Cockcroft&Gault and CKD-EPI equations: are these equations concordant to adjust drug dosage?

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Objectives

When obese patients are considered, one important issue is the question of body surface area (BSA) indexation. In Pharmacology, the Cockcroft&Gault (CG) equation is still recommended to adapt drug dosage. In Nephrology, KDIGO recommend using CKD-EPI equation to estimate glomerular filtration rate (eGFR) and « de-indexing » this equation to adjust drugs. Both in Pharmacology and in Nephrology, the "weight" variable matters in the context of obesity. Therefore, adjusted ideal body weight (AIBW) is sometimes preferred to actual body weight for these patients. In this study, we test the concordance of the different equations to adjust drug dosage.

Methods

Patients with body mass index (BMI) higher than 30 kg/m^2 were included in the study. AIBW is calculated as follows:

$$AIBW = Ideal\,Body\,Weight + (0.4 * (Actual\,Body\,Weight - Ideal\,Body\,Weight))$$

In this work, we compare results obtained with CKD-EPI and with CG and CG$_{AIBW}$. CKD-EPI is « de-indexed », as recommended (calculated by multiplying eGFR by each individual's body surface area and by dividing this intermediate result by 1.73 m^2). CG and CG$_{AIBW}$ are nonindexed and also expressed in mL/min. We calculated bias (defined as the mean difference between CKDEPI$_{deindexed}$ and CGs), precision (defined as the SD around the bias) and accuracy 30%(defined as the percentage of CKD-EPI$_{deindexed}$ within ± 30% of CGs). All patients were then classified according to the level of GFR (stage 1: eGFR > 90, stage 2: eGFR 60-90, stage 3: eGFR 30-60 and stage 4: eGFR<30 mL/min). We then calculated the concordance between these equations in each of these groups.

Population (n=366)

Age (year)	55 ± 14 [18-86]
Female	185 (51%)
Weight (kg)	100 ± 22 [67-258]
Height (cm)	166 ± 10 [144-193]
African origin	50 (14%)
Body mass index (kg/m²)	36 ± 7 [30-77]
BSA (Gehan and Georges formula m²)	2 ± 0 [2-2]
Creatinine (mg/L)	16 ±11 [5-74]
CKDEPI	60 ± 33 [8-137]
EDTA mGFR non indexed (mL/min)	71 ± 35 [11-169]
Chronic Kidney Disease (CKD) stage	
1. GFR≥90 mL/min	110 (30%)
2. GFR 60-89 mL/min	100 (27%)
3. GFR 30-59 mL /min	107 (29%)
4. GFR 15-29 mL /min	49 (13%)
Hyperfiltrating status (GFR>120 mL/min)	37 (10%)

Results

The population included 366 patients (185 women) from two different areas. Mean age was 55 ± 14 years and mean BMI was 36 ± 7 kg/m^2. Mean eGFR by CG and CG$_{AIBW}$ were 96 ± 64 and 73 ± 45 mL/min, respectively. Mean eGFR by CKD-EPI$_{deindexed}$ was 77 ± 44 mL/min. In the global population, when we considered CG and CKD-EPI$_{deindexed}$, mean bias was -18.8 ± 24.7 and accuracy 30% between the equations was 86%. When we used CG$_{AIBW}$, mean bias was +3.6 ± 8.6 and accuracy 30% was 99% (p<0.0001). Regarding the classification of the patients, the concordance between CG and CKD-EPI$_{deindexed}$ and the concordance between CG$_{AIBW}$ and CKD-EPI$_{deindexed}$ were 79.2% and 84.9%, respectively (p=0.06).

Tables

	CG vs CKD-EPI$_{deindexed}$	CG$_{AIBW}$ vs CKD-EPI$_{deindexed}$
Biais	-18.8	3.6
Precision	24.7	8.6
Accuracy 30%	86	99
Concordance %	79.2	84.9

Conclusions

In the context of obesity, we observed a good concordance between the results given by the CG equation and CKD-EPI$_{deindexed}$ if the AIBW is considered. Using actual weight induces discrepancies between the equations with potential consequences on drug dosage adjustment. Our study illustrates these potential discrepancies but it remains to be definitively proven that CKD-EPI$_{deindexed}$ (or CG$_{AIBW}$) performs better than CG with actual weight for the adjustment of drug dosage in obese patients.

References

1. Chin P *et al*. The performances of the CG, MDRD and CKD-EPI equations in predicting gentamicin clearance. *Annals of Clinical Biochemistry 2013;* 50(6): 546–557.
2. Delanaye P *et al*. Errors induced by indexing glomerular filtration rate for body surface area: reductio ad absurdum. *Nephrol Dial Transplant 2009;* 24: 3593-3596.