



Is Cystatin C Valuable Marker of Glomerular Filtration Rate in Living Kidney Donors After Uninephrectomy?

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ABSTRACT

Background. The determination of kidney function plays a pivotal role in living donors renal assessment because of the long-term hazards of life with one kidney. Guidelines recommend estimation of glomerular filtration rate (GFR) by the Modification of Renal Disease (MDRD) or Cockcroft-Gault equations for people with normal or near-normal renal function. Cystatin C (CysC) has been introduced as an alternative endogenous marker of GFR.

Objective. The objective of the study was to evaluate residual renal function among living kidney donors by comparing serum CysC concentrations and estimated GFR according to the MDRD formula or the Cockcroft-Gault equation.

Patients and methods. Forty living kidney donors showed a mean age of 46.14 years. Their GFR was estimated according to the abbreviated MDRD (aMDRD) and Cockcroft-Gault formula adjusted for body surface area. Twenty-two donors underwent diethylenetriamine-pentaacetic acid (DTPA) renal studies. Serum CysC concentrations were measured during the last follow-up visit. GFR values according to Cockcroft-Gault formula and MDRD formula were correlated with CysC concentrations using Pearson's linear correlation.

Results. Mean GFR according to the aMDRD formula and Cocroft-Gault formula decreased after nephrectomy. The Cockcroft-Gault formula overestimated the DTPA GFR in our study. No significant differences were observed between DTPA GFR and GFR estimated using the aMDRD equation. The rate of GFR decrease was approximately 0.8 mL/min/1.73m² per year. No significant correlation was observed between serum CysC concentration and GFR. Microalbuminuria was observed in one patient after nephrectomy.

Conclusions. aMDRD equation to estimate GFR is more precise than Cockcroft-Gault formula and cystatin C in living kidney donors after nephrectomy and should be preferred model in these patients.

AN accurate estimate of glomerular filtration rate (GFR) is one of the most significant finds in nephrology.¹ The determination of kidney function plays a pivotal role in assessment of living kidney donor because of the long-term hazard to life with only one kidney. In addition, a higher GFR in the donor is independently associated with better allograft outcomes.² Serial measurements of serum creatinine and urinary clearance are used to assess and monitor renal function among prospective donors.³ However, it is now well established that serum creatinine alone is a relatively poor marker of GFR. Serum creatinine concentrations can be within the normal range even when the GFR is approximately 60 mL/min/1.73 m² resulting in a "creatinine-blind range."⁴ Urinary creatinine clearance is often inaccurate on collec-

tions. K/DOQI guidelines suggest the use of prediction formulas like Cockcroft-Gault and the Modification of Renal Disease (MDRD) for renal patients in chronic kidney

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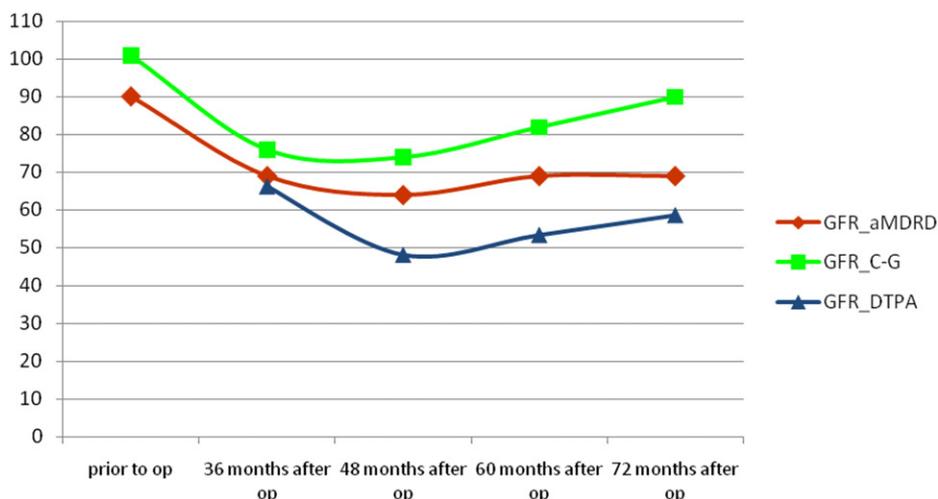


Fig 1. Mean glomerular filtration rate depends on method.

disease (CKD) stage higher than CKD2.⁵ The new guidelines recommend GFR estimates using the MDRD or Cockcroft-Gault equations for people with normal or near-normal renal function.⁶

An alternative endogenous marker of GFR is cystatin C (CysC), a nonglycated basic housekeeping protein (MW 13 359) in a superfamily of cysteine proteinase inhibitors.³ CysC is produced by all nucleated cells, readily filtered, not secreted, and completely degraded in the proximal tubular cells and it does not return to the systemic circulation.⁷ Its production rate is unaltered under inflammatory conditions.³ The CysC plasma concentration is independent of muscle mass. CysC shows a minor not clinically relevant difference between men and women. CysC increases with aging (>50 years of age), reflecting the naturally decreased renal function in advanced age.⁸ The clinical use of serum CysC concentrations as a measure of GFR was first proposed in 1985 by Grubb et al⁹ and by Simonsen et al.¹⁰

The objectives of this study was to evaluate residual renal function among living kidney donors and to compare serum CysC concentrations and GFR estimate according to the MDRD formula and the Cockcroft-Gault equation.

