI 95%: 3.3, 6.0). [Fig.1]

Figure 1. Bland-Altman plot to evaluate the limits of agreement between volumes based and DTPA based differential function

DISCUSSION

Evaluation of renal function by estimation and/or measurement of GFR in a prospective donor are mandatory because low GFR can have a negative impact on both the donor as well as the recipient.[7] Various guidelines around the world have recommended minimum GFR required for prospective donors to be eligible for living renal transplant programs. Although serum creatinine-based calculations are simple to apply, they are not particularly accurate; hence guidelines suggest using a second approach to confirm the predicted GFR.[7] Radioisotope labeled exogenous markers like inulin and alternatively DTPA are considered more accurate methods of measurement and usually used for GFR estimation.[12] This study evaluated the role of CT based renal volume for estimation of GFR in prospective donors.

The reported mean age of the donors around the world is variable and range from 37-72 years.[13,14] The mean age in the current study was 42.8 ± 10.9 years. Similarly, male prospective donors were older as compared to female prospective donors. Most of the male donors are usually parents or guardians which could explain the age discrepancy of male and female donors. Majority of the study population were females (70%). Reported literatures around the world also show a sex discrepancy in the percentage of donor.[5]

The mean total renal volume of the current study population was 200 ± 42.4 ml (117- 301). The right kidney with the mean volume of 100.6 ± 22.4 ml were marginally larger than the left with the mean volume of 98.9 ± 22.2 ml. In comparison to the Western literature, the volumes of kidney in Nepalese donors were smaller, but it appears to be comparable to those reported from India.[15,16] The smaller volume kidney m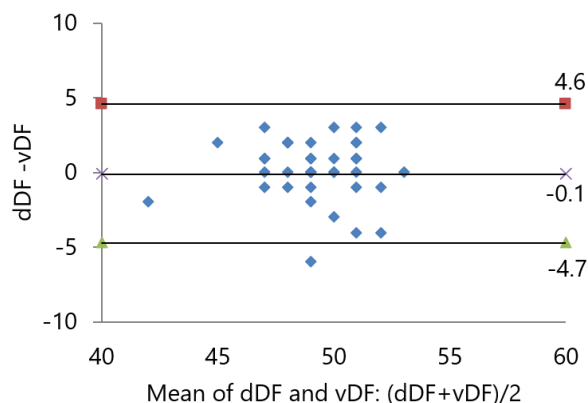ay be associated with smaller body masses in South Asians as compared to the Western population. The size difference between the right and left kidneys has been reported to be variable, with some reporting left, some reporting right, and some reporting no difference.[17]

DTPA renogram is the routinely used radioisotope for measurement of GFR in our country. The mean mGFR was 86.9 ± 9.4 ml/min/1.73m² in the current study. Although comparable to the mean GFR reported for Indian population (86.4 ± 17.4 ml/min/1.73 m²) but is comparatively lower than that reported in Western literature.[10,18] The decreased renal volume in our population compared to the western donor pool could be one explanation for the lower mean dGFR. When compared to inulin clearance, DTPA has also been shown to underestimate GFR.[19] Using renal volume to estimate renal function, the mean GFR (vGFR) of the prospective donors in the study was 91.9 ± 11.4 ml/min/1.73m² which was higher than dGFR. The mean difference (bias) between vGFR and dGFR was 2.51±3.7 ml/min/1.73m² which was significant. Dixit et al also reported a higher volume estimated GFR, with a mean difference of 9.68 ml/min/1.73m², however in contrast to our study they did not find a significant difference between the volume based and DTPA based GFR in their study.[18] Similarly, Goh et al also reported a higher estimated vGFR.[20] Higher volume based GFR estimates in the studies may be the outcome of including overall renal volume, which includes both the excretory tissues as well as non excretory component of renal parenchyma like interstitium and vascular bed. There was

moderate positive correlation (r=0.76) between vGFR and dGFR in our study. Hertz et al in the original study reported a correlation of 0.42, though they compared the vGFR to iodothalamate based measurement.[10] Dixit et al and Goh et al reported a correlation between vGFR and dGFR of 0.47 and 0.5 respectively in their study.[18,20] Since, the only variability in assessment of vGFR in various reports is the technique of renal volume measurement, better volumetric assessment may explain a better correlation in the current study.

But without any comparative studies assessing the best method of renal volume measurements there is no data to support the given reason for correlation. However, 68.4% of the values were within 10% of dGFR which is better than those reported by Goh et al.[20]

The main advantage of radioisotope renogram over creatinine based estimate of renal function is its ability to differentiate individual kidney function. If two kidneys' split renal functions are significantly different, the kidney with the lower function is considered for donation.[21] In our study, volume based split renal function (vDF) was not significantly different from DTPA (dDF) based estimate, with moderate degree of correlation (r=0.71). Soga et al. used various methods to estimate CT-based renal volume and found excellent correlation to nuclear split renal function in their study.[11]

Main drawback of the current study is, although CT volume can be used to estimate renal function, we have not evaluated multiple reported techniques to estimate renal volume from CT. Hence, they also need to be tested to get the most accurate technique to measure volume which can have better correlation to measured GFR (dGFR).

CONCLUSION

CT volume based GFR estimates shows a moderate correlation with DTPA but correlation was better compared to all creatinine based estimates. Volume based estimate however overestimated GFR compared to DTPA. CT volumetry based estimated differential function was not significantly different when compared to DTPA.

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CONFLICT OF INTEREST

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