A practice update on medication dose estimate in people with chronic renal disease

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Abstract
The increasing prevalence of chronic kidney disease (CKD) and the disparities in treatment availability make it a pressing public health issue. A person's glomerular filtration rate (GFR) is the most essential metric for drugs that the kidneys filter out of the blood, and it is also the most reliable indicator of general renal function. It is common practice in clinical practice to utilize equations that estimate GFR based on verified prediction equations. Clinical pharmacists from the Australian Society of Hospital Pharmacists (SHPA) Specialty Practice streams in nephrology, oncology and haematology, critical care, and infectious diseases formed the Working Group that drafted this practice update. For clinical pharmacists who make dosage choices based on estimated GFR using equations, this article is meant to provide practical advice. Summarized and contrasted with direct measurements of kidney function using exogenous markers are the limitations of the many equations in use, including the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), the Modification of Diet in Renal Disease, and the Cockcroft-Gault equation. Regular use of the CKD-EPI equation as the principal metric for renal function is advised. When deciding on a new dosage, it is important to take the patient's and the disease's specific characteristics into account. Monitoring the signs, symptoms, and illness outcomes, the appearance of adverse reactions or medication-induced diseases, and the use of therapeutic drug monitoring (if available) to modify dosages appropriately are all important ways to continually check kidney function and the response to treatment.

Keywords:chronickidneydisease,medicationdosing,eGFR,estimationofkidneyfunction,glomerularfiltrationrate.

INTRODUCTION

The increasing prevalence of chronic kidney disease (CKD) and the disparities in treatment availability make it a pressing public health issue.About 1.7 million persons, or one in ten, in Australia suffer from chronic kidney disease (CKD).As a result of socioeconomic determinants of health, the prevalence of chronic kidney disease (CKD) is double among individuals of Aboriginal and Torres Strait Islander descent compared to non-Indigenous adults, and rates are much higher for those residing in rural and isolated locations.3. Nevertheless, only around 10% of the population is aware that they have CKD, which means that treatments that might decrease the disease's progression are not started until much later. Individuals at risk are also more likely to take their medications incorrectly, which may worsen their acute kidney damage (AKI).Approximately 20% of all AKI cases are medication-induced, and this kind of AKI may either cause new instances of CKD to develop or worsen preexisting CKD.To avoid unfavorable medication-related consequences, such as renal function loss and other metabolic problems, and to ensure that patients get the best possible therapy, it is crucial to accurately estimate kidney function in order to diagnose AKI or CKD.6. The most essential way to describe the clearance of medications that are removed by the kidneys is by measuring the glomerular filtration rate (GFR), which is widely recognized as the greatest overall indicator of kidney function. In clinical practice, validated prediction equations for estimated GFR (eGFR) are often used.
Standards of practice in nephrology, oncology and haematology, critical care, and infectious illnesses have been developed by the Society of Hospital Pharmacists of Australia (SHPA) to outline the best practices for the safe and effective administration of medications to patients. Clinical pharmacists from various Specialty Practice streams formed a SHPA Working Group to develop this practice update. For clinical pharmacists who employ GFR estimation equations in medicine dosage choices, it is meant to provide realistic recommendations. It explains potential sources of bias or imprecision and draws attention to the many shortcomings of these equations.

GLOMERULARFILTRATIONRATE

By monitoring the serum concentrations of endogenous filtration markers or the clearance of exogenous filtration markers, one may determine the glomerular filtration rate (GFR), which is the rate at which the kidney glomerulus filters plasma to create an ultrasound.10

Assaying Glomerular Filtration Rate using External Filtration Markers

Serial measurements of glomerular filtration rate (GFR) utilizing an external marker constitute the gold standard for accurate evaluation of renal function. Medication dosage selections in routine clinical practice do not need the time-consuming and expensive procedure. For this aim, exogenous filtration markers including inulin, sinistrin, iohexol, and iothalamate are used. These markers are neither reabsorbed or released by the tubules, and they are freely filtrated by the glomerulus.10

Determining Glomerular Filtration Rate from Endogenous Filtration Markers Concentrations in Serum

Estimates of glomerular filtration rate (eGFR) are derived using formulas that take into account serum concentrations of endogenous filtrates, and they are used to guide dosage choices for medications that are cleared by the kidneys. Endogenous filtration indicators such as creatinine and cystatin C are the most used.

