Estimation of glomerular filtration rate: an evaluation of the use of different equations in the clinical context of older patients

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Abstract

Objective: To verify the level of agreement between the Chronic Kidney Disease Epidemiology Collaboration 2021 (CKD-EPI 2021) and Cockcroft-Gault (CG) equations regarding medication dose adjustment for renal function in older patients, and to analyze whether these estimates imply changes in clinical management. *Methods:* Observational study with a longitudinal and prospective design, including individuals aged 60 years or older, followed during hospitalization. Agreement between dose adjustments based on CKD-EPI 2021 and CG was assessed using the Kappa (κ) test. *Results:* A total of 54 medical records were analyzed, of which the majority were male (53.7%) and younger than 73 years (57.4%). The level of agreement ranged from very good to excellent for atenolol, spironolactone, morphine, metformin, and escitalopram. However, medications such as meropenem, domperidone, piperacillin tazobactam, vancomycin, metoclopramide, regular insulin, and enoxaparin showed moderate to low agreement. In addition, the results indicate that a change in clinical management would occur in 40.40% of the medications that did not present a good level of agreement when one equation or the other was selected. *Conclusion:* There is potential interchangeability between CKD-EPI 2021 and CG for medications that demonstrated a good level of agreement. However, caution is warranted when selecting the equation for medications not included in this group, as the choice may alter clinical management and affect therapeutic effectiveness or increase the risk of toxicity.

Keywords: Kidney Function Tests. Chronic Kidney Disease. Drug Utilization. Elderly.

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INTRODUCTION

The demographics of aging are changing rapidly as a result of increased life expectancy. It is estimated that by 2030 approximately 12% of the world population will consist of individuals aged 60 years or older. In Brazil, data from the 2022 census conducted by the Brazilian Institute of Geography and Statistics (IBGE) estimated that the population aged 60 years or older reached 32,113,490 individuals (15.6%), representing an increase of 56.0% compared with 2010[1,2].

Aging can be described as a process of irreversible deterioration of physiological activities related to survival and fertility, resulting in impaired tissue and organ function over the life course. This process is one of the most relevant risk factors for the development of a large proportion of chronic diseases, as demonstrated in major population-based studies[3,4].

Systemic changes resulting from prolonged human lifespan range from alterations in body composition to bioenergetic imbalance and neurodegeneration. These changes may lead to reductions in resting cardiac output, maximal respiratory capacity, nerve conduction velocity, and glomerular filtration rate (GFR), which are among the most frequently observed alterations[3,4].

In this context, nephrosenescence refers to the progressive decline in renal function associated with aging, which occurs even in healthy individuals. As life advances, the likelihood of developing chronic kidney disease (CKD) increases. For patients in the hospital setting, estimating renal function is essential, whether for diagnostic purposes and/or CKD management, or for dose adjustment of medications excreted via the renal route[5-7].

In clinical practice, renal function is estimated using equations based on serum creatinine (sCr). The first equation developed was the Cockcroft-Gault equation, in 1976, which estimates creatinine clearance (CrCl) rather than GFR. This is because both glomerular filtration and tubular secretion contribute to creatinine clearance. Tubular secretion of creatinine may account for up to 50% of its total clearance, particularly in the presence of impaired renal function and comorbidities such as obesity. Consequently, GFR may be overestimated when calculated using this equation. The Cockcroft-Gault formula estimates renal clearance based on body weight, age, and sex[5, 8-10].

In 2009, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) research group in the United States conducted a study aimed at developing and validating a new sCr-based estimation equation. The first version of this equation considered, in addition to sCr, factors such as sex, age, and race. Adopted by the Kidney Disease Improving Global Outcomes (KDIGO) initiative since 2012, it has become the most widely used method worldwide. In 2021, the CKD-EPI formula was updated following a publication by the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN), which removed race-based modifiers, as they are not biological parameters[10-12].

Within this framework, the predictive performance of drug pharmacokinetics may differ depending on whether the estimated glomerular filtration rate (eGFR) or estimated CrCl is calculated using an equation different from that employed in the original pharmacokinetic study. In both clinical pharmacology and drug development, the Cockcroft-Gault (CG) equation has served as the reference standard for decades. Therefore, to consider equivalence between estimation methods, the same medication must be evaluated using different formulas to calculate GFR and demonstrate similar performance within the same previously established population pharmacokinetic model[5].

