

ORIGINAL RESEARCH ARTICLE

Establishing discordance rate of estimated glomerular filtration rate between serum creatinine-based calculations and cystatin-C-based calculations in critically ill patients

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Abstract

Introduction: The use of serum creatinine (SCr) for drug dosing has significant limitations and is influenced by many non-kidney factors. Cystatin C (cysC) is an alternative or additional marker of kidney function that is less affected by non-kidney factors. Although cysC may be useful in hospitalized patients, the use of cysC to calculate drug dosing in critically ill patients has been incompletely investigated.

Objective: The objective of this study was to determine the rate of discordance in estimated glomerular filtration rate (eGFR) between SCr-based calculations and SCr/cysC-based calculations that affect drug dosing in critically ill patients.

Methods: This was a single-center, retrospective, observational cohort study at an academic medical center including critically ill adult patients admitted in 2023 with SCr and cysC ordered. Data were collected via chart review. Demographic data were analyzed via descriptive statistics. Discordance, defined as the percentage of times at which there is at least one discrepancy in kidney dosing for a medication using Cockcroft-Gault (CG) creatinine clearance versus Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR creatinine-cystatin C (eGFRcr-cys) equations, was analyzed via Wilcoxon matched pair signed ranked sum. eGFR calculations were normalized for patients' body surface area for comparison.

Results: The study population included 232 patients (53.02% female; mean age 58.7 \pm 14.9 years; with 62.5% in medical, 23.28% in surgical, and 8.62% in neurological intensive care) with a median SCr of 0.94 mg/dL IQR [0.57–1.58] and median cysC of 1.92 mg/L IQR [1.27–2.77]. The median clearance rates were 68.5 mL/min (45.3–111.5) for CG and 53.9 mL/min (30.9–80.7) for CKD-EPI eGFRcr-cys; $p < 0.001$. The discordance rate across all study drugs was 32.3% (75/232). The four most common study drugs demonstrating discordance were cefepime 40.6% (52/128), vancomycin 38.3% (46/120), levetiracetam 35.1% (13/37), and piperacillin/tazobactam 11.6% (5/43).

Conclusion: Clinically significant discordance exists between SCr and SCr/cysC-based estimates of kidney function. This study established a discordance rate, as defined by drug dosing, of 32.3% in adult patients admitted to the ICU.

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KEYWORDS

creatinine, critical illness, cystatin C, discordance rate, kidney function

1 | INTRODUCTION

Assessment of kidney function is critical to optimizing efficacy and safety of medication dosing. Traditional assessment strategies include urine output and serum creatinine (SCr). Serum creatinine, a muscle breakdown product that is freely filtered across the glomerulus with some proximal tubule secretion, has specific limitations to assessing kidney function, especially in patients with acute kidney injury.^{1,2} Several non-kidney determinants may influence SCr levels, including sepsis, volume status, rhabdomyolysis, muscle mass/body composition extremes, nutritional status, hyperglycemia, pregnancy, age, and others.^{1,3-6} Despite these limitations, urine output and SCr remain the standard of care for assessing and defining kidney function, oftentimes by using the Cockcroft-Gault (CG) equation.⁷⁻¹¹

In response to these limitations, there has been evolving support for alternative formulas to estimate kidney function. In the late 1990s, the Modification of Diet in Renal Disease (MDRD) estimated glomerular filtration rate (eGFR) study equation was developed as an alternative to CG.¹² In 2009, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR equations were developed and thought to be more accurate than the MDRD equations.¹³ In 2021, these equations were updated to remove race from the calculation.¹⁴ Although these equations are helpful in addressing the limitations of the CG formula, the limitations of SCr remain.

Cystatin C (cysC), a low molecular weight protein, has been proposed as an additional or alternative marker of kidney function that appears to be less affected by non-kidney determinants compared to SCr.¹⁵⁻¹⁷ CysC is released from all nucleated cells and filtered by the glomerulus prior to catabolism in the proximal tubules.¹⁵ Considered a functional biomarker, cysC is not without its own limitations. Baseline levels of cysC may be affected by uncontrolled thyroid disease, corticosteroid use, active smoking, high levels of C-reactive protein, coronary artery disease, and malignancy.^{15,18-21} However, data supporting its use in clinical practice is promising.¹⁰ In the inpatient environment, CysC-based estimates of kidney function have been explored in dosing vancomycin and in medication dosing for older adults.²²⁻²⁴ The CG formula, which relies on SCr, is commonly used to estimate kidney function to inform drug dosing in clinical practice.¹¹ Several major national kidney organizations recommend against using CG formula due to many limitations, instead favoring CKD-EPI eGFR equations.^{10,25,26} Since the original validation study of the CKD-EPI eGFR equation, the CKD-EPI eGFR equation has evolved into a set of eGFR equations based on SCr, cysC, or both SCr and cysC that are more inclusive of all patients.^{13,14,27} Of the three CKD-EPI equations studied and validated, the equation estimating glomerular filtration rate using both SCr and cysC has performed best.^{11,27}

Despite these advances related to cysC utilization in estimating kidney function, widespread adaptation into acute care clinical practice has been slow.^{21,28} Preliminary studies have investigated the use of cysC in hospitalized patients with promising results.²⁹ Limited data exist regarding use of cysC in critically ill patients, specifically. CysC was made available as an in-house laboratory order for use by all providers and pharmacists at our institution in 2023. The purpose of this study is to establish the discordance rate of kidney drug dosing between SCr-based calculations and SCr/cysC-based calculations in critically ill patients.