Protein level

Creatinine is a byproduct of muscle metabolism that is mostly eliminated from the blood via glomerular filtration; less than 15% of its clearance is due to tubular secretion, therefore it may be used as a suitable filtration measure in most cases.10

Although shifts in serum creatinine concentration could indicate glomerular function, this is not always the case. To put it another way, any creatinine-based estimating equation will provide inaccurate eGFR results in the following cases.

Some factors that may influence the metabolic production of creatinine include a phenobarbital-and/or a very high-protein diet, as well as the use of creatine or protein supplements in excess of the recommended daily dose.10 Elevated blood creatinine concentrations have been associated with intense exercise-induced muscle metabolism. These situations may cause an increase in serum creatinine levels, which might give the impression that the GFR is lower than it really is. On the flip side, low serum creatinine concentration may occur in clinical settings when a patient's muscle mass is reduced, such as in cases of paralysis, prolonged periods of immobility, or connective tissue illnesses. In such cases, a low blood creatinine concentration could provide the impression that renal function is sufficient.

The cellular transporter proteins in the proximal tubule are inhibited, leading to a rise in blood creatinine content. This effect is well-known to be caused by media such as cimetidine, trimethoprim, dolutegravir, and tyrosine kinase inhibitors.ten to thirteen A medication-induced rise in serum creatinine concentration causes an artificially decreased estimated glomerular filtration rate (eGFR).false-negative AKI that resolves itself after the relevant medication is discontinued and does not reflect a real decrease in GFR.

Aspirin C

An ever-present in the body's protein inventory is cystatin C, a small molecular weight protein. Very little is discharged in urine because it is readily filtered by the glomerulus and metabolized after tubular reabsorption.14 Because of this, measuring urine cystatin C concentrations to predict GFR is not possible; nonetheless, equations that take serum cystatin C concentrations into account have been devised. While creatinine is more sensitive to changes in food and muscle mass, cystatin C has its own distinct restrictions that must be taken into account. It has been shown that equations including both creatinine and cystatin C levels perform better than those involving either one of these parameters.10

Although cystatin C estimating equations are not yet widely used due to cost and availability concerns, they have been used selectively in patients with chronic illness or muscle wasting to provide an accurate estimate of kidney function, which is important for clinical decision making.

Formulas for Determining Renal Function

As a result of the clarity mechanism, the exogenous filtration marker, and the tests themselves, all approaches for assessing renal function are associated with systematic or random mistakes.10 For all patient populations, no one approach to guiding medicine dosage has emerged as the clear winner.15 At least one estimated GFR should be available to clinicians, and the best reliable approach for GFR estimation is presently the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.15

Below is a short history of the equations that are most regularly employed. Using serum creatinine concentration as a filtration measure, all of the presented equations are constrained by the aforementioned factors that influence creatinine production and tubular secretion.

A standardized body surface area (BSA) of 1.73 m2 is used as an indicator in many formulae, including the CKD-EPI and the Modification of Diet in Renal Disease (MDRD). To prevent erroneous dosing, it is necessary to adjust the indexed eGFR for the patient's real BSA when using it to determine medicine dosage in obese or underweight patients. This is because the patient's BSA varies from a standardized BSA.16

Equation of Cockcroft and Gault

Since its publication in 1976, the Cockcroft-Gault (CG) equation has been used to estimate creatinine clearance (CrCl), a proxy indication of a patient's renal function.16 Because measured CrCl (mCrCl) requires collecting urine, this equation was revolutionary because it could determine a patient's CrCl with only one serum creatinine concentration. Supporting dosage of potentially nephrotoxic medications was deemed to provide the most benefits.17 A total of 249 adult males, ranging in age from 18 to 92 years, who were admitted to a Canadian veterans' hospital for medical purposes formed the population from which this equation was derived.17 An estimated CrCl (eCrCl) may be calculated using the CG equation by combining a serum creatinine concentration with readily available patient information. Patient factors like age, sex, weight, muscle mass, illness status, nutrition, and specific treatments cause variances dictated by the inherent limits of this equation.2,18–22 The original equation derivation research notably omitted female participants. A 15% drop in projected CrCl was arbitrarily added using estimates from other studies to account for the fact that women and men have differing proportions of fat and muscle.18

The CG equation has been around for 40 years, making it an impressive part of the academic and regulatory structures of medicine and pharmacy throughout that time.17 To be sure, the CG equation is becoming less used in clinical practice throughout the world.

