

A comparison of carboplatin dosing using the Cockcroft-Gault equation versus BSA-adjusted eGFR_{CKD-EPI} equation

Linda Nguyen¹, Ian Kei Yee², Neil Kim Chiu Lam¹

1. Icon Wesley Pharmacy, Icon Cancer Centre, Brisbane, QLD, Australia 2. School of Pharmacy, University of Queensland, Brisbane, QLD, Australia

Background

Carboplatin is a chemotherapy drug used to treat a variety of cancers. Its dosing is based on the Calvert Formula and requires the patient's glomerular filtration rate (GFR) in its calculation. Historically, the Cockcroft-Gault (CG) equation was used to determine estimated GFR (eGFR), by calculating creatinine clearance. However, with the recently introduced International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD), the Chronic Kidney Dysfunction-Epidemiology Collaboration 2009 equation (eGFR_{CKD-EPI}) is recommended to replace the Cockcroft-Gault equation in determining eGFR due to increased precision and accuracy.¹

Aim

This study aimed to compare the carboplatin dose variation between the Cockcroft-Gault and body surface area (BSA) adjusted eGFR_{CKD-EPI} equations.

Method

- Retrospective audit of initial carboplatin doses (n=127) administered between 1st January and 31st December 2022 to adult cancer patients at a day oncology clinic
- Patient characteristics collected include age, sex, weight, height, serum creatinine and target area under the curve (AUC)
- Carboplatin doses were calculated using the Calvert formula
- GFR was calculated using the CG and BSA-adjusted eGFR_{CKD-EPI} equations (refer to Table 1 and 2). Note that creatinine clearance [CrCl] was capped at 125mL/min when calculating the carboplatin dose using the CG equation
- Statistical analysis included:
 - Paired t-test – to compare the mean carboplatin dose calculated using the CG and BSA-adjusted eGFR_{CKD-EPI} equations
 - Pearson correlation coefficient – to investigate the relationship between patient characteristics and percentage dose variation.

Table 1: Calvert Formula, Cockcroft-Gault and BSA-adjusted eGFR_{CKD-EPI} equations¹

	Equation
Calvert Formula	Carboplatin dose = (GFR + 25) x target AUC
Cockcroft-Gault (CG) Equation	Creatinine Clearance [CrCl] = [(140-age) x weight [kg]] / [0.814 x SCr [micromol/L]] [x 0.85 for females]
BSA-adjusted eGFR_{CKD-EPI} Equation	BSA-adjusted eGFR _{CKD-EPI} [mL/min] = [eGFR _{CKD-EPI} [mL/min/1.73 m ²] x BSA [m ²]] / 1.73

Table 2: eGFR_{CKD-EPI} equations¹

Sex	Serum creatinine (SCr)	eGFR _{CKD-EPI} equation
Female	≤ 62 micromol/L	eGFR _{CKD-EPI} [mL/min/1.73m ²] = 144 x [SCr [micromol/L] x 0.0113/0.7] ^{-0.328} x [0.993] ^{age}
	> 62 micromol/L	eGFR _{CKD-EPI} [mL/min/1.73m ²] = 144 x [SCr [micromol/L] x 0.0113/0.7] ^{-1.209} x [0.993] ^{age}
Male	≤ 80 micromol/L	eGFR _{CKD-EPI} [mL/min/1.73m ²] = 141 x [SCr [micromol/L] x 0.0113/0.9] ^{-0.411} x [0.993] ^{age}
	> 80 micromol/L	eGFR _{CKD-EPI} [mL/min/1.73m ²] = 141 x [SCr [micromol/L] x 0.0113/0.9] ^{-1.209} x [0.993] ^{age}

Conclusion

With the implementation of the BSA-adjusted eGFR_{CKD-EPI} equation in practice, this study will provide insight and reassurance to clinicians regarding the dose variation between the two methods. However, further study is required to determine its clinical significance.

