Exploration of Estimated Renal Function and Gabapentin Clearance in Older Adults

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INTRODUCTION

The best formula to estimate glomerular filtration rates (eGFR) in older adults, particularly in very old populations is unknown. Gabapentin (GBP) is eliminated by glomerular filtration and used clinically in older adults, affording the opportunity to compare gabapentin clearance to various estimates of glomerular filtration rates (GFR). The goal of this study was to determine which GFR estimation formula most closely correlates with GBP clearance in older adults.

OBJECTIVE

To determine the relationship between steady-state GBP concentrations and eGFR formulas that incorporate serum creatinine and/or cystatin C measurements, and age, with and without race.

METHODS

Study Design

Sampling of steady-state GBP, creatinine, and cystatin concentrations in medically stable nursing home residents $\geq$ 60 years of age. GBP and serum creatinine were measured at University of Minnesota, cystatin C was measured at UCSF.

Data Analysis

➢ Estimates of GFR were obtained using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[1,2], CG[3] and Modifications of Diet in Renal Disease (MDRD-4) formula.[4]

➢ Population pharmacokinetic analyses were conducted via non-linear mixed effects modeling (NONMEM, version 7.5). Post-hoc of GBP clearance values (GBP~iCL) were used for calculation. Correlation between GBP~iCL and eGFR values was tested using Spearman's rank correlation test.

Table 1. Demographic Charateristics

Charateristics	Median [range]; N(%)
Age (years)	81 [61-97]
Sex (Men/Women) (%)	15(25.4) / 44 (74.6)
Race (Caucasian/African American) (%)	52 (88.1) / 7 (11.9)
Weight (kg)	73.64 [44.73-168.40]
Creatinine (mg/dL)	0.9 [0.39-3.35]
Cystatin C (mg/dL)	1.45 [0.79-3.84]
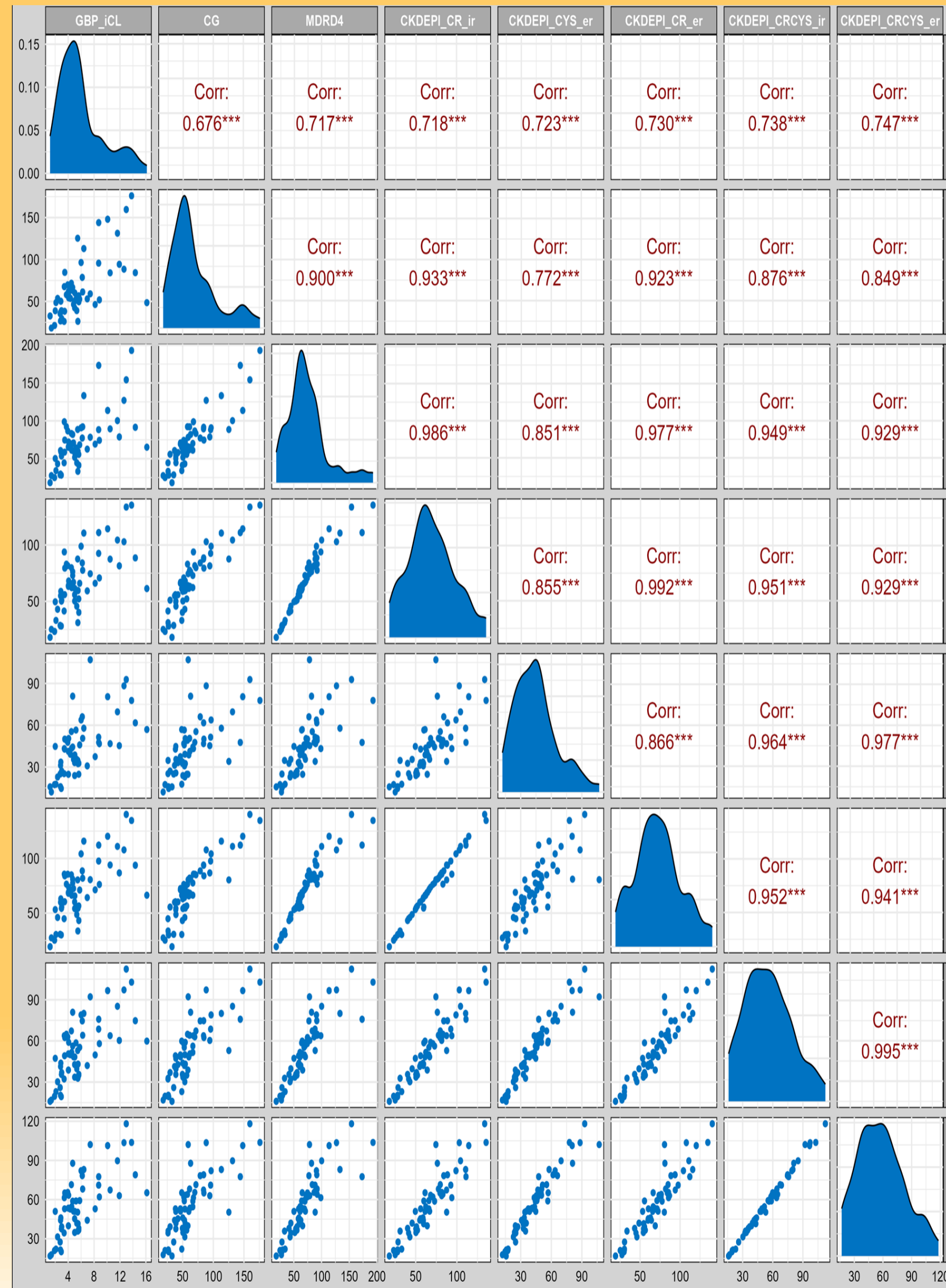
REFERENCES