2 | METHODS

2.1 | Objectives

The primary objective of this study was to determine the discordance rate of kidney drug dosing between the SCr-based calculation (CG) and the SCr and cystatin C-based calculation (CKD-EPI eGFRcr-cys) in critically ill patients. A secondary analysis was comparing CKD-EPI eGFRcr-cys to 2012 CKD-EPI cystatin C-based calculation (CKD-EPI eGFRcys). Study equations can be found in the Appendix A. Discordance rate, the primary outcome, was defined as the percentage of times at which there was a discrepancy in drug dosing for at least one medication for a patient using the CKD-EPI eGFRcr-cys compared to CG estimates of kidney function.³⁰ A secondary endpoint was the discordance rate in drug dosing between eGFRcr-cys and eGFRcys. Other secondary endpoints were rates of discordance at which eGFRcr-cys was more than 30% lower than CG or eGFRcys and discordance rate for which there was an absolute difference between eGFRcr-cys of 15 mL/min or more compared to CG or eGFRcys.^{31,32}

2.2 | Design

This study was designed according to retrospective chart review methodology best practices and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.^{33,34} This was a single-center, observational, retrospective cohort study at a large academic medical center that was determined exempt from Institution Review Board review by the Office of Responsible Research Practice. Patients who were 18 years and older who were admitted to an intensive care unit (ICU) between January 1, 2023 and December 31, 2023 with a cysC level collected during ICU admission were included in this study. For patient with multiple cysC collections in the ICU, only the first collection was included. Patients were excluded if they were

incarcerated, pregnant/lactating, receiving kidney replacement therapy within 72 h of cysC lab collection, had a history of kidney transplant, or if specified admission was for kidney transplant.

2.3 | Data collection

Prior to data collection, study personnel were properly trained to collect data, which included iterative pilot testing until accuracy and consistency between study personnel was confirmed. Data were collected from the electronic medical record (EMR) via reporting and chart review. Data were recorded in a REDCap database. Patient demographic data included age, sex, height, weight, body surface area, and race. Past medical history was collected with a focus on disease-relevant disease states. A Sequential Organ Failure Assessment (SOFA) score was calculated for the day cysC was ordered.³⁵ Details of the specified hospital admission were collected, including presentation location, medical service, and lengths of stay. Laboratory results including albumin, SCr, and cysC from the day of the cysC lab draw were collected. Administration of select kidney-adjusted medications (Table 1), medications known to influence SCr (cimetidine, high dose trimethoprim, pyrimethamine, cobicistat, dolutegravir, olaparib, rucaparib, dronedarone, cefoxitin, flucytosine, and tyrosine kinase inhibitors), and conditions thought to influence cysC were recorded.

Estimates of kidney function were recorded from the EMR including CG creatinine clearance and CKD-EPI eGFRcr-cys. The EMR-calculated CG equation utilized actual body weight (ABW) if the patient's ABW was less than the ideal body weight (IBW). If the

patient's ABW was $\geq 120\%$ of the IBW, adjusted body weight (adjBW) was used for the calculation.³⁰ eGFR results were normalized to the patient's body surface area to result in comparable units of mL/min for analysis. Equations are available in the Appendix A.^{11,14,36,37}

Select kidney-adjusted medications were chosen for evaluation based on frequency of use in critical care populations. Dosing breakpoints for kidney-adjusted medications were defined based on institutional policy and package insert recommendations.³⁰ For each patient, these medications were classified by pre-specified kidney dosing cutoffs based on each of the calculated kidney function estimate results.

2.4 | Statistical analysis

Data was analyzed via Statistical Package for Social Sciences version 29.0 (SPSS®) statistics software. Sample size, and consequently power, was not calculated given the study design and scarcity of data comparing CG to CKD-EPI estimates of kidney function in this patient population. Demographic and baseline data was analyzed via descriptive statistics. Nominal data were presented as percentage, normally distributed date and mean \pm standard deviation (SD) and non-normally data as median [25%–75% interquartile range, IQR]. Discordance, defined as the percentage of time at which there is at least one discrepancy in kidney dosing for a medication using CG creatinine clearance versus CKD-EPI eGFRcr-cys equations, was analyzed via Wilcoxon matched pair signed ranked sum. eGFR calculations were normalized for patients' body surface area for comparison to CG.

TABLE 1 Select kidney-adjusted medications, dosing breakpoints, and discordance rates.