The objective of this study was to assess the level of agreement between the CKD-EPI 2021 and Cockcroft-Gault equations, based on estimated glomerular filtration rate (eGFR) and estimated creatinine clearance (CrCl), respectively, regarding medication dose adjustment for renal function in older patients, and to determine whether these estimates imply changes in clinical management.

METHODS

This was an observational study with a longitudinal and prospective design involving older adults followed

during hospitalization at Hospital das Clínicas of the Federal University of Pernambuco (HC-UFPE), Brazil. Data were collected through review of patients' medical records using the *Aplicativo de Gestão para Hospitais Universitários (AGHUx)*, the electronic health record system used in Brazilian federal university hospitals, between August and November 2023.The convenience sample comprised older adults of either sex, aged 60 years or older, who were hospitalized during the study period and were using at least one medication listed in their prescription.

Exclusion criteria were as follows: absence of at least one recent serum creatinine (sCr) test result in the medical record, defined as a test performed within 72 hours before or after hospital admission; electronic prescriptions containing only medications prescribed as needed or at the physician's discretion; and absence of recorded body weight during hospitalization, as this information is essential for calculating estimated glomerular filtration rate (eGFR). Patients admitted directly to the Intensive Care Unit (ICU) or to the surgical block immediately after hospital admission were excluded. Patients initially admitted to a general ward and subsequently transferred to the ICU or surgical block were followed only until the time of transfer, as clinical instability and rapid fluctuations in clinical status in these settings could increase sample heterogeneity.

The following sociodemographic, clinical, and laboratory variables were recorded: sex, age in years, educational level, body weight in kilograms (kg), height in meters (m), body mass index (BMI), calculated as weight divided by height squared (kg/m^2), comorbidities, medication-related information (name, dose, route of administration, and total number of prescribed medications), and sCr (mg/dL), used to calculate eGFR and estimated creatinine clearance (CrCl).

After data collection, eGFR and estimated CrCl were calculated for all included patients using the CKD-EPI 2021 and CG equations, respectively, as available electronically on the National Kidney Foundation® platform. Prescriptions were analyzed regarding indication, dose, and dosing regimen, as well as evaluated in relation to renal function impairment. Medication-related information was obtained from the UpToDate® database, institutional protocols, and manufacturer prescribing information.

Data analysis was conducted using descriptive and inferential statistics. Qualitative variables were expressed as frequencies and proportions, whereas quantitative variables were presented as mean, median, range, and standard deviation. Agreement between dose adjustments based on CKD-EPI 2021 and Cockcroft-Gault was assessed using the Kappa (κ) test. This test, proposed by Cohen in 1960, uses the Kappa agreement coefficient. A κ value equal to 1 indicates perfect agreement between the evaluated methods, whereas values closer to zero indicate agreement attributable to chance. In this study, the following thresholds were adopted: values above 0.80 excellent, between 0.79 and 0.60 very good, between 0.59 and 0.40 moderate, and below 0.39 low[13]. Analyses were performed using a significance level of 0.05.

The study was submitted to and approved by the Research Ethics Committee of the Hospital das Clínicas of Pernambuco, under Certificate of Presentation for Ethical Consideration (CAAE) No. 69009823.4.0000.8807 and approval opinion No. 6045723, in accordance with Resolution No. 466/2012 of the Brazilian National Health Council (CNS), with a waiver of written Informed Consent Form (ICF). Ethical principles were observed throughout the study, and participant confidentiality and anonymity were strictly maintained.

HC-UFPE is managed by the *Empresa Brasileira de Serviços Hospitalares* (Ebserh), a federal public company that supports teaching, research, and extension and outreach activities at affiliated federal universities. The hospital is a medium and high complexity referral center for the Brazilian Unified Health System (SUS) in the state of Pernambuco and provides outpatient and inpatient care, including services in nephrology. The equations evaluated in this study were already used in routine hospital practice; however, there was no standardized guidance regarding which calculator should be used or the specific contexts for selecting one equation over the other.

DATA AVAILABILITY

The entire dataset supporting the results of this study is available upon request to the corresponding author.

RESULTS

During the study period, data were obtained from 88 patient medical records, of which 34 were excluded. Among these, 30 (88.2%) did not have creatinine results within 72 hours before or after hospital admission; 2 (5.9%) had prescriptions containing only medications prescribed as needed; 1 (2.9%) underwent surgery almost immediately after admission; and 1 (2.9%) did not have body weight recorded in the medical record by any professional category. Consequently, 54 medical records were analyzed, and their sociodemographic and clinical characteristics are described in Table 1.