The Dietary Modification Equation in Chronic Kidney Disease

To estimate GFR, the MDRD equation was developed in 1999. The developers aimed to enhance the identification of renal illness in people by developing it from 1600 patients. The goal was to simplify the assessment of kidney function so that automated reporting could be done using easily acquired laboratory findings.23 Age, sex, race (Black and non-Black), and serum creatinine are the independent variables in the MDRD equation.23 Due to its limitations, the MDRD equation is not suitable for use when kidney function is more than 60 mL/min/1.73 m2. Additionally, older equations were deemed more suitable since more than 10% of all predicted findings differed by more than 30% to a measured GFR.24

A Joint Formula for the Study of Chronic Kidney Disease Epidemiology

The first CKD-EPI equation, which was established in 2009 using a huge database merged from ten research and then verified using data merged from sixteen more investigations, calculates GFR.25

For factors other than glomerular filtration rate (GFR) that affect serum creatinine levels, the first CKD-EPI formula substituted age, race, and sex.24 These factors are linked to muscular mass, which is the primary factor that determines creatinine levels.the next. The imprecision of GFR estimations implies that non-GFR drivers of blood creatinine may predominate over age, race, and sex, and that these factors may not fully explain all variance in serum creatinine.25, 26, and 28 Australian pathology reports using the CKD-EPI equation do not account for racial differences, and a similar trend toward using the more recent 2021 CKD-EPI without racial adjustments is being seen on a global scale.29

When it comes to primary care CKD staging, the CKD-EPI equation is more trustworthy than the MDRD study equation since it is more accurate and has a smaller bias for GFR larger than 60 mL/min/1.73 m2,22. That is why, for the last ten years, CKD-EPI has been the go-to formula for reporting eGFR in clinical labs throughout Australia. It explains why the creatinine test, which debuted in 2010, is now standardised.28,30

To make this equation more applicable to certain patient groups, there is always room for improvement by adding disease- and medication-level components.18, 24, 31, 32 Better eGFR equations that account for other variables (such as blood glucose concentrations in diabetic individuals) should be developed for these groups.18,32

CLINICALDECISIONMAKINGFORMEDICATIONDOSINGINPATIENTSWITHCKD

Somemedicinesarecontraindicatedbelowcertainthresholds of GFR and many medicines that are clearedby the kidneys require dose adjustments.[29]Medicationdosing decision in patients with CKD is performed on acase-by-case basis. Factors such as baseline kidney func-tion, duration and magnitude of the change to kidneyfunction should be considered. The burden of adversemedication reactions is high in patients with CKD, par-ticularlythosewitheGFR<30mL/min/1.73m^2.[33]

Calculating an eGFRor eCrCl toguide initial dosingis only one part of this decision-making process.[28]TheCGequationandeCrClhavebeenusedfordosingadjustmentsinmanyclinicaltrialsandsubsequentlyincluded in the product information (PI) for the relevantmedicines when licensed. In practice, using eGFR (CKD-EPI)inplaceofeCrCl(CG)islikelytoonlyresultinsmall changes in estimates of kidney function and negli-gible clinical significance when making dosing decisionsthatshouldutiliseabroaderthoughtprocess.