Medication	Dosing Breakpoints (mL/min)				Discordance Rate (% , number of incidences of dose discordance/number of patients receiving medication)
Acyclovir	>50	25–50	10–24	<10	14.0%; 3/13
Aminoglycosides	≥ 60	40–59	20–39	<20	0.0%; 0/2
Ampicillin/sulbactam	≥ 50	30–49	15–29	<15	9.1%; 1/11
Cefepime	≥ 60	30–59	<30		40.6%; 52/128
Ceftaroline	≥ 50	30–49	15–29	<15	66.7%; 2/3
Ceftazidime/Avibactam	≥ 50	30–49	15–29	5–14	100%; 1/1
Daptomycin	≥ 30	<30			34.8%; 8/23
Enoxaparin	≥ 30	<30			4.05%; 3/74
Lacosamide	≥ 30	<30			14.3%; 1/7
Levetiracetam	>80	50–80	30–49	<30	35.1%; 13/37
Levofloxacin	>50	20–50	<20		33.3%; 2/6
Meropenem	≥ 50	26–49	10–25	<10	45.0%; 9/20
Piperacillin/tazobactam	≥ 20	<20			11.6%; 5/43
Rivaroxaban (atrial fibrillation)	>50	15–50	<15		50%; 1/2
Sotalol (atrial fibrillation)	≥ 60	40–59	<40		0.0%; 0/1
Sulfamethoxazole/trimethoprim	≥ 30	15–29	<15		28.6%; 4/14
Valganciclovir	≥ 60	40–59	<40–20	<20	16.7%; 1/6
Vancomycin	≥ 60	30–59	<30		38.3%; 46/120

3 | RESULTS

A total of 358 patients had a cysC and SCr collected during the study period. A total of 126 patients were excluded, leaving 232 patients included in the study. Reasons for exclusion were non-ICU patients when cysC was collected (82); received kidney replacement therapy within 72 h of cysC collection (20); history of kidney transplant (17); and multiple exclusion (7). Patients were an average age of 58.7 \pm 14.9 years old; 53.02% were female. Patients had the following relevant past medical histories: currently smoking (44), thyroid disease (43), current cancer (32), chronic kidney disease (27), paralysis (26), cirrhosis (16), and current corticosteroid use prior to admission of greater than or equal to prednisone 40 mg or equivalent (22). Additional demographic information is included in Table 2. The mean height and median weight of the study population were 168.4 \pm 11.5 cm and 78.1 IQR [61.3–103.2] kg, respectively. Median body surface area (BSA) was 1.89 m² IQR [1.65–2.2] and median body mass index (BMI) was 27.3 kg/m² IQR [22–35.3].

Kidney function is described in Table 3. Median markers of kidney function were as follows: SCr 0.94 mg/dL IQR [0.57–1.58] and cysC 1.92 mg/L IQR [1.27–2.77]. There was a lower estimate of kidney function using the 2021 CKD-EPI eGFRcr-cys equation (normalized for BSA) compared to CG: 53.9 mL/min IQR [30.9–80.7] versus 68.5 mL/min IQR [45.3–111.5], respectively, $p < 0.001$. There was also a lower estimated of kidney function using 2012 CKD-EPI eGFRcys compared to 2021 CKD-EPI eGFRcr-cys (normalized for BSA): 36.6 mL/min IQR [20.8–55.3] versus 53.9 mL/min IQR [30.9–80.7], respectively, $p < 0.001$.

Overall discordance rate based on drug dosing between 2021 CKD-EPI eGFRcr-cys and CG was determined to be 32.3% (75/232). Similarly, rate of discordance between 2021 CKD-EPI eGFRcr-cys and 2012 CKD-EPI eGFRcys was 31.3% (72/232). Figure 1 depicts a plot of kidney function estimates by CG versus CKD-EPI eGFRcr-cys. Comparing CG to CKD-EPI eGFRcr-cys, the rate at which kidney function estimates differed by 30% or more was 52.2% (121/232 patients). The rate at which kidney function estimates differed by an absolute difference of 15 mL/min or more was 58.2% (135/232 patients). Comparing CKD-EPI eGFRcr-cys to CKD-EPI eGFRcys the rate at which the kidney function estimates differed by 30% or more was 47.8% (111/232), and 51.3% (119/232) had an absolute difference of greater than 15 mL/min. Table 3 shows the primary objective comparing CG to CKD-EPI eGFRcr-cys for discordance rates for specific medications. The top five drugs by volume and discordance rates based on drug dosing were as follows: cefepime 40.6% (52/128), vancomycin 38.3% (46/120), levetiracetam 35.1% (13/37), piperacillin/tazobactam 11.6% (5/43), and enoxaparin 4.05% (3/74). and Though medications known to influence SCr were recorded, there were no incidences of these medications noted in the study population.

4 | DISCUSSION

This study revealed clinically significant discordance in drug dosing between the creatinine-based estimate of kidney function and the

TABLE 2 Patient demographics (N=232).