The most prevalent comorbidities were systemic arterial hypertension and diabetes. CKD was present in a small proportion of the study population. Regarding BMI, 19 patients (35.2%) had values at the extremes of the classification, either underweight or with some degree of obesity. With respect to medications, a total of 504 drugs included in the institution's standardized formulary were prescribed (median = 8, mean = 9.3, standard deviation = ±5.3). Of these, 130 (25.8%) had recommendations for dose adjustment based on renal function.

The analysis of the level of agreement between the CKD-EPI 2021 and Cockcroft-Gault equations regarding the need for medication dose adjustment is presented in Table 2.

Table 3 presents the percentage of dose adjustment recommendations according to both equations for medications that showed moderate to low levels of agreement. Considering eGFR, 18 patients required dose adjustment for at least one medication. Among these patients, a total of 141 dose adjustments would have been required, taking into account the days on which the medications remained prescribed. Furthermore, considering this latter aspect, 57 adjustments (40.40%) would have resulted in different clinical management decisions depending on whether one equation or the other was used.

Table 1. Demographic, social, and clinical characteristics of the older adults included in the study (N = 54). Recife, Pernambuco, Brazil, 2023.

Characteristics	Values
Male sex – n (%)	29.0 (53.7)
Age (years) – m (± SD)	72.5 (8.8)
Age group – n (%)	
60-73	31.0 (57.4)
73 ≥	23.0 (42.6)
Body weight (kg) – m (± SD)	67.2 (17.9)
Height in meters (m) – m (± SD)	1.6 (0.1)
BMI, kg/m² – n (%)	
≤ 18.5 – Underweight	5.0 (9.3)
18.6–24.9 – Normal weight	19.0 (35.2)
25.0–29.9 – Overweight	16.0 (29.6)
30.0–34.9 – Obesity class I	10.0 (18.5)
35.0–39.9 – Obesity class II	2.0 (3.7)
≥ 40.0 – Obesity class III	2.0 (3.7)

to be continued

Continuation of Table 1

Characteristics	Values
Educational level – n (%)	
No formal education	21.0 (38.9)
Incomplete elementary education	14.0 (25.9)
Complete elementary education	9.0 (16.7)
Incomplete high school	1.0 (1.9)
Complete high school	7.0 (13.0)
Incomplete higher education	1.0 (1.9)
Complete higher education	1.0 (1.9)
Non-smokers and non-alcohol users – n (%)	50.0 (92.6)
Comorbidities* – n (%)	
Systemic arterial hypertension	46.0 (26.4)
Diabetes	28.0 (16.1)
Oncological diseases	16.0 (9.2)
Cardiac system diseases	15.0 (8.6)
Vascular diseases	15.0 (8.6)
CKD	6.0 (3.4)
Other**	48.0 (27.6)
No reported drug allergy – n (%)	52.0 (96.3)
Number of prescribed medications – m (± SD)	10.3 (5.5)
Length of hospital stay – m (± SD)	12.4 (12.7)
eGFR – CKD-EPI 2021 – n (%)	
≥ 90	14.0 (25.9)
60-89	21.0 (38.9)
30-59	15.0 (27.8)
≤29	4.0 (7.4)
CrCl – CG*** – n (%)	
≥ 90	10.0 (18.5)
60-89	14.0 (25.9)
30-59	24.0 (44.4)
≤29	6.0 (11.1)

Source: Study data, 2023; SD = standard deviation; CKD = chronic kidney disease; BMI = body mass index; kg = kilogram; kg/m² = kilograms per square meter; m, SD = mean and standard deviation; n, % = absolute and relative frequency; eGFR = estimated glomerular filtration rate expressed in mL/min/1.73 m²; CrCl = creatinine clearance expressed in mL/min. *Considering n = 174 as the sum of comorbidities across all patients. **"Other" includes conditions such as hypothyroidism, dyslipidemia, respiratory, gastrointestinal, hepatic, hematological, neurological, urological, and bone diseases. ***Cockcroft-Gault.

Table 2. Agreement between the CKD-EPI 2021 and Cockcroft-Gault equations regarding the need for medication dose adjustment according to the Kappa test. Recife, Pernambuco, Brazil, 2023.