Table1Medication-specificcharacteristics

Whattoask	Whattoconsiderand/oraction
Whatistheproportionofthemedicationeliminatedby kidney?	Themedicationisdeemedtobeeliminated*via*thekidneyswhen>30%ofthethekidmedicationoritsactivemetabolite,iseliminatedbythekidneys Inpatientswithimpairedkidneyfunctionusealternativemedicationorreducethedoseand/orextenddosinginterval.Followthedosingguidelines,monitorkidneyfunctionandpatientresponseforeffectivenessandsafety,andadjustaccordingly
Isthemedicationnephrotoxic(directlydamagingtothe kidney)?	Avoidnephrotoxicmedicationsinelderlypatients,patientswithAKIand/orCKD,kidneytransplantrecipientsandpatientsonperitonealdialysiswithresidualkidneyfunction Inpatientsonhaemodialysis,nephrotoxicityisnotrelevant(e.g.NSAID)
Isthepatienttakinganyotherpotentiallynephrotoxic ication(s)?	Combinationsofnephrotoxicmedicationsincreaseriskforkidneyinjury(e.g.medNSAIDand radiocontrast,aminoglycosideand cisplatin,NSAID,ACEI/ARBanddiuretic)
Whatarethepharmacokineticdifferencesinpatients causesdownregulationwithnormalkidneyfunctioncomparedtoimpaired kidneyfunction?	AccountforalteredpharmacokineticsnotingthatCKDofhepaticcytochromeP450metabolismanddrugtransporters Decreasedproteinbindingduetohypoalbuminemialeadstoincreasedfreefractionofthemedication(pharmacologicallyactive)
Doesthemedicationhaveactiveortoxicmetabolites thatarepredominantlyeliminatedbythekidneys?	Medicationsthatarepredominantlymetabolisedbytheliverto pharmacologicallyactiveortoxicmetabolitesthatareexcretedbythekidneys canaccumulateinpatientswithkidneyimpairment Exampleofactivemetabolites: Morphine?morphine-6-glucuronide?CNSsideeffects Exampleoftoxicmetabolites: Pethidine?norpethidine?CNSeffects(seizures)
Aretheredosingguidelinesforimpairedkidney ionavailableforthemedicationinquestion?	Adjustthedosesofthemedication(s)thatareeliminatedbythekidneysfunctaccordingtotheguidelines
Doesthemedicationhaveanarrowtherapeuticindex?	Asmallchangeinplasmaconcentrationscanleadtotoxicityoraless efficacioustreatment Availableestimatesofkidneyfunctionalonewillbeinadequatetoguidedosingandtheuseofvalidatedbiomarkersortherapeuticdrugmonitoringshouldbeused,inadditiontoclosemonitoringforclinicalresponse
Istherevalidatedtherapeuticdrugmonitoring ilable?	Monitorserumconcentrationsandadjustdosesaccordingtovalidatedtargetavaranges
Whataretherisksofadverseeffectsfrom mulation?	Befamiliarwiththeincidenceofadverseeffectsinpatientswithckdandaccumonitoraccordingly
Hasthepatientbeentakinganymedicationsthat inhibittubulardrugtransporters?	Extensiveuptakeofpotentiallynephrotoxicmedicationsbytubularcells*via*bothapicalandbasolateraltransportsystemscanleadtokidneyinjury Inhibitionofapicaleffluxtransporterssuchasmultidrug-resistanceproteintransporters,humanmultidrugandtoxinextrusionproteintransporters(hMATE1,hMATE2)andP-glycoproteindiminishesdrugexitfromrenaltubularcellsleadingtoaccumulation,nephrotoxicityandsystemictoxicity
Hasthepatientbeentakinganymedicationsknownto interferewithrenalcreatininehandling?	Somemedicationsmayreducetubularsecretionofcreatinine(and correspondingincreaseinserumcreatinine)thatresultsinafalsereductionin reported eGFR.Some examples includetrimethoprim,cimetidine and tyrosinekinaseinhibitors

ACEI=angiotensinconvertingenzymeinhibitor;ARB=angiotensinreceptorblocker;CKD=chronickidneydisease;CNS=centralnervoussystem;eGFR=estimatedglomerularfiltrationrate;hMATE1=humanmultidrugandtoxincompoundextrusion-1;hMATE2=humanmultidrugandtoxincompoundextrusion-2;NSAID=non-steroidalanti-inflammatorydrugs.

toguidepractice,particularlyinpatientswithadvancedCKD,whoareoftenexcludedfromoriginalresearch.

For patients with kidney dysfunction, dosing at thespecificthresholdsfordosechangerecommendationscanbecomplexandhavesignificantimpactonthesepatients. For example, a threshold of 30 mL/min is usedfor many medicines, with eGFR/eCrCl values below thisrequiringadosedecrease.However,theinaccuracyofall equations means that dose reduction should consideradditionalmedication-specific,patient-relatedanddisease-related characteristics (Tables 1–3). The potentialimpact of toxicity from the medicine being dosed needstobeweighedagainsttheriskofunderdosing,espe-cially in critical situations such as antimicrobial therapyinsepsis.

