# Comparison of the Cockcroft-Gault, MDRD and CKD-EPI equations for estimating ganciclovir clearance

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Accurately estimating kidney function is essential for the safe administration of renally cleared drugs like ganciclovir (GCV). Current practice recommends adjusting renally eliminated drugs according to the Cockcroft-Gault equation. There is no data on the utility of the Modification of Diet in Renal Disease (MDRD) and Chronic Kideny Disease Epidemiology Collaboration (CKD-EPI) equations in GCV dosing.

## Objectives

To evaluate which renal function equation best predicts GCV clearance.

## Results

-112 patients were selected/ 100 patients were analyzed.
-Learning group: 74 patients; validation group: 26

Table 1. Characteristics of the 100 patients treated with IV GCV

| | Mean ± SD | Median (min-max) |
|---|---|---|
| Age (years) | 55.2 ± 14.6 | 57.0 (18.0–91.0) |
| Sex (N men/women) | 67/33 | |
| Weight (kg) | 66.9 ± 16.0 | 66.0 (36.0-117.0) |
| BSA (m2) † | 1.76 ± 0.24 | 1.78 (1.24-2.41) |
| Serum creatinine (m2) † | 1.0 ± 0.6 | 0.9 (0.3–3.9) |
| Daily dose (mg/kg/day) | 7.8 ± 4.0 | 8.1 (0.8 – 22.5) |
| Cmin (mcg/ml) | 1.8 ± 1.4 | 1.4 (0.1-6.0) |
| CrCl Cockcroft-Gault (ml/min) | 79.6 ± 36.5 | 71.2 (16.7–199.2) |
| GFR MDRD4-IDMS (ml/min/1.73 m2) § | 121.4 ± 96.7 | 87.5 (16.6–742.2) |
| GFR MDRD4-IDMS·BSA (ml/min) †,§ | 120.0 ± 89.8 | 91.1 (16.2–659.2) |
| GFR CKD-EPI (ml/min/1.73 m2) § | 92.3 ± 36.4 | 96.4 (16.4–205.5) |
| GFR CKD-EPI·BSA (ml/min) †,§ | 92.4 ± 35.5 | 93.7 (16.1–182.5) |
| $C_0$ (mcg/ml) | 5.7 ± 2.0 | 5.3 (2.5 – 13.3) |
| Kel (h$^{-1}$) | 0.108 ± 0.073 | 0.108 (0.011 – 0.381) |
| Cl (ml·kg/ml) | 2.0 ± 1.4 | 2.0 (0.2 – 7.1) |
| $T_{1/2}$ (h) | 11.5 ± 10.9 | 6.4 (1.8 – 60.9) |
| AUC (mcg·h/ml) | 92.8 ± 84.3 | 51.0 (10.9 – 407.3) |
| AUC 24h (mcg·h/ml) | 137.2 ± 103.8 | 93.1 (21.9 – 457.3) |

AUC: area under the plasma concentration-time curve; Cl: total plasma clearance; Cmin: minimum (or trough) plasma concentration; CrCl: creatinine clearance; $C_0$: concentration at time 0; GFR: glomerular filtration rate; Kel: elimination rate constant; $T_{1/2}$: terminal half-life
†BSA was calculated using Mosteller equation.
‡Serum creatinine levels were determined when GCV blood levels were monitored
§The five equations showed significant correlation with each other, with a correlation coefficient of > 0.8 (P<0.001, in all cases).