Medication	n	κ	*p*	Level of agreement
Atenolol	33	1.000	< 0.001	Excellent
Spironolactone	19	0.883	<0.001	Excellent
Morphine	13	0.843	0.002	Excellent
Metformin	12	0.750	0.007	Very good
Escitalopram	18	0.640	0.004	Very good
Meropenem	12	0.500	0.079	Moderate
Domperidone	24	0.357	0.022	Low
Piperacillin + Tazobactam	17	0.354	0.056	Low
Vancomycin	19	0.336	0.050	Low
Metoclopramide	13	0.316	0.120	Low
Regular insulin	24	0.149	0.459	Low
Enoxaparin	91	0.109	0.120	Low

Source: Study data, 2023; κ = Kappa coefficient; n = sample size; p = significance level.

Table 3. Percentage of dose adjustment recommendations based on estimated glomerular filtration rate calculated using the CKD-EPI 2021 and Cockcroft-Gault equations for medications with κ values below 0.6. Recife, Pernambuco, Brazil, 2023.

Medication	CKD-EPI 2021			Cockroft-Goult		
	n (%)	m*	CI	n (%)	m**	CI
Meropenem	7 (58.3)	44.0	3.4	6 (50.0)	38.2	11.3
Domperidone	4 (16.7)	24.5	5.9	1 (4.2)	28.0	***
Piperacillin + Tazobactam	4 (23.5)	27.0	9.5	10 (58.8)	32.3	4.1
Vancomycin	12 (63.2)	17.9	6.9	17 (89.5)	25.6	4.6
Metoclopramide	1 (7.7)	52.0	***	4 (30.4)	46.3	11.1
Regular insulin	13 (54.2)	35.3	6.0	15 (62.5)	42.2	9.8
Enoxaparin	2 (2.2)	26.5	31.8	12 (13.2)	25.1	2.0

Source: Study data, 2023; n = absolute frequency; % = relative frequency; m = mean; CI = confidence interval. *Mean estimated glomerular filtration rate expressed in mL/min/1.73 m²; **Mean estimated creatinine clearance expressed in mL/min; ***Confidence interval could not be calculated due to the sample size consisting of only one observation.

DISCUSSION

The results of the present study show that the level of agreement between the CKD-EPI 2021 and Cockcroft-Gault (CG) equations for medication dose adjustment based on renal function varies according to the medication being adjusted. Complementarily, the choice of equation for this purpose may alter clinical management, which can positively or negatively affect treatment safety or effectiveness.

The κ values for atenolol, spironolactone, morphine, metformin, and escitalopram indicate a degree of variation between the two equations that may be considered negligible. This finding opens the possibility of discussing renal dose adjustment for these medications regardless of which of the two equations is used.

In 2011, the KDIGO initiative published a statement addressing recommendations on this topic, focusing on chronic kidney disease (CKD)

and acute kidney injury (AKI). According to this document, no specific equation is defined as the best option for this purpose. The recommendation is to use the method that provides the greatest accuracy, regardless of whether it is estimated creatinine clearance (CrCl), estimated glomerular filtration rate (eGFR), or measured creatinine clearance obtained from a 24-hour urine collection[14].

There is no evidence confirming the superiority of any single method for medication dose adjustment across all patient populations or clinical situations. In its most recent update, the KDIGO practical guidelines for CKD adopt a less favorable position regarding the use of the CG equation; however, they emphasize that, to date, few studies have compared different eGFR equations in the context of medication dosing[15].

Two equations, known as the Berlin Initiative Study equations 1 and 2 (BIS 1 and BIS 2), were developed and validated with the aim of estimating GFR specifically in older adults. This work consisted of a cross-sectional study conducted in Germany with 600 patients and used creatinine as the biomarker[16]. Despite the relevance of the initiative and its contributions, the sample comprised only White individuals older than 75 years, which limits extrapolation to other populations, including the one evaluated in the present study.

In addition, the KDIGO statement addresses the controversies surrounding the main equations, including CKD-EPI and CG. Methodological differences between equations strongly influence estimated values. In this regard, KDIGO recommends selecting a single formula for estimation, patient follow-up, and medication dose adjustment, as this approach may provide greater safety with respect to changes occurring in renal function[15].

Some pharmacokinetic studies evaluating drug clearance across different levels of renal function do not clearly specify which equation was applied in their methodology. These studies underpin clinical reference tools widely used in practice, such as UpToDate®, and this lack of clarity may represent a confounding factor in equation selection. Furthermore, the way adjustment ranges are presented in these tools, whether based on estimated CrCl or eGFR and expressed in mL/min or mL/min/1.73 m², respectively, may induce preference for a particular equation.