Following the initial medication dosing decision, theresponse to therapy should be continuously assessed bymonitoring the signs, symptoms and disease outcomes.For medications with a narrow therapeutic index, wherea small change in medication concentration can causetoxicity or loss of efficacy, validated biomarkers or thera-peutic drug monitoring should be used in addition toclose monitoring for clinical response. Ongoing assess-mentofkidneyfunctionis,ofcourse,essential.

PharmacokineticandPharmacodynamicConsiderationsinPatientswithCKD

Thepharmacokineticsofmanymedicationscanbealteredinpatientswith CKD,althoughforsomenodosechangesarerequired.

A decrease in glomerular filtration or tubular secre-tion will reduce clearance of medications as well as theactive and toxic metabolites typically cleared by thosemechanisms.[15]Some have significant tubular secretion,which may result in higher clearances than their eGFRmay otherwise suggest, such as amoxycillin, cefalexin,meropenem and metformin.[34–36]Furthermore, the activ-ityofkidneydrugtransportersmaybeaffectedbypharmacogeneticdifferencesanddrug–druginteractions.[37]Forexample,inhibitionofapicaleffluxtransporters may reduce drugexit from renal tubularcells, leading to accumulation, nephrotoxicity and sys-temictoxicity.[38]Additionally,somemedicationshaveincreasedclearance*via*otherelimination routes,forexample increased transintestinal clearance of ciproflox-acin has beendescribedin severe kidneydysfunctionprovidingan‘extrarenalsafetyfactor’,meaningthatlinear dose adjustments with decreasing GFR would behighlyinappropriate.[39]

Table2(*continued*)

Whattoask	Whattoconsiderand/oraction
Isthepatientakidneytransplantrecipient?	Mostpatientswillonlyreceiveasinglekidneytransplant,makingthemmore susceptibletofutureacutekidneyinsults.Choosemedicationscarefullyandconsul ttransplantteamifunsureofsafety
Whatmodalityofdialysisisapatientreceiving?	Estimatingequationswillbeinaccurateinthispopulationandshouldnotbeusedto guidemedicationdosingdecisions Adjustthedosesaccordingtoinformationavailablefortheindividual’sdialysismodalit yandfrequencyofdialysis
Doanypharmacogenomicfactorsneedtobe Medicationsconsidered?	Cytochrome P450 polymorphism may affect medication metabolism. thatexhibitpolymorphicmetabolismmaybeatmuchhigherriskofadverse medicationreactionsinpeoplewithCKD

ACEI=angiotensinconvertingenzymeinhibitor;AKI=acutekidneyinjury;ARB=angiotensinreceptorblocker;BMI=bodymassindex;CG=Cockcroft–Gault;CKD=chronickidneydisease;CKD-EPI=ChronicKidneyDiseaseEpidemiologyCollaboration; eGFR=estimatedglomerularfiltrationrate;GFR=glomerularfiltrationrate;mGFR=measuredglomerularfiltrationrate;NSAID=non-steroidal anti-inflammatory drugs; SCr=serum creatinine; SGLT2=sodium glucose cotransporter 2 inhibitor; U&E=urea andelectrolytes.

[a]Bodymassindex(BMI)=weight(kg)/height(m)^2.

[b]AbsoluteGFR=(bodysurfacearea[BSA]indexedeGFR9patient’sBSA)/1.73m^2=mL/min.

Table3Disease-relatedcharacteristics

Whattoask	Whattoconsiderand/oraction
Whatistheindication?	Usemedicationsonlyifthereisadefiniteindication
	Choosethemedicationwithminimumnephrotoxicity
Isthepatientcriticallyill?	Considerthehospitalsettingsuchasregularward,highdependencyorICUIsthereclinicalsi
gnificancetoanyunderdosing?	Considertheacuityandtheseverityofthediseasethatrequirestreatment
	Unnecessarydecreasesindosagemayresultinundertreatment
Isasingledoseormorethanonedoserequired?	Administrationofinappropriatelyhighdosesofmedicationsinpatientswith impairedkidneyfunctioncanresultintoxicity aftermultipledosing,ratherthanafterthefirstdose
Whatisthedurationoftherapy?	Theriskofadversemedicationeffectsincreaseswiththedurationoftherapy
Areothertreatment optionsmoresuitablefor	Ifpossible,usemedicationsthatarenotorminimallyeliminatedbythekidneys
someonewithkidneyimpairment?	