Age (mean \pm SD, years)	58.7 \pm 14.9
<40 years	24 (10.3%)
40–65 years	124 (53.4%)
>65 years	84 (36.2%)
Sex n (%)	
Male	109 (46.98%)
Female	123 (53.02%)
Race n (%)	
White	182 (78.45%)
Black/African American	34 (14.66%)
Asian	2 (0.86%)
Native Hawaiian/Other Pacific Islander	1 (0.43%)
Unknown/Not Reported	13 (5.6%)
Ethnicity n (%)	
Not Hispanic or Latino	224 (96.55%)
Hispanic or Latino	5 (2.16%)
Unknown	3 (1.29%)
Past Medical History	
Diabetes	73 (31.47%)
Currently Smoking	44 (18.99%)
Thyroid Disease	43 (18.53%)
Current Cancer	32 (13.79%)
Chronic Kidney Disease	27 (11.64%)
Cirrhosis	16 (6.90%)
Paralysis	26 (11.21%)
Corticosteroid Use	22 (9.48%)
Clinical Characteristics	
Height (mean \pm SD, cm)	168.4 \pm 11.5
Weight (median [IQR], kg)	78.1 [61.3–103.2]
Body Surface Area (median [IQR], m ²)	1.89 [1.65–2.2]
Body Mass Index (median [IQR], kg/m ²)	27.3 [22–35.3]
Body Mass Index category	
<20	37 (15.9%)
20–<25	58 (25.0%)
25–<30	48 (20.7%)
>30	89 (38.4%)
SOFA Score (median [IQR])	6 [3–8]
Albumin (mean \pm SD, g/dL)	2.8 \pm 0.6
Hospitalization Details	
Intensive Care Unit Type n (%)	
Medical	145 (62.5%)
Surgical	54 (23.28%)
Neurocritical	20 (8.62%)
Oncology Medical	10 (4.31%)
Cardiac	3 (1.29%)
Length of Stay (median [IQR], days)	
Intensive Care Unit	13 [7–26]
Hospital	23 [13.3–36.0]

Abbreviations: IQR, interquartile range, SD, standard deviation, SOFA, Sequential Organ Failure Assessment.

SCr/cysC-based estimate of kidney function in critically ill patients. The overall discordance rate defined by drug dosing between CG and CKD-EPI eGFRcr-cys was determined to be 32.3%. As depicted in Figure 1, patients with poorer kidney function appeared to have less discordance compared to patients with intact kidney function. This may suggest that patients with normal or slightly diminished kidney function may benefit more from using a cysC-based estimate of kidney function as another piece of clinical data (alongside urine output and blood urea nitrogen, for example) to base medication dosing compared to patients with poor kidney function. These trends suggest that the limitations of SCr and CG have less of an effect on drug dosing in patients with lower clearances.

Discordance rate in this study was based on medication dosing, specifically. Other studies have suggested alternative definitions of discordance rate, such as “the rate at which eGFRcr-cys was more than 30% lower than eGFRcr.”³¹ Based on this definition, investigators reported a discordance rate of 29% (543/1869 patients), which is lower than this study's finding of a rate of 52.2% (121/232 patients).³¹ Another study focused on patients with cancer admitted to the hospital, whereas our study only included 32 (13.79%) patients with cancer who were admitted to the ICU.

TABLE 3 Kidney function.

Serum creatinine (median [IQR], mg/dL)	0.94 [0.57–1.58]
Cystatin C (median [IQR], mg/L)	1.92 [1.27–2.77]
Cockcroft-Gault (median [IQR], mL/min)	68.5 [45.3–111.5]
CKD-EPI eGFRcr-cys (median [IQR], mL/min)	53.9 [30.9–80.7]
CKD-EPI eGFRcys (median [IQR], mL/min)	36.6 [20.8–55.3]
Discordance Rate by drug dosing	32.3% (75/232)
Discordance Rate by 30% or more difference	52.2% (121/232)
Discordance Rate by absolute difference of 15 mL/min or more	58.2% (135/232)

Abbreviations: CKD-EPI eGFRcr-cys, Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate by serum creatinine and cystatin C; IQR, interquartile range.

Discrepancies in these rates may be explained by the variability in patient populations. It has been proposed that active cancer may increase baseline levels of cysC and patients admitted to the ICU may suffer from ICU-associated weakness which may decrease SCr.^{38,39}

Other studies have considered an “intraindividual difference” in eGFRcr versus eGFRcr-cys.³² Assuming an absolute difference of 15 mL/min based on these findings, but normalized for body surface area, our study's rate of discordance by this definition was 58.2% (135/232 patients).³² Although this discordance rate is much higher than our drug dosing definition, it remains unclear which definition has the highest clinical utility. Variability in results between definitions may be explained by differences in patient population. In the previous study analyzing intraindividual differences, only 47% of patients were in the ICU, including 31% in a medical ICU and 16% in a surgical ICU. It is unknown if this included neurocritical and cardiac ICU patients or not. Additionally, our study excluded patients outside of the ICU and those receiving kidney replacement therapy at the time of cysC lab draw, while the other study included those patients.