Results

- 70.9% of doses [90/127] had ≤10% dose variation between the CG and BSA-adjusted eGFR_{CKD-EPI} method (Figure 1)
- 23.6% of doses [30/127] had a >10% to ≤20% dose variation (Figure 1)
- Mean carboplatin dose between the two methods did not reach statistical significance (p=0.06)
- Weak correlation between weight and percentage dose variation was observed (r=-0.39)[Figure 2]
- Weak correlation between body mass index (BMI) and percentage dose variation was observed (r=-0.52)[Figure 3]

Figure 1: Waterfall plot comparing the percentage dose variation between Cockcroft-Gault and BSA-adjusted eGFR_{CKD-EPI} equations for individual patients

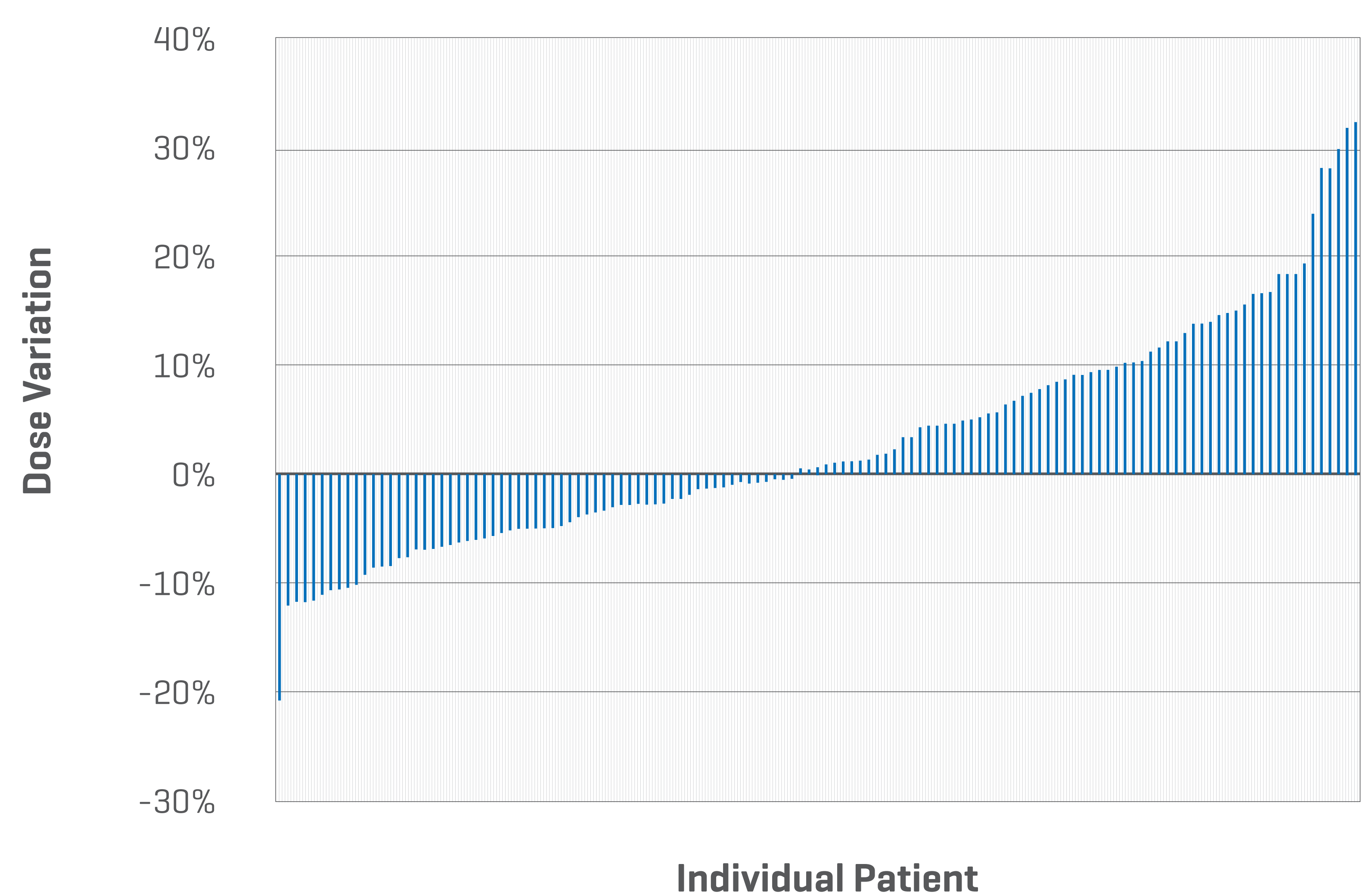


Figure 2: Scatter plot comparing percentage dose variation between Cockcroft-Gault and BSA-adjusted eGFR_{CKD-EPI} equations versus weight