RESULTS

➢ 59 individuals provided 227 GBP concentrations (Table 1). Total daily dose was 600 [50-3000] mg and median GBPss concentration was 4.29 [0.14-23.43] μg/mL. GBP PK were best described by a one-compartment linear model with proportional error, including interindividual variability on clearance (CL) and its parameters agreed with past literature[5,6]

➢ The correlation between GBP~iCL and eGFR formulas ranged from 0.68 to 0.75. The highest correlation (r = 0.75) was between GBP~iCL and CKD-EPI 2021 which incorporates serum creatinine and cystatin C, but excludes race. The lowest correlation (r = 0.68) was between GBP~iCL with the CG formula. (Figure 1)

Table 2. Formula to Estimates GFR

Formula	Equations
Cockcroft-Gault (CG) (1973)[3]	eGFR = (140 – age) x weight / 72 x SCr; Multiply by 0.85 if female; No race
MDRD-4 (1999)[4]	eGFR = 186.3 x (SCr/k)^-1.154 x (Age)^-0.203; Multiply by 0.742 if female, Multiply by 1.21 if Black
CKD-EPI (2009)[2]	eGFR = 141 x min(SCr/k, 1)^α x max(SCr/k, 1)^-1.209 x 0.9929^Age; Multiply by 1.018 if female; Multiply by 1.159 if Black; k:0.7 for females and 0.9 for males; α: -0.329 for females and -0.411 for males
CKD-EPI (2021)[1]	eGFR = 142 x min(SCr/k, 1)^α x max(SCr/k, 1)^-1.200 x 0.9938^Age; Multiply by 1.012 if female, No race; k:0.7 for females and 0.9 for males; α: -0.241 for females and -0.302 for males

CONCLUSION

➢ GBP~iCL was best correlated with CKD-EPI 2021 formula suggesting it is preferable over other eGFR methods for estimation of glomerular filtration in older adults.

➢ As the lowest correlation was seen with the CG formula, this suggests it may not be the best formula for use in older adults.

➢ Further research is needed to validate these findings in larger and more diverse older adult populations.

Figure 1. Pairwise matrix plot of several eGFR and its Correlation with GBP~iCL; *_ir=inclusion race; _er: exclusion race; _iCL:individual clearance; CG: Cockcroft-Gault formula