Drug-specific discordance rates suggest when a cystatin-C-based estimate of kidney function might be useful for drug dosing. Medications with lower and one dosing breakpoint, like enoxaparin (30 mL/min) or piperacillin/tazobactam (20 mL/min), demonstrated lower rates of discordance, 4.05%, and 11.6%, respectively, when compared to medications with more and higher dosing breakpoints. The lower rates of discordance for lower dosing breakpoint medications are consistent with the discordance rate trend in Figure 1. Medications with higher dosing breakpoints, like cefepime (60 mL/min and 30 mL/min) and vancomycin (60 mL/min and 30 mL/min) demonstrated higher rates of discordance (40.6% and 38.3%, respectively). Thus, cysC may be useful in drug dosing for medications with higher dosing breakpoints. Beta-lactam levels at our institution are a “send-out” lab, which takes several days to result, thus limiting the clinical utility of these levels in ICU patients with dynamic kidney function. CysC, an in-house lab

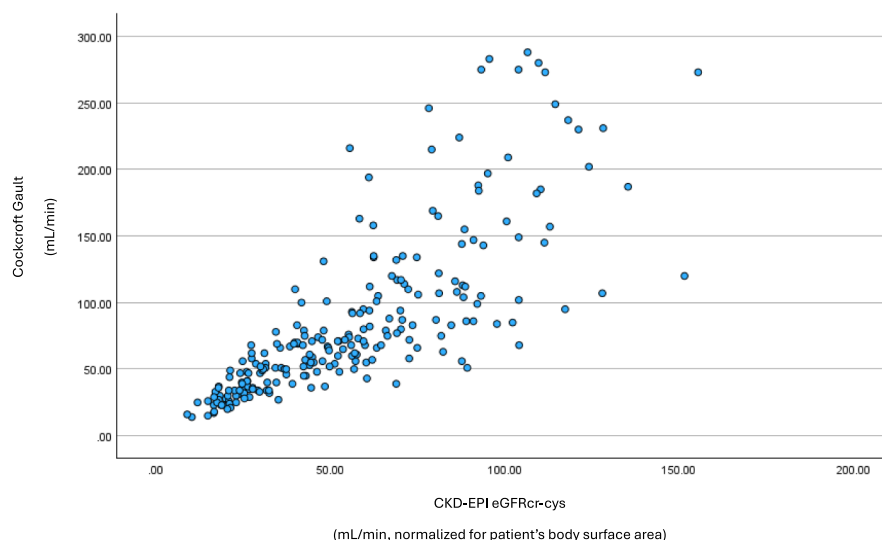


FIGURE 1 Kidney function estimates by Cockcroft Gault versus CKD-EPI eGFRcr-cys.

at our institution with roughly a 3-hour turnaround time, maybe more practical to inform drug dosing. There is evolving evidence to support that utilizing cysC-based estimates of kidney function to inform cefepime dosing results in greater accuracy and precision in dosing.²⁹ With regard to vancomycin, it has been proposed that cysC is useful in determining the initial dose and in therapeutic drug monitoring.^{22,23,40}

There are certain limitations inherent to this research given its retrospective, single-center design. Based on design, clinical outcomes were not assessed. For practicality, a list of kidney-adjusted medications was determined a priori, so it is reasonable to consider that incidences of concordance/discordance were not captured in this study. The study population was defined as patients having a cysC order, which was left to provider discretion. The study period took place prior to any formal provider education on cysC. Cardiac ICU patients were under-represented which is a reflection of local patterns of cysC use and an inherent limitation of retrospective research. Compared to datasets used to validate CKD-EPI equations, there was a higher percentage of patients with a body mass index less than 20 kg/m² in our data which may have affected the results.¹⁴ We also did not collect if a patient was a kidney donor candidate. Including all ICU patients, except those on kidney replacement therapy, resulted in lower SOFA scores than if these patients were included. Since drug dosing while on renal replacement therapy is not based on creatine or cystatin-C based estimates of kidney function, there was no clinical utility in including these patients in this study. Excluding those on kidney replacement therapy resulted in diversity of kidney function, which increased external validity as patients with decreased kidney function and intact kidney function were represented in this study. However, patients with poor kidney function were better represented in the study population, and patients with augmented kidney clearance were not well represented. The role of cysC in estimating kidney function in the setting of augmented kidney clearance should be investigated further. The timing of cysC relative to each patient's hospitalization was not recorded so we cannot comment on the possible utility of cysC in patients with prolonged hospitalizations.

The results of this study support further inquiry into describing risk factors for discordance, comparing CKD-EPI eGFRcr-cys to other markers of kidney function like urine creatinine, and identifying clinical circumstances where one estimate of kidney function is preferred over the other.

