Estimation of renal function using the Cockroft-Gault, CKD-EPI and MDRD in chronic kidney disease patients not on renal replacement therapy

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Introduction

- CKD is an important health problem due to its increased morbidity and growing prevalence worldwide.
- Proper early diagnosis and stadialization is a must for a better disease management and prognosis.
- ***GFR*** is a product of the average filtration rate of each nephron, the filtering unit of the kidneys, multiplied by the number of nephrons in both kidneys.

Marker	Method of administration	Comments
Inulin	Continuous IV infusion	Gold standard
Iothalamate	Bolus IV or SC	Overestimation of GFR
99mTc-DTPA	Bolus IV injection	Underestimation of GFR
51Cr-EDTA	Bolus IV injection	10% lower clearance than inulin
Iohexol	Bolus IV injection	Comparable to inulin; expensive and difficult to perform

Table 1: Exogenous filtration markers for estimation of GFR

- ***Clearance*** of a substance: volume of plasma cleared of a marker by excretion per unit of time.

$$C_x = U_x \times V/P_x$$

- Equations for GFR :

Cockroft-Gault Formula

Clcr (ml/min)=(140-Age)xWeight(kg)x0.85 (if F)/72xScr (mg/dl)

MDRD Study Equation

GFR (ml/min/1.73m^2)=175xStand.Scr (mg/dl)$^{-1.154}$xAge$^{-0.203}$ x0.742 (if F)x1.210 (if black)

CKD-EPI Equation

GFR (ml/min/1.73m^2)=141xmin(Scr/κ,1)$^{\alpha}$xmax(Scr/κ,1)$^{1.209}$ x0.993 ^{Age}x1.018 (if F)x1.157 (if black),

where: κ is 0.7 (F)/0.9(M); λ is-0.329(F)/-0.411(M)

CKD-EPI Serum Cystatin C Equation

GFR (ml/min/1.73m^2)=133xmin(Scys/0.8,1)$^{-0.499}$x max(Scys/0.8,1)$^{-1.328}$ x0.996 ^{Age}x0.932 (if F)

CKD-EPI SCys and SCrc Equation

GFR (ml/min/1.73m^2)=135xmin(Scr/κ,1)$^{\alpha}$xmax(Scr/κ,1)$^{-0.601}$ xmin(Scys/0.8,1)$^{-0.375}$x max(Scys/0.8,1)$^{-0..711}$x0.995 ^{Age} x0.969 (if F)x1.08 (if black)

where: κ is 0.7 (F)/0.9(M); λ is-0.329(F)/-0.411(M)

Objectives

To assess the acuracy of different formula-based equations for renal function compared with measurement of creatinin clearance in CKD patients not on renal replacement.

Methods

- Cross-sectional study in new CKD patients.
- CKD was classified in 5 stages by measurement of creatinin clearance (CrCl) from 24-hour urine sample and compared with formula-based equations (Cockroft-Gault, MDRD and CKD-EPI).

Stage	Description	GFR (ml/min/1,73 m^2)
1	Kidney injury with normal/↑ GFR	≥90
2	Mild kidney injury with small ↓ of GFR	60-89
3	Moderate ↓ of GFR	30-59
4	Severe ↓ of GFR	15-29
5	End stage renal disease	<15 or dialysis

Table 2: CKD stadialization

- SPSS ver 16: kappa test with values for κ between **0.61-0.80** showing a high consistency of results.
- ***Accuracy***, a combination between bias and precision, was used to define the best formula.

Results

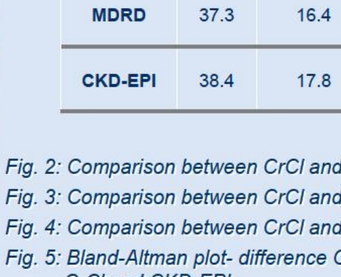
Fig. 2

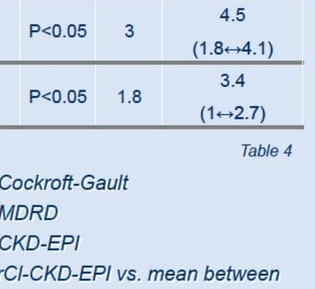
Fig. 3


Fig. 4

Fig. 5

Method	Mean	Standard deviation	P	Bias	Precision (95% CI)
CrCl	39.6	16.7	-	0	-
Cockcroft-Gault	37.8	13.2	P<0.05	1.85	6.3 (0.3 ↔ 3.3)
MDRD	39	15.3	P<0.05	0.6	3.8 (-0.3↔1.5)
CKD-EPI	38.5	15.6	P<0.05	1	3.3 (0.3↔1.9)