-The coefficient of determination ($R^2$) was 0.28 for Cockcroft-Gault, 0.30 for CKD-EPI·BSA, 0.31 for MDRD4-IDMS·BSA, 0.32 for MDRD4-IDMS and 0.36 for CKD-EPI.
-Analysis of the validation group confirmed these results. The R2 was 0.20 for Cockcroft-Gault, 0.21 for MDRD4-IDMS·BSA, 0,27 for CKD-EPI·BSA, 0.29 for MDRD4-IDMS and 0.42 for CKD-EPI (Figure 1).
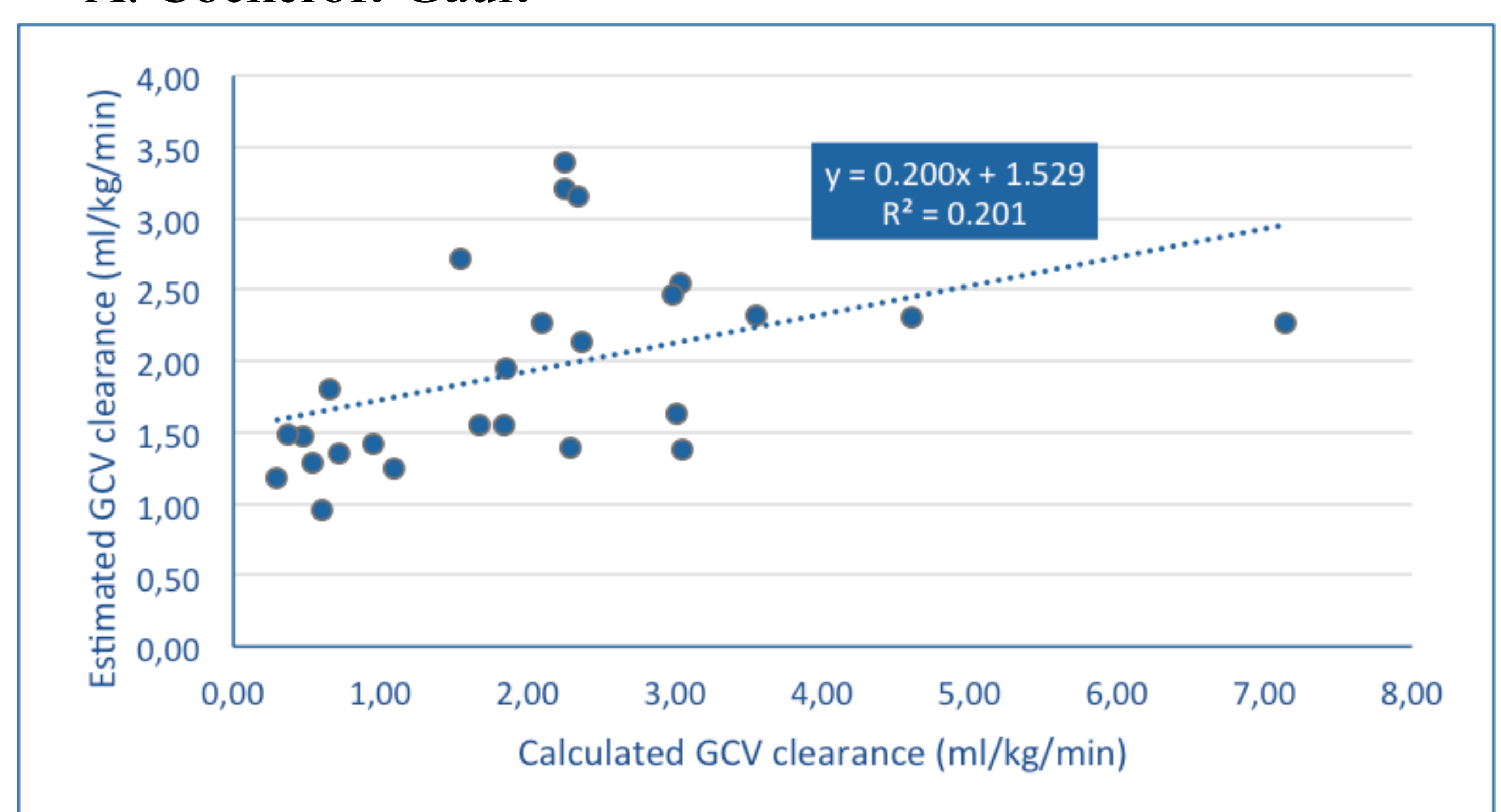
## Conclusions

The CKD-EPI equation correlates better with GCV clearance than the Cockcroft-Gault and MDRD4-IDMS equations. However, further studies are needed in order to recommend new GCV doses according to the CKD-EPI equation.

## Material and Methods

•The performance of the Cockcroft-Gault equation, isotope dilution mass spectrometry (IDMS)-traceable 4-variable MDRD study (MDRD4-IDMS) equation, and CKD-EPI equation in determining GCV clearance were assessed retrospectively in patients treated with GCV from 2004-2015.
•The MDRD4-IDMS and CKD-EPI equations adjusted to individual body surface area (MDRD4-IDMS·BSA and CKD-EPI·BSA, respectively) were also evaluated.
•Patients with IV GCV peak and trough concentrations in their medical records were included in the study.
•GCV clearance was calculated from serum concentrations using a two-compartment model.
•The five equations were compared based on their predictive ability, the coefficient of determination, through a linear regression analysis.
•The results were validated in a group of patients.

Figure 1. Calculated GCV clearance vs GCV clearance estimated from the Cockcroft-Gault (A) and CKD-EPI (B), based on the 26-patient validation group

A. Cockcroft-Gault



B. CKD-EPI

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