5 | CONCLUSION

Clinically significant discordance exists between SCr and SCr/CysC-based estimates of kidney function. This study established a discordance rate, as defined by drug dosing, of 32.3% in adult patients admitted to the ICU. Additional studies should identify risk factors for discordance and further compare CKD-EPI eGFRcr-cys to other estimates of kidney function.

ACKNOWLEDGMENTS

The authors would like to acknowledge Sarah Okefor for her help with data collection. Dr. Williams would also like to acknowledge her cohort from the ACCP Foundation's Mentored Research Investigator Training (MeRIT) program for their continued support of her research endeavors.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

- Kashani K, Rosner MH, Ostermann M. Creatinine: from physiology to clinical application. *Eur J Intern Med*. 2020;72:9-14. doi:[10.1016/j.ejim.2019.10.025](https://doi.org/10.1016/j.ejim.2019.10.025)
- Sharma A, Mucino MJ, Ronco C. Renal functional reserve and renal recovery after acute kidney injury. *Nephron Clin Pract*. 2014;127(1-4):94-100. doi:[10.1159/000363721](https://doi.org/10.1159/000363721)
- Levey AS, Inker LA. Assessment of glomerular filtration rate in health and disease: a state of the art review. *Clin Pharmacol Ther*. 2017;102(3):405-419. doi:[10.1002/cpt.729](https://doi.org/10.1002/cpt.729)
- Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem*. 1992;38(10):1933-1953. doi:[10.1093/clinchem/38.10.1933](https://doi.org/10.1093/clinchem/38.10.1933)
- Doi K, Yuen PST, Eisner C, et al. Reduced production of creatinine limits its use as marker of kidney injury in sepsis. *J Am Soc Nephrol*. 2009;20(6):1217-1221. doi:[10.1681/ASN.2008060617](https://doi.org/10.1681/ASN.2008060617)
- Musso CG, Michelangelo H, Vilas M, et al. Creatinine reabsorption by the aged kidney. *Int Urol Nephrol*. 2009;41(3):727-731. doi:[10.1007/s11255-008-9508-7](https://doi.org/10.1007/s11255-008-9508-7)
- Khawaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-c184. doi:[10.1159/000339789](https://doi.org/10.1159/000339789)
- Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the second international consensus conference of the acute dialysis quality initiative (ADQI) group. *Crit Care*. 2004;8(4):R204-R212. doi:[10.1186/cc2872](https://doi.org/10.1186/cc2872)
- Mehta RL, Kellum JA, Shah SV, et al. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):1-8. doi:[10.1186/cc5713](https://doi.org/10.1186/cc5713)
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1-150.
- Cockcroft DW, Gault H. Prediction of creatinine clearance from serum creatinine. *Nephron*. 2008;16(1):31-41. doi:[10.1159/000180580](https://doi.org/10.1159/000180580)
- Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med*. 1999;130(6):461-470. doi:[10.7326/0003-4819-130-6-199903160-00002](https://doi.org/10.7326/0003-4819-130-6-199903160-00002)
- Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612. doi:[10.7326/0003-4819-150-9-200905050-00006](https://doi.org/10.7326/0003-4819-150-9-200905050-00006)

14. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737-1749. doi:[10.1056/NEJMoa2102953](https://doi.org/10.1056/NEJMoa2102953)
15. Shlipak MG, Mattes MD, Peralta CA. Update on cystatin C: incorporation into clinical practice. *Am J Kidney Dis*. 2013;62(3):595-603. doi:[10.1053/j.ajkd.2013.03.027](https://doi.org/10.1053/j.ajkd.2013.03.027)
16. Barreto EF, Rule AD, Voils SA, Kane-Gill SL. Innovative use of novel biomarkers to improve the safety of renally eliminated and nephrotoxic medications. *Pharmacotherapy*. 2018;38(8):794-803. doi:[10.1002/phar.2149](https://doi.org/10.1002/phar.2149)
17. Stevens LA, Schmid CH, Greene T, et al. Factors other than glomerular filtration rate affect serum cystatin C levels. *Kidney Int*. 2009;75(6):652-660. doi:[10.1038/ki.2008.638](https://doi.org/10.1038/ki.2008.638)
18. Ye Y, Gai X, Xie H, Jiao L, Zhang S. Impact of thyroid function on serum cystatin C and estimated glomerular filtration rate: a cross-sectional study. *Endocr Pract*. 2013;19(3):397-403. doi:[10.4158/EP12282.OR](https://doi.org/10.4158/EP12282.OR)
19. Knight EL, Verhave JC, Spiegelman D, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. *Kidney Int*. 2004;65(4):1416-1421. doi:[10.1111/j.1523-1755.2004.00517.x](https://doi.org/10.1111/j.1523-1755.2004.00517.x)
20. Luc G, Bard JM, Lesueur C, et al. Plasma cystatin-C and development of coronary heart disease: the PRIME study. *Atherosclerosis*. 2006;185(2):375-380. doi:[10.1016/j.atherosclerosis.2005.06.017](https://doi.org/10.1016/j.atherosclerosis.2005.06.017)
21. Chen DC, Potok OA, Rifkin D, Estrella MM. Advantages, limitations, and clinical considerations in using cystatin C to estimate GFR. *Kidney360*. 2022;3(10):1807. doi:[10.34067/KID.0003202022](https://doi.org/10.34067/KID.0003202022)
22. Tanaka A, Suemaru K, Otsuka T, et al. Estimation of the initial dose setting of vancomycin therapy with use of cystatin C as a new marker of renal function. *Ther Drug Monit*. 2007;29(2):261-264. doi:[10.1097/FTD.0b013e31803bcfd2](https://doi.org/10.1097/FTD.0b013e31803bcfd2)
23. Frazee E, Rule AD, Lieske JC, et al. Cystatin C-guided vancomycin dosing in critically ill patients: a quality improvement project. *Am J Kidney Dis*. 2017;69(5):658-666. doi:[10.1053/j.ajkd.2016.11.016](https://doi.org/10.1053/j.ajkd.2016.11.016)
24. Iversen E, Bodilsen AC, Klausen HH, et al. Kidney function estimates using cystatin C versus creatinine: impact on medication prescribing in acutely hospitalized elderly patients. *Basic Clin Pharmacol Toxicol*. 2019;124(4):466-478. doi:[10.1111/bcpt.13156](https://doi.org/10.1111/bcpt.13156)
25. Sharma A, Sahasrabudhe V, Musib L, Zhang S, Younis I, Kanodia J. Time to rethink the current paradigm for assessing kidney function in drug development and beyond. *Clin Pharmacol Ther*. 2022;112(5):946-958. doi:[10.1002/cpt.2489](https://doi.org/10.1002/cpt.2489)
26. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN task force on reassessing the inclusion of race in diagnosing kidney disease. *Am J Kidney Dis*. 2022;79(2):268-288. doi:[10.1053/j.ajkd.2021.08.003](https://doi.org/10.1053/j.ajkd.2021.08.003)
27. Inker LA, Schmid CH, Tighiouart H, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012;367(1):20-29. doi:[10.1056/NEJMoa1114248](https://doi.org/10.1056/NEJMoa1114248)
28. Markos JR, Schaepe KS, Teaford HR, et al. Clinician perspectives on inpatient cystatin C utilization: a qualitative case study at Mayo Clinic. *PLoS One*. 2020;15(12):e0243618. doi:[10.1371/journal.pone.0243618](https://doi.org/10.1371/journal.pone.0243618)
29. Barreto EF, Rule AD, Murad MH, et al. Prediction of the renal elimination of drugs with cystatin C vs creatinine: a systematic review. *Mayo Clin Proc*. 2019;94(3):500-514. doi:[10.1016/j.mayocp.2018.08.002](https://doi.org/10.1016/j.mayocp.2018.08.002)
30. Brown AR, Lavelle RI, Gerlach AT. Discordance of renal drug dosing using estimated creatinine clearance and measured urine creatinine clearance in hospitalized adults: a retrospective cohort study. *Int J Crit Illn Inj Sci*. 2020;10(Suppl 1):1-5. doi:[10.4103/IJCIIS.IJCIIS_61_19](https://doi.org/10.4103/IJCIIS.IJCIIS_61_19)
31. Hanna P, Wang Q, Strohhenn I, et al. Medication-related adverse events and Discordancies in cystatin C-based vs serum creatinine-based estimated glomerular filtration rate in patients with cancer. *JAMA Netw Open*. 2023;6(7):e2321715. doi:[10.1001/jamanetworkopen.2023.21715](https://doi.org/10.1001/jamanetworkopen.2023.21715)
32. Teaford HR, Rule AD, Mara KC, et al. Patterns of cystatin C uptake and use across and within hospitals. *Mayo Clin Proc*. 2020;95(8):1649-1659. doi:[10.1016/j.mayocp.2020.03.030](https://doi.org/10.1016/j.mayocp.2020.03.030)
33. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573-577. doi:[10.7326/0003-4819-147-8-200710160-00010](https://doi.org/10.7326/0003-4819-147-8-200710160-00010)
34. Bauman JL, Jackevicius C, Zillich AJ, Parker RB, Phillips BB. On the methodology of retrospective chart reviews. *JACCP J Am Coll Clin Pharm*. 2019;2(1):6-7. doi:[10.1002/jac5.1064](https://doi.org/10.1002/jac5.1064)
35. Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med*. 1998;26(11):1793-1800. doi:[10.1097/00003246-199811000-00016](https://doi.org/10.1097/00003246-199811000-00016)
36. Pai MP, Paloucek FP. The origin of the "ideal" body weight equations. *Ann Pharmacother*. 2000;34(9):1066-1069. doi:[10.1345/aph.19381](https://doi.org/10.1345/aph.19381)
37. Bauer LA. (Eds.), *Applied Clinical Pharmacokinetics*, 3e. McGraw-Hill Medical; 2015. Accessed October 26, 2023. accesspharmacy.mhmedical.com/content.aspx?aid=1106302597
38. Jung C, Kim HW, Han SH, Yoo T, Kang S, Park JT. Creatinine-cystatin C ratio and mortality in cancer patients: a retrospective cohort study. *J Cachexia Sarcopenia Muscle*. 2022;13(4):2064-2072. doi:[10.1002/jcsm.13006](https://doi.org/10.1002/jcsm.13006)
39. Teixeira JP, Mayer KP, Griffin BR, et al. Intensive care unit-acquired weakness in patients with acute kidney injury: a contemporary review. *Am J Kidney Dis*. 2023;81(3):336-351. doi:[10.1053/j.ajkd.2022.08.028](https://doi.org/10.1053/j.ajkd.2022.08.028)
40. DeCarolis DD, Thorson JG, Marraffa RA, Clairmont MA, Kuskowski MA. Comparison of equations with estimate renal function to predict serum vancomycin concentration in patients with spinal cord injury—does the use of cystatin C improve accuracy? *Ther Drug Monit*. 2014;36(5):632. doi:[10.1097/FTD.0000000000000065](https://doi.org/10.1097/FTD.0000000000000065)