Table 3

Method	Mean	Standard deviation	P	Bias	Precision (95% CI)
ClCr	40.3	19.7	-	0	-
Cockcroft-Gault	46.1	20.5	P<0.05	-5.8	8.4 (-8 ↔ -3.6)
MDRD	37.3	16.4	P<0.05	3	4.5 (1.8↔4.1)
CKD-EPI	38.4	17.8	P<0.05	1.8	3.4 (1↔2.7)

Table 4

Fig. 2: Comparison between CrCl and Cockroft-Gault
Fig. 3: Comparison between CrCl and MDRD
Fig. 4: Comparison between CrCl and CKD-EPI
Fig. 5: Bland-Altman plot- difference CrCl-CKD-EPI vs. mean between CrCl and CKD-EPI
Table 3: Accuracy of GFR formula in elderly patients
Table 4: Accuracy of GFR formula in obese patients

Results

- 223 patients included (106F, 117M, mean age 60.8 ± 14.2 years)

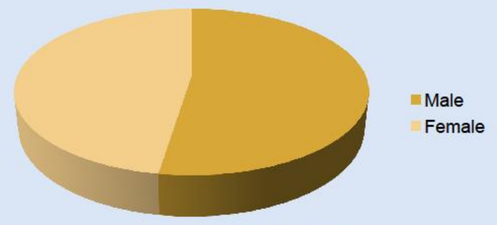

Fig. 1: Gender distribution

- CKD-EPI had the highest accuracy (Fig. 4)
  - ✓ correct stadialization of 85% patients (κ=0.76)
  - ✓ overestimation in 9% of the cases
  - ✓ underestimation in 6% of the cases.
- MDRD was very close to CKD-EPI, with a 82% accuracy (κ=0.73) (Fig. 3).
- Cockroft-Gault overestimated GFR for earlier CKD stages and underestimated GFR for more advanced CKD (Fig. 6). CKD-EPI had the highest accuracy compared to CrCl (Fig. 5,6)

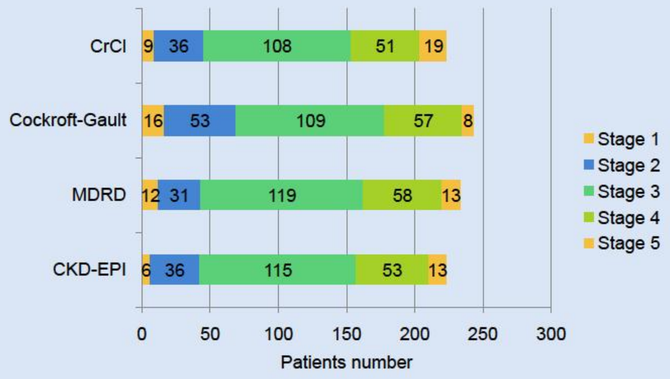

Fig.6: Comparison between GFR estimation formula depending on CKD stages

- In obese (*n*=61, 27.4%) and in elderly patients (>70 yrs, *n*=69), CKD-EPI had the highest precision (3.4 in obese, 3.3 in elderly) followed very close by MDRD (precision of 4.5 in obese and 3.8 in elderly) (Tables 3 and 4)

Conclusions

CKD-EPI and MDRD had similar results, with reasonable estimation of kidney function.

CKD-EPI had a better consistency for different CKD stages, but especially for stages 1 to 4 of CKD.

For end stage renal disease it seems that these formula based equations are not as good as clearance measurement.

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J1) Chronic Kidney Disease. Lab methods, GFR measurement, urine proteomics

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