Drug dosing in Chronic Kidney Disease: Is the Cockcroft-Gault Formula always the Best Estimator of Renal Function to Prevent Overexposure?

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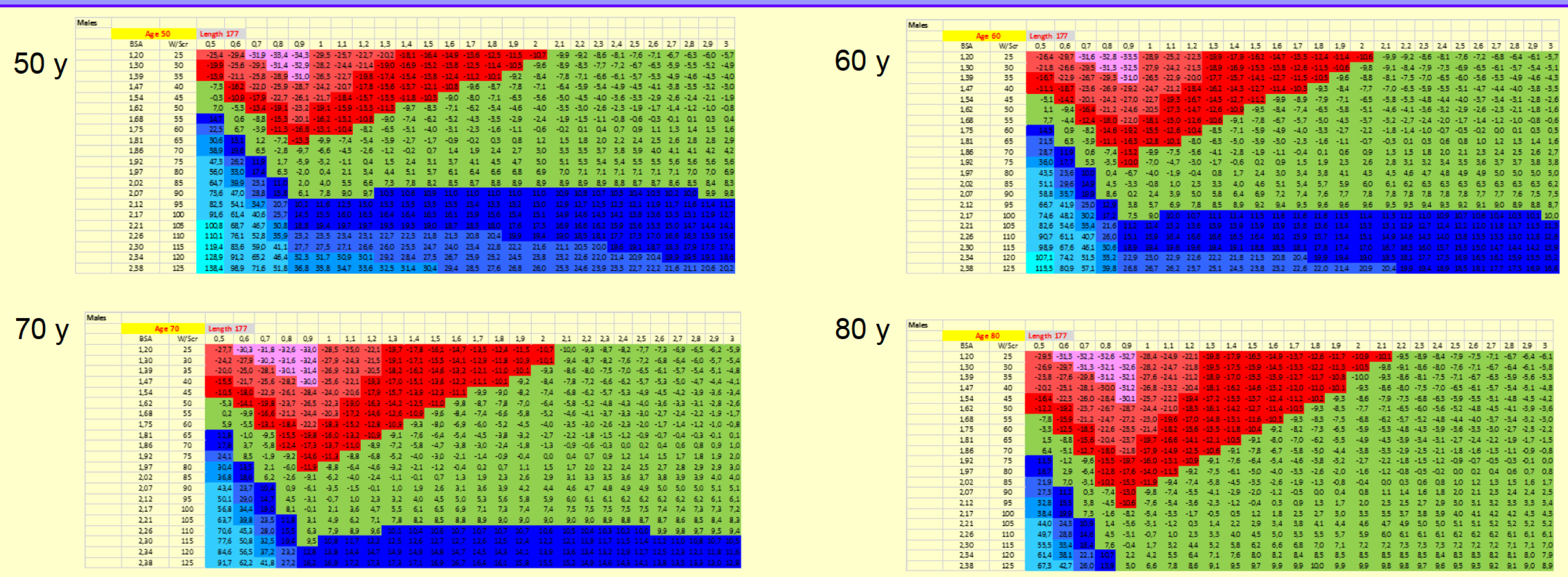
Objectives:

Which creatinine-based GFR equation should preferentially be used in the context of drug dosing is highly debated. While most Nephrology guidelines recommend the use of the CKD-EPI equation, other specialists such as geriatricians keep on favoring the use of the Cockcroft-Gault equation (C-G). Along with the fact that dosing recommendations were most often initially done based on C-G, the main justification is that this equation usually provides lower value of GFR as compared to the CKD-EPI equation, and thus minimizes the risk of overdosing. Herein, we wanted to verify whether this assertion was systematically true regardless of demographic characteristics.

Methods:

We developed a software program that explores, for different age strata and gender, more than 500 combinations of weight and serum creatinine values. For each combination, GFR was estimated by both CKD-EPI and C-G and the difference (CKD-EPI – C-G) was calculated. We considered a difference in eGFR between -10 ml/min and + 10 ml/min as a good agreement between CKD-EPI and C-G. Alternatively, a difference < -10 ml/min and > +10 ml/min was considered as, respectively, a significant higher and lower GFR estimation given by G-C as compared to CKD-EPI.



Concordant (green cases) and discordant results (red and blue) when age increases from 50 to 80 y. Results are expressed as absolute difference in mL/min.
Red color will correspond to cases where CG equation give significantly lower values than CKD-EPI, blue color will correspond to cases where CKD-EPI gives higher results

Results:

Overall, levels of agreement were significantly improved for the highest strata of ages with 36% and 62% of concordant GFR values for 40 and 80 years of age, respectively ($p<0.01$). For strata of ages above 70 years, C-G systematically gave lower GFR value for a weight below 60 kg and for a serum creatinine in the range of normal or near normal values. For weights above 90 kg, C-G-based values were never lower than CKD-EPI irrespective of the serum creatinine value. For strata of ages below 55 years, C-G provided significantly lower value of GFR in only less than 10% of the simulations.

Conclusions:

Our data challenge the notion that C-G systematically gives lower value of GFR as compared to CKD-EPI. Age, weight and serum creatinine value are critical factors influencing the agreement between C-G and CKD-EPI. The typical situation in which C-G results in lower GFR estimates is a patient of 70 years old or more who tends to be underweight and with a low/normal serum creatinine value. Our data do not support the notion that disagreement between C-G and CKD-EPI should favor the use of C-G for preventing drug overdosing.

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