How to cite this article: Williams VL, Gerlach AT. Establishing discordance rate of estimated glomerular filtration rate between serum creatinine-based calculations and cystatin-C-based calculations in critically ill patients. *Pharmacotherapy*. 2025;45:161-168. doi:[10.1002/phar.70000](https://doi.org/10.1002/phar.70000)

APPENDIX A

Equations used to calculate estimations of kidney function

Equations used to calculate estimations of kidney function		
Equation	Formula	Legend
Cockcroft-Gault Formula for creatinine clearance (CrCL) ¹¹	$\text{CrCL (mL/min)} = \{[(140 - \text{age}) \times \text{weight}] / (72 \times \text{SCr})\} \times 0.85$ (if female)	Age (years) Weight (kg)* SCr (mg/dL)
Estimated Glomerular Filtration Rate by Creatinine (eGFRcr) ¹⁴	$\text{eGFRcr (mL/min/1.73m}^2\text{)} = 142 \times \min(\text{SCr}/\kappa, 1)^\alpha \times \max(\text{SCr}/\kappa, 1)^{-1.200} \times 0.9938^{\text{Age}} \times 1.012$ [if female]	SCr (mg/dL), age (years) $\kappa = 0.7$ (females) or 0.9 (males) $\alpha = -0.241$ (female) or -0.302 (male) min(SCr/ κ , 1) is the minimum of SCr/ κ or 1.0 max(SCr/ κ , 1) is the maximum of SCr/ κ or 1.0
Estimated Glomerular Filtration Rate by Creatinine and Cystatin C (eGFRcr-cys) ¹⁴	$\text{eGFRcr-cys (mL/min/1.73m}^2\text{)} = 135 \times \min(\text{SCr}/\kappa, 1)^\alpha \times \max(\text{SCr}/\kappa, 1)^{-0.544} \times \min(\text{cysC}/0.8, 1)^{-0.323} \times \max(\text{cysC}/0.8, 1)^{-0.778} \times 0.9961^{\text{Age}} \times 0.963$ [if female]	SCr (mg/dL), cysC (mg/L), age (years) $\kappa = 0.7$ (females) or 0.9 (males) $\alpha = -0.219$ (female) or -0.144 (male) min(SCr/ κ , 1) is the minimum of SCr/ κ or 1.0 max(SCr/ κ , 1) is the maximum of SCr/ κ or 1.0 min(cysC/0.8, 1) is the minimum of CysC/0.8 or 1.0 max(cysC/0.8, 1) is the maximum of cysC/0.8 or 1.0
Converting from eGFR in mL/min/1.73m ² to mL/min	$\text{eGFR (mL/min/1.73m}^2\text{)} \times (\text{BSA}/1.73\text{m}^2) = \text{mL/min}$	BSA = body surface area (m ²) Weight (kg) Height (cm)
Equations Used to Calculate Weight		
Ideal Body Weight for Males ³⁶	$\text{IBW for males (kg)} = 50 + (2.3 \times \text{height} - 60)$	Weight (kg) Height (inches)
Ideal Body Weight for Females ³⁶	$\text{IBW for females (kg)} = 45.5 + (2.3 \times \text{height} - 60)$	Weight (kg) Height (inches)
Adjusted Body Weight (AdjBW) ³⁷	$\text{adjBW (kg)} = [(\text{actual weight} - \text{IBW}) \times 0.4] + \text{IBW}$	Weight (kg)

Abbreviations: cysC, cystatin C; SCr, serum creatinine.

*Use actual weight if actual weight < ideal body weight (IBW); use adjusted body weight (adjBW) if actual body weight is >120% IBW.