PATIENTS AND METHODS

Approval from our Ethics Committee was obtained before study initiation. Between 1995 and 2005, 66 living donor cases were performed with open nephrectomies. Mean ages were 40.66 years (range, 27 to 60 y) at donation and 46.14 years (range, 31 to 69) at the last follow-up visit. The donors were females in 52.5% of cases. Left-sided nephrectomy was performed in 75% of procedures. Physical examinations as well as blood and urine tests were performed before surgery and at every follow-up visit. GFR was estimated according to the abbreviated MDRD (aMDRD) and Cockcroft-Gault formula adjusted for body surface area (BSA). In additions, 22 donors underwent ^{99m}Tc-diethylenetriamine-pentaacetic acid (DTPA) renal studies. Serum CysC concentrations were measured by immunonephelometry at the last follow-up visit. GFR according to Cockcroft-Gault formula and MDRD formula were correlated with CysC concentrations using Pearson's linear analysis. The observation period ranged from 25 to 156 months. Twenty-

six donors did not report for a follow-up visit. The statistical analysis was performed using SPSS version 13.0 with $P < .05$ considered to be statistically significant.

RESULTS

Mean GFR according to the aMDRD formula decreased from 89.9 mL/min before to 64.36 mL/min ($P = .001$), 69.1 mL/min ($P = .006$), and 68.6 mL/min ($P = .007$) at 36, 60 and 72 to 156 months after nephrectomy, respectively. Mean GFR according to Cockcroft-Gault formula decreased from 100.7 mL/min before to 74.1 mL/min ($P = .005$), 81.7 mL/min ($P = .007$), and 89.9 mL/min (not significant) at 36, 60, and 72 to 156 months after donation, respectively (Figure 1) A regression model to estimate the GFR decrease revealed approximately 0.8 mL/min/1.73m² per year. The Cockcroft-Gault formula adjusted for BSA overestimated DTPA GFR ($P = .003$). No significant differences were observed between DTPA GFR and GFR estimates using the aMDRD equation. Mean serum CysC concentrations were 0.772 mg/L, 0.8 mg/L, and 0.825 mg/L at 25 to 36, 48, and 60 months after nephrectomy, respectively (Table 1) Serum CysC concentrations did not depend on donor gender or age. Serum CysC concentrations at 5 or more years after nephrectomy were higher among older versus younger patients albeit not significantly. GFR according to Cockcroft-Gault or MDRD formulae were correlated with CysC concentrations using Pearson's linear analysis. CysC concentrations negatively correlated with GFR ($R = -0.065$). There was no significant correlation between serum CysC concentrations and estimated GFR in this study ($P = .797$). Microalbuminuria was observed in one patient (2.5%) at 84 months after nephrectomy.

DISCUSSION

It is essential to monitor renal function in living kidney donors after unilateral nephrectomy to ensure the safety of the procedure. We observed previously that mean GFR according to the Cockcroft-Gault formula or aMDRD equa-

Table 1. Serum Concentration of Cystatin C Depends on Age and Time After Nephrectomy in Living Kidney Donors

Time After Nephrectomy	Serum Concentration of Cystatin C			
	All Patients	Age of the Donor (y)		
		< 40	40 to 49 lat	> 50 lat
24 to 36 months	0.772	0.753	0.788	—
48 months	0.8	0.833	0.75	0.8
60 to 156 months	0.825	0.6	0.8	0.95

Abbreviation: lat,

tion decreased by 30% after donation.¹¹ In this study we noted that mean GFR according to Cockcroft-Gault formula decreased by 10.7% and mean GFR according to the aMDRD equation, by 24%. The average estimated GFR was 72% of the age-predicted value upon long-term follow-up of living kidney donors.¹² The estimated GFR decreased in relation to increasing age. The average decrease in GFR was estimated as 1 mL/min/1.73 m² per year. The GFR decrease was approximately 0.8 mL/min/1.73m² per year in our study. Therefore, the residual renal function among kidney donors did not deteriorate more rapidly than that expected from aging.

Lin et al reported that the MDRD and abbreviated MDRD equations were more precise and accurate within 30% versus the Cockcroft-Gault formula among healthy potential kidney donors. However, the MDRD equations consistently underestimated DTPA GFR, whereas Cockcroft-Gault consistently overestimated it.¹ Our study confirmed that the Cockcroft-Gault formula overestimated DTPA GFR in kidney donors after nephrectomy. Unexpectedly, we noticed no significant difference between DTPA GFR and GFR estimated using the aMDRD equations.

CysC has recently been evaluated as a screening test for impaired GFR among living kidney donors.^{3,13–15} Examining 28 living kidney donors, John et al reported serial CysC estimation to be a poor method to detect reduced renal function as compared with serum creatinine or serum B2 microglobulin.¹⁵ Herget-Rosenthal et al observed CysC to detect rapid GFR decreases 1 to 2 days earlier than serum creatinine.¹³ Louvar et al assessed the performance of seven CysC and two creatinine-based GFR prediction equations among 187 former kidney donors versus iothexol GFR measurements. They observed the MDRD equation to be superior to CysC-based equations to estimate GFR among, former kidney donors.¹⁴ They recommended continued use of the traditional measures of kidney function for preoperative screening and postoperative follow-up of living kidney donors ending development and evaluation of other new markers of kidney function. The CysC concentration did not depend on the donor gender or age in this study. However, serum CysC concentrations at 5 or more years after nephrectomy were higher among older versus younger patients. Our study confirmed that the aMDRD equation was superior to serum CysC to estimate GFR among former kidney donors.

In conclusions, living kidney donation results in a reduced GFR. Residual kidney function did not deteriorate

more rapidly than that expected from aging. The aMDRD equation to estimate GFR was more precise than the Cockcroft-Gault formula and correlated with CysC concentrations in living kidney donors after nephrectomy and should be the preferred model for these patients.

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