Additionally, the publication date of an article may be another factor influencing the choice of calculator. It is known that the first version of the CKD-EPI equation, which included race as a modifier, was created and validated in 2009[11]. Prior to that, few calculators were available, including the CG equation, originally published in 1976[9]. It is also noteworthy that pharmacokinetic testing related to renal function only became an official requirement in 1998, following guidance issued by the United States Food and Drug Administration[16]. This historical context may further influence equation selection, particularly regarding the use of CG for the purpose addressed in this study; however, it cannot be definitively stated that this was the equation used in studies conducted prior to the development of CKD-EPI.

As an example of the issues discussed above, atenolol was the medication with the highest $\varkappa$ value in this study, with the following dose adjustment recommendation described in UpToDate®: a maximum dose of 50 mg for CrCl between 10 and 30 mL/min and 25 mg for CrCl below 10 mL/min[17,18]. Pharmacokinetic studies evaluating the renal clearance of this drug do not specify which equation was used for estimation; however, they predate the development of the CKD-EPI equation.

From a practical standpoint, the greatest concern involves medications that showed moderate or poor agreement, that is, $\varkappa$ values below 0.60. In this study, antimicrobial agents, antiemetics, anticoagulants, and hypoglycemic agents, which are frequently used in hospital clinical practice, exhibited this pattern.

Among the antiemetic and gastrointestinal prokinetic agents identified in this study are domperidone and metoclopramide, medications that are often prescribed to oncology patients and that have potential cardiotoxicity[19]. In this study, oncological and cardiac diseases ranked third and fourth, respectively, in terms of prevalence. The routine use of these agents in this population is justified both by the patients' underlying clinical condition and by adverse reactions resulting from the

use of chemotherapeutic agents, which are essential for the treatment of several oncologic conditions[20].

Given the vulnerability of patients undergoing cancer treatment, it is essential to adopt assertive measures, such as medication dose adjustment based on renal function. The objectives of these measures are to reduce and prevent complications, such as loss or worsening of effective renal function due to the use of potentially nephrotoxic medications, including some chemotherapeutic agents. For patients who already have concomitant CKD at any stage, the goal is to minimize the impact of drug accumulation for medications that rely primarily on the renal route for clearance[14].

It is also noteworthy that metoclopramide is classified as potentially inappropriate for older adults according to the Beers Criteria[21], both when used alone, due to associated extrapyramidal effects, and when used concomitantly with other medications, because of drug drug interactions. Therefore, metoclopramide is a medication for which cautious use is recommended in older patients[21].

Another medication with low κ agreement was regular insulin, which is also frequently prescribed in the hospital setting, mainly for glycemic correction, but also in other conditions, such as hyperkalemic emergencies[22]. Used in the treatment of diabetes, this disease is one of the main causes of CKD and was the second most prevalent comorbidity in this study[17].

In the case of regular insulin, the issue lies in the fact that, in addition to its clearance, insulin is metabolized by the kidneys. This may lead to drug accumulation in patients with impaired renal function, potentially resulting in hypoglycemia[22]. However, dose adjustment based on renal function for this medication is not routinely performed in the hospital context, as capillary blood glucose is typically monitored frequently, and dose variations are generally guided by point of care glucose testing results.

With regard to antimicrobial agents, several studies have addressed safety and effectiveness in patients with impaired renal function. Meropenem, piperacillin with tazobactam, and vancomycin were also among the medications showing low agreement between formulas in the present study. A key consideration for these drugs is the influence of pharmacokinetic and pharmacodynamic factors (PK/PD) on the selection of dosing regimens used to treat infections, particularly those associated with healthcare delivery and caused by resistant microorganisms[23].

Further regarding these therapeutic agents, factors such as molecular hydrophilicity, volume of distribution (VD), clearance pathway, half-life, sepsis, infection focus, tested minimum inhibitory concentration (MIC), as well as renal function itself, among others, guide the choice of antibiotic dose. In addition, the risk of nephrotoxicity associated with these agents also influences therapeutic decision making, especially for vancomycin and piperacillin with tazobactam when used alone or concomitantly[17,23].

Finally, the medication with the poorest κ value in this study was enoxaparin, an anticoagulant used both for the treatment and prophylaxis of thromboembolic events. This drug tends to accumulate when CrCl is below 30 mL/min, in which case dose reduction or switching to unfractionated heparin is generally recommended[24].