ICU=intensivecareunit;U&E=ureaandelectrolytes.

There may be changes in the clearance of some drugs in individuals with chronic kidney disease (CKD) that are unrelated to renal function. As an example, it has been shown that cytochrome P450 3A4 (CYP3A4) isoenzyme activity decreases in end-stage kidney disease (ESKD), perhaps due to uraemia.40 However, ESKD patients may see a 27% rise in CYP3A4 activity after hemodialysis.35 Because many patients with CKD also have other medical conditions that might impact the dosage of their medications, it is necessary to take these other diseases into account when making treatment decisions. Medications have a longer half-life when clearance is reduced.

When dosing patients with chronic kidney disease, it is important to keep in mind the medicine's pharmacodynamics and the therapeutic objectives that are particular to the medication.15 Therapy objectives may include preserving a minimum inhibitory concentration (MIC) or the ratio of the drug's area under the concentration time curve (AUC) to the MIC, or maintaining a peak, trough, or average steady-state concentration, depending on the relationship between medication concentration and clinical response.15 Although there is usually a minimal threshold exposure required by most drugs for ongoing clinical benefits during the dose period, especially for chronic comorbidities, there are exceptions. Examples of antimicrobials include aminoglycosides, which kill bacteria in relation to their concentration, and beta-lactams, which kill bacteria in relation to their time in the presence of the drug. Maximum bacterial killing and a better chance of clinical cure are related with concentration-dependent drugs having a peak concentration to minimum inhibitory concentration (peak/MIC) ratio greater than 10. High peak concentrations do not provide any therapeutic benefit or extra bacterial killing, but for beta-lactams, it is more significant to maintain concentrations above the MIC throughout the dosage period. drug toxicity concentrations (toxicokinetics) may be more related to peak or trough concentrations, or even total drug exposure, than to clinical efficacy or bacterial killing. The pharmacodynamic and toxicokinetic properties of a medicine should be considered by the physician when deciding on an adjusted dosage for CKD patients. This will guarantee the medication's highest potential for clinical efficacy with the lowest possible risk of toxicity. For critically sick patients with sepsis and obesity, it has been suggested to optimize antimicrobial dosage techniques by considering specific pharmaceutical features and pharmacokinetic/pharmacodynamic principles.33,42

In Table 1 we can see a summary of the medication-related factors that should be considered when estimating renal function and making dosage adjustments.

Important Factors to Consider When Dosing Certain Medications

Therapeutic Drug Monitoring for Antibiotic Dosage

The goal of therapeutic drug monitoring (TDM) is to measure the concentrations of medications in a biological matrix, most often blood, and then adjust the patient's dosage so that they reach an exposure (measured concentrations) that is associated with efficacy while minimizing the risk of toxicity. Medication having a limited therapeutic index, such as glycopeptides and aminoglycosides, is often dosed in this method, however TDM is suggested for the administration of many drugs.42 Prior to the availability of TDM, eGFR becomes significant only for empiric dosing in certain cases, and the first dosage estimates should be based on the eGFR equation that has the highest accuracy for that medication-patient combination. Because TDM informs the exact drug exposure that eGFR aims to forecast, it will always be more trustworthy than eGFR, so TDM should be used instead of eGFR as long as it is performed consistently enough. In cases when TDM is not an option, such as when the assay is unavailable or when blood samples are difficult to obtain, eGFR should be considered in addition to TDM when making dosage choices.

