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مرکز همایش‌های بین‌المللی روزبه



GFR Estimation in AKI

Dr. Shahrzad Shahidi

Professor of Nephrology

Isfahan University of Medical Sciences

Objects

- **Introduction**
- **Implications of GFR for Critical Care**
- **KeGFR**
- **Shortened CrCl**
- **Diagnosing AKI ahead of time**
- **Medication management in critically ill patients with AKI**

Nephrol Dial Transplant (2020) 35: 1834–1836

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IF: 6.1
(2022)

Estimating glomerular filtration rate in patients with acute kidney injury

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The 