# Comparison of Creatinine Based and Kidney Volume Based Methods of Estimating Glomerular Filtration Rates in Potential Living Kidney Donors

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**Abbreviations and Acronyms**

BMI = body mass index
CrCl = creatinine clearance
CT = computerized tomography
dGFR = directly measured GFR
eGFR = creatinine based equation estimated GFR
GFR = glomerular filtration rate
SCr = serum creatinine
vGFR = volume based equation estimated GFR

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**Purpose:** Accurate assessment of kidney function is critical to evaluate living kidney donors. Direct glomerular filtration rate measurement using isotopes is currently the gold standard but it is complex and costly. We evaluated the performance of surrogate markers of the glomerular filtration rate in living kidney donors by comparing direct measurement of the rate to the creatinine based equation estimated rate, the kidney volume based estimated rate using a newly developed equation and creatinine clearance.

**Materials and Methods:** We first statistically compared direct glomerular filtration rate measurement to the results of the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) creatinine based equations, and to creatinine clearance in 54 potential renal donors from 2006 to 2010. In 32 donors with cross-sectional computerized tomography available we used measured functional renal volume with age, gender, weight and serum creatinine to estimate the rate based on kidney volume according to a previously reported model. Kidney volume based measurement was compared to direct glomerular filtration rate measurement and assessed against the results of the best performing creatinine based equation.

**Results:** In the first group of 54 donors the correlation index of the estimated glomerular filtration rate according to MDRD and CKD-EPI creatinine based equations, and to creatinine clearance was low compared to direct measurement. In the subset of 32 potential donors the kidney volume based estimated rate correlated better with direct measurement than MDRD equation results with higher accuracy (estimated 87.5% and 75.0% within 30% and 10% of direct rate measurement, respectively).

**Conclusions:** To estimate the glomerular filtration rate in healthy individuals a volume based model correlated better than the MDRD equation, which is the best performing creatinine based equation used to estimate the rate. By providing a more robust estimation of the glomerular filtration rate in healthy potential kidney donors, the volume based model adds value to routine preoperative computerized tomography above that of anatomical evaluation.

**Key Words:** kidney, living donors, kidney function tests, creatinine, organ size



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THE current optimal treatment of end stage renal failure is living kidney transplantation, which is performed as frequently as cadaveric donor kidney transplantation.[1] For successful living kidney transplants accurate renal function determination, ideally in a reproducible, cost-effective manner, is critical during potential donor evaluation.[2] The accepted reference standard of measuring GFR is direct measurement using radiotracer labeled compounds, which is costly and not readily available.[3]

Alternatives using creatinine based equations were developed as surrogate determinants of measured GFR. Most of these formulas, including the MDRD and CKD-EPI equations, were derived from patients with impaired renal function and excluded individuals with a GFR of greater than 70 ml/minute/1.73 $m^2$. Although it is currently advocated by the Amsterdam Forum on living donors and widely used to assess donors,[2] concern arises regarding the performance of these equations in healthy individuals with limited attempts at validation in kidney donor populations.[4]

Reports that the volume of a healthy kidney is related to body parameters led Jeon et al to directly correlate the kidney volume of donors measured on contrast enhanced CT with nephrectomized kidney weight and various kidney function measures.[5] This correlation of CT measured kidney volume with renal function was incorporated by Herts et al into a novel mathematical model to estimate GFR in potential kidney donors.[6] Since cross-sectional CT is the standard practice for evaluating potential kidney donors, this vGFR is potentially convenient and cost-effective. Using renal volume in addition to the standard parameters of age, weight and SCr, the volume based model outperformed the MDRD equation when forward tested in 100 white donors.[6]

We determined the optimal method of estimating GFR in potential kidney donors at our institution. This was done in 2 parts. 1) We compared the performance of the MDRD and CKD-EPI creatinine based equations, and 24-hour CrCl to dGFR, which is the current reference standard. 2) In a subset of these individuals who donated a kidney and had CT available, we compared the performance of the volume based model and the best performing creatinine based equation.

## PATIENTS AND METHODS

### Study Population

This retrospective, institutional review board approved study included 79 consecutive healthy potential renal donors who were reviewed for potential living related kidney donation between June 2006 and September 2010. In 54 potential donors in whom borderline GFR was determined by creatinine based equations we selectively measured dGFR by $^{99m}$Tc-diethylenetriaminepentaacetic acid scintigraphy. Baseline demographics and clinical characteristics of the potential donors were retrieved from the transplantation database. All 54 potential kidney donors in whom GFR was measured directly were recruited for study to compare the performance of creatinine based equations. We excluded 22 donors due to dGFR less than 80 ml/minute/1.73 $m^2$ or to voluntary withdrawal after evaluation. In the remaining 32 donors CT was performed and the kidney was donated. These 32 donors were recruited for volume based GFR estimation. All laboratory and anthropometric measurements were made within a month of GFR direct measurement.

### Performance

***Creatinine based equations and CrCl.*** To study creatinine based equations we determined eGFR in all recruited donors with the MDRD and CKD-EPI equations using the National Kidney Foundation calculator (http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm). In all donors 1 measurement was made of 24-hour CrCl. Samples were considered adequate if 24-hour urine creatinine was more than 15 and 20 mg/kg per day in females and males, respectively. Our laboratory provides standardized creatinine values traceable to the National Institute of Standards and Technology sample.

We used 3 equations. 1) The MDRD equation is GFR in ml/minute/1.73 $m^2 = 175 \times (SCr)^{-1.154} \times (age)^{-0.203} \times 0.742$ (if female) $\times$ 1.212 (if black).[7] 2) The CKD-EPI equation is GFR in ml/minute/1.73 $m^2 = 141 \times \min(SCr/\kappa,1)^{\alpha} \times \max(SCr/\kappa,1)^{-1.209} \times 0.993^{age} \times 1.018$ (if female) $\times$ 1.159 (if black), where SCr is in mg/dl, $\kappa$ is 0.7 for females and 0.9 for males, $\alpha$ is $-0.329$ for females and $-0.411$ for males, min represents the minimum of SCr/$\kappa$ or 1 and max indicates the maximum of SCr/$\kappa$ or 1.[8] 3) For CrCl we used the equation, CrCl = (UCr $\times$ V)/SCr (adjusted for body surface area using 1.73 $m^2$), where UCr represents 24-hour urine creatinine and V represents 24-hour urine volume. All results were compared against dGFR for precision, accuracy and bias, as described.

***Kidney volume based equation.*** In 32 donors with contrast enhanced CT available we first measured kidney volume by a technique adapted from liver volumetry using National Institutes of Health ImageJ tissue segmentation software.[9] CT images obtained in the arterial phase were saved in JPEG format. Using ImageJ, the functional nephron mass was manually outlined on the transverse section by a single surgeon, excluding renal sinus fat, cysts, blood vessels and the pelvicalyceal system (fig. 1). The area of outlined functional renal mass was multiplied by slice thickness to obtain renal volume. Total renal volume was calculated by summing all volumes in the measured boundaries of the 2 kidneys after exporting results into Windows® Excel®. Volume measurement and calculation for each kidney required an average of 30 minutes.

We calculated vGFR in donors using the regression and forward tested model of Herts et al.[6] The equation used was vGFR in ml/minute/1.73 $m^2 = 70.77 - 0.444(age) + 0.366(W) + 0.200(V) - 37.317(SCr)$, where W represents