It was also observed that, among the medications with an indication for dose adjustment included in this study, enoxaparin was the most frequently prescribed, appearing almost three times as often as the second most prescribed medication. This finding should be interpreted cautiously, as it raises the question of whether agreement results might have differed if prescription frequencies had been balanced across medications. Conversely, it is important to highlight that there was a considerable proportion of differing clinical decisions regarding dose adjustment depending on whether one equation or the other was adopted.

Thus, it is essential that the equation used be the one that ensures the most appropriate dose adjustment for treatment. Studies referenced by the UpToDate® tool for dose adjustment of meropenem, vancomycin, piperacillin, and enoxaparin used the CG equation to estimate CrCl[24-27]. In contrast, for domperidone, dose adjustment is based on expert opinion; for metoclopramide, studies do not specify which calculator was used; and for regular insulin, no reference is provided.

In this study, for most medications that showed moderate or low agreement, CG was the equation associated with higher percentages of dose adjustment. These findings suggest a potentially more conservative stance of the CG equation, in the sense of recommending dose modifications to preserve current renal function or to reduce the risk of toxicity resulting from decreased excretory capacity, despite the limitations reported. Conversely, meropenem and domperidone showed a higher number of dose adjustments when CKD-EPI 2021 was used, which also supports a conservative role of this latter equation for these two medications.

As discussed above, the equations used in this study have inherent limitations. For CKD-EPI, when comparing eGFR between obese and non-obese individuals with the same sCr value, results tend to be similar, as the equation uses a standard body surface area (BSA) of 1.73 m^2, based on the average BSA of Americans in 2009. In contrast, the CG equation is more closely related to estimating measured CrCl than to true GFR, as creatinine undergoes tubular secretion. Moreover, the development of the CG equation predates the standardization of creatinine measurement using isotope dilution mass spectrometry (IDMS) by the National Institute of Standards and Technology (NIST) in 2005, which may lead to overestimation of CrCl when CG is applied using current standardized assays[9,14].

Among the limitations of this study, the small number of participants should be highlighted. This was mainly due to the short period available for data collection and the absence of sCr measurements within the time frame established in the inclusion criteria, the latter being the primary reason for the exclusion of potential candidates. Another limitation was the performance of a single body weight measurement for all patients at the beginning of the study, without longitudinal follow-up aligned with sCr assessments, particularly among patients with longer hospital stays. Body weight is a variable that may undergo significant changes during hospitalization, especially in individuals with fluid retention secondary to cardiovascular conditions, CKD, and AKI.

Nevertheless, it is noteworthy that this study presents an important strength by addressing a topic that remains underexplored in the Brazilian scientific literature, despite its high relevance to clinical practice. In the context of older adults, the findings underscore the importance of conscious, careful, and rational healthcare, contributing to more effective therapies and to the reduction of health-related complications, with an emphasis on patient safety. In addition, the study may support healthcare services in minimizing patient harm, reducing length of hospital stay, and lowering healthcare costs. It also contributes to improving clinical reasoning and promoting the alignment of interprofessional practices within the institution where the study was conducted.

CONCLUSION

The findings reveal the existence of disagreements among the various stakeholders involved in the medication use process regarding the estimation of kidney function and dose adjustment. Significant uncertainty persists as to which equation should be preferred or which provides the most appropriate support for clinical decision making. In this study, the CKD-EPI 2021 and Cockcroft-Gault equations demonstrated levels of agreement ranging from very good to excellent for dose adjustment of certain medications, suggesting the possibility of interchangeability between them in these cases. This may represent a favorable aspect for patients using such medications.

It should be emphasized that the considerations presented in this study are not intended to define clinical conduct nor to allow extrapolation beyond the institutional setting in which the research was carried out. However, the findings highlight the need for further investigations on this topic, given that renal function-based medication dose adjustment has direct implications for both treatment effectiveness and patient safety.

AUTHORSHIP

- Anderson Félix da Cruz – responsibility for all aspects of the study; project administration; conceptualization; data curation; writing – review & editing; methodology; funding acquisition; resources; and software.

- Matheus Eduardo do Nascimento Barreto – study conception and design; critical revision; project administration; conceptualization; data curation; writing – review & editing; methodology; funding acquisition.
- Francisca Sueli Monte Moreira – study conception and design; critical revision; approval of the final version; supervision; validation; visualization; formal analysis.
- Renally Cristina Lima da Silva – conception; data analysis; critical revision.
- Ricardo Brandão – study conception and design; critical revision; approval of the final version; supervision; validation; visualization; formal analysis.
- Erika Michelle do Nascimento Facundes Barbosa – supervision; validation; visualization; formal analysis.

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