Direct Oral Anticoagulant Dosage

No definitive evidence has been found to guide the optimal equation for assessing kidney function to aid in the dosage of direct oral anticoagulants (DOACs). Despite the practicality of employing eGFR CKD-EPI at the bedside due to its accessibility, research has shown that various equations lead to varying dosage recommendations.43–45

Out of 39,239 individuals diagnosed with atrial fibrillation (AF), 11,185 were studied using direct-occurring anticoagulants (DOACs), while 2,323 were studied using warfarin. It was shown that using MDRD or CKD-EPI instead of CG would lead to DOACs being dosed inappropriately, mostly in the form of overdose. For determining eGFR and determining DOAC dosage, the authors concluded that the CG equation should be the de facto norm.43 Similar findings were seen in a recent research conducted by Rohla et al., which also included 1288 individuals with AF.44 In as many as 25% of patients, the dosage recommendations for dabigatran, edoxaban, and rivaroxaban were different when MDRD or CKD-EPI was used instead of CG. Patients whose CG and CKD-EPI results did not match had a distinct risk profile, with increased incidence of hemorrhage and thromboembolic complications.44 Alternatively, a research with 6,392 AF patients found that both the CG and non-CG equations differed in their ability to estimate kidney function; nonetheless, the risks of thromboembolism and severe bleeding were comparable to those with warfarin, irrespective of the equation utilized.45

At the bedside, estimated GFR CKD-EPI may be utilized to dose a DOAC for the first time. The effectiveness and negative effects should be closely monitored. Regular evaluation of renal function to detect worsening and adequate dosage should be considered for complicated patients, especially those on longer-term treatment, with DOAC that has shown safety at lower eGFR.

Administering Anticancer Drug Doses

The gold standard for determining glomerular filtration rate (mGFR) is direct measured GFR testing. It is advised for use with certain cancer treatments, such as carboplatin, cis-platin, and methotrexate (≥500 mg/m2), in patients with abnormally large or small bodies, amputees, paraplegics, or those with skeletal muscle disorders.46 Due to capacity issues at bigger centers and a lack of availability at smaller facilities, mGFR is presently only used in cases when a more precise dosage is required, such as when administering carboplatin.45 When comparing eCrCl to other equations for dose selection for kidney-excreted anticancer drugs at the bedside, studies in cancer contexts have shown that mGFR is the most accurate.26,47

It is advised to use eGFR CKD-EPI as the standard and routine estimate of kidney function, and to use BSA-adjusted eGFR CKD-EPI for carboplatin dosing using the Calvert equation, in accordance with the recently developed International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD) by eviQ and Cancer Institute NSW.46 An exhaustive literature search provided the basis for the development of the ADDIKD. Direct referral to the ADDIKD and associated protocols is required for practitioners seeking individualized recommendations on certain drugs and unique populations (e.g., obesity, AKI).46

Particular Patient Populations and Dosage Considerations

Table 2 summarizes the patient-related factors to be considered for medication dosage estimate based on kidney function, and Table 3 summarizes the disease-related features to be considered. The following is a synopsis of the suggestions made for various patient populations.

Dosage of Medications for Patients Who Are Obese

Hypertrophy, glomerular hyperfiltration, and increased blood flow to the kidneys are all symptoms of obesity.48–50 Research shows that the CG-based equations still don't work very well in this group, even after accounting for weight. When adjusting dose at glomerular filtration rates (GFRs) between 30 and 45 mL/min, the CKD-EPI de-indexed equations and the MDRD de-indexed by BSA (also called BSA-adjusted) equations are very similar and work well.14, 15, 16, 51, 52

For obese individuals with a GFR of 30-80 mL/min, the MDRD and CKD-EPI indexed by the BSA provide very accurate GFR estimates.numbers 48, 51, and 53 Standardized BSA 1.73 m2 indexes eGFR CKD-EPI. It is important to modify the indexed eGFR for the patient's actual BSA when utilizing eGFR for drug dosage. This will help prevent erroneous dosing in patients who are obese or underweight.16 In those who are very obese and have a glomerular filtration rate (GFR) below 30 mL/min, the usefulness and precision of all equations diminish.52 This is where mGFR comes in handy, especially when taking drugs with a small therapeutic index.48,52

CONCLUSION

For therapeutic purposes, such as tracking the development of kidney disease and dosing drugs that the kidneys clear, an accurate estimate of renal function is essential. For the majority of patients, the CKD-EPI equation should be the go-to tool for gauging kidney function. Every case calls for an individualized assessment based on medication-specific, patient-related, and disease-related factors; clinical judgment is the key. It is important to regularly evaluate kidney function and treatment response by keeping an eye on symptoms, illness outcomes, adverse reactions, medication-induced diseases, and TDM (where available) to determine dosage adjustments.

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