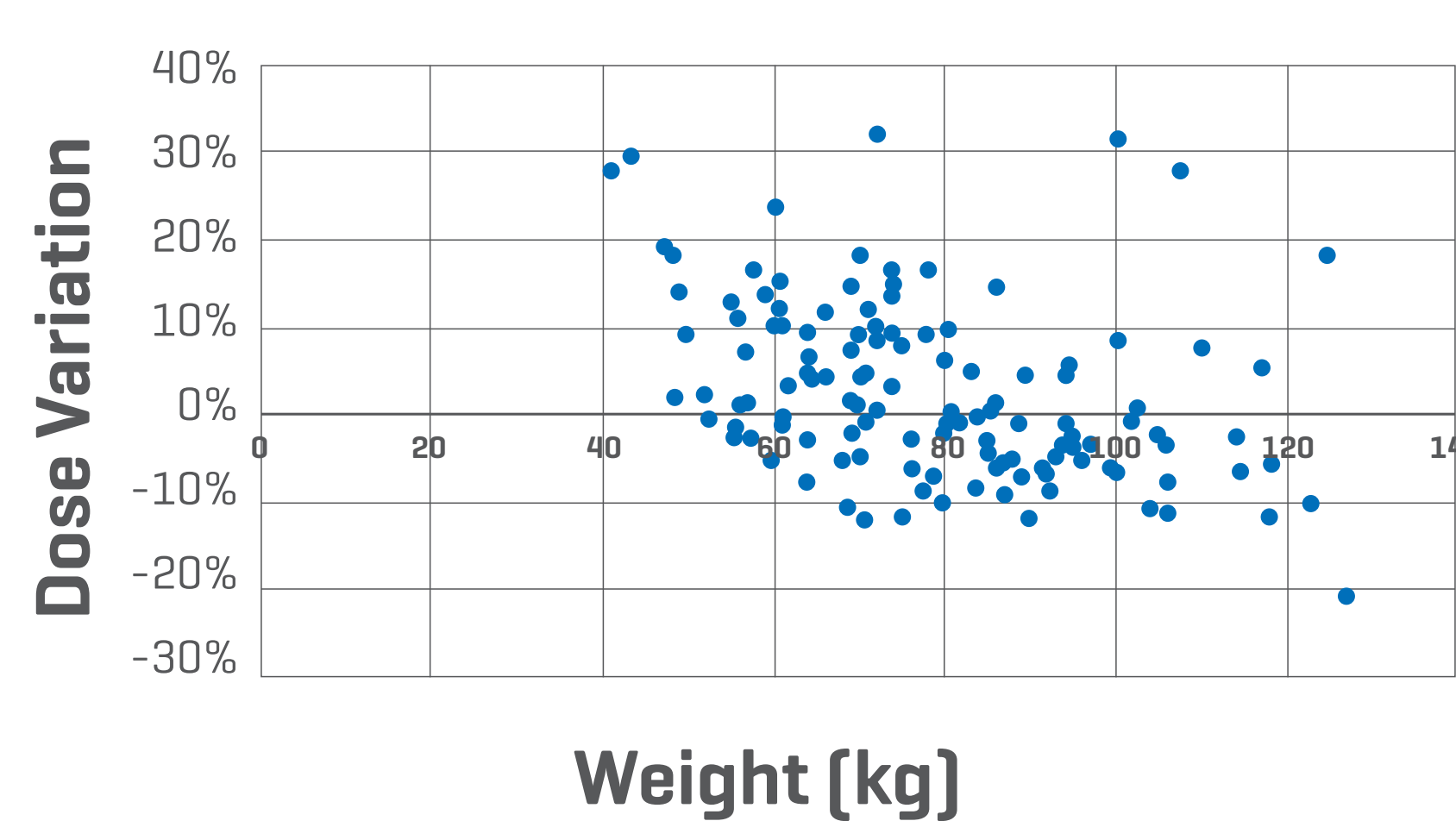
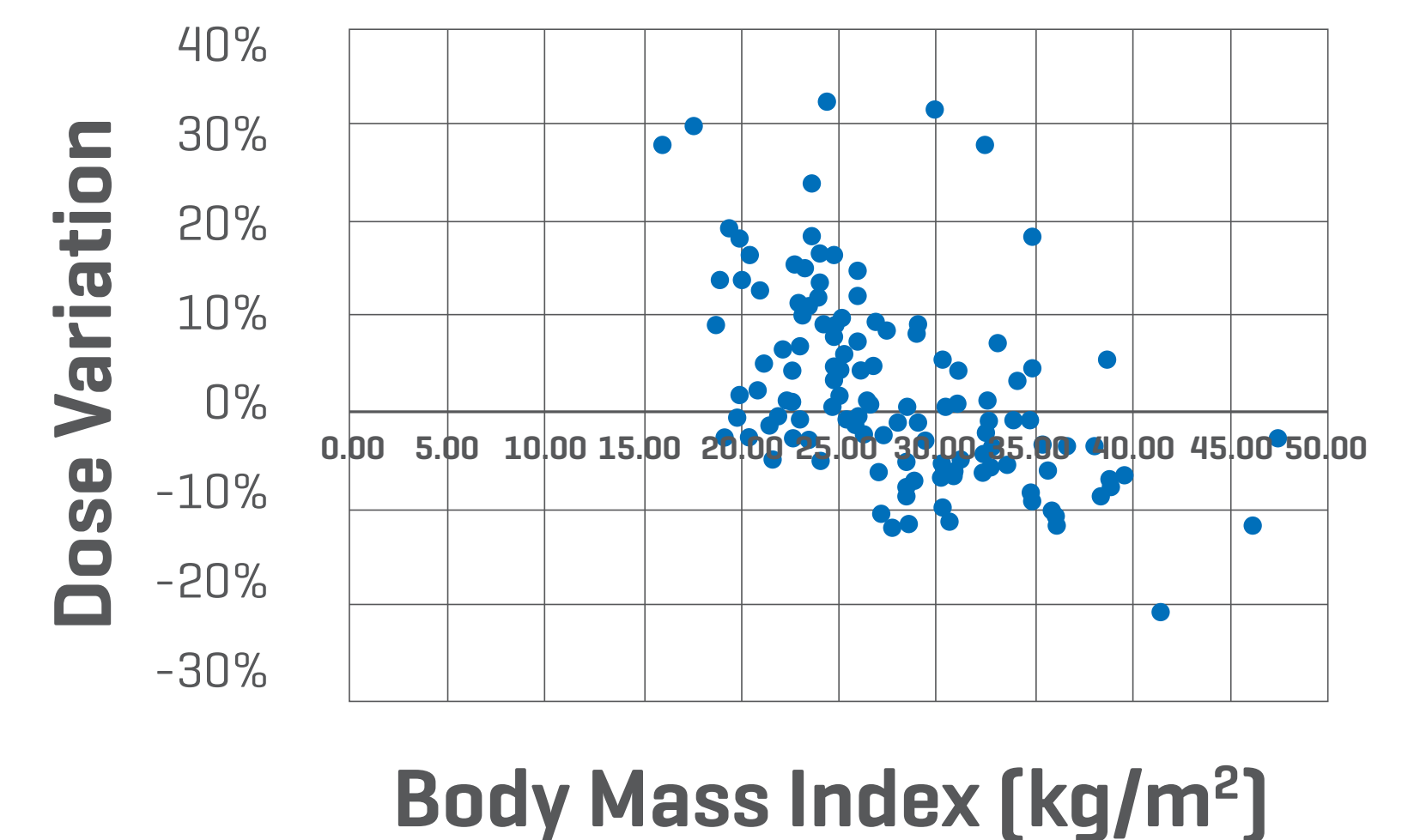


Figure 3: Scatter plot comparing percentage dose variation between Cockcroft-Gault and BSA-adjusted eGFR_{CKD-EPI} equations versus body mass index (BMI)



Discussion

In this study, the majority of doses calculated using the BSA-adjusted eGFR_{CKD-EPI} equation were within 20% compared to the CG equation. 5.5% of doses (n=7) had a >20% dose variation. This result shows some similarity with another study that investigated carboplatin dose calculations including the BSA-adjusted eGFR_{CKD-EPI} equation.² However, a lack of information from the literature regarding an acceptable percentage dose difference makes the interpretation of results difficult.

It was also observed that extremes in body weight and BMI had a larger percentage dose variation, although these were weak correlations.

Study limitations include the small sample size and single centre. Additionally, the clinical significance on patient outcomes were not assessed, but would be an area of interest for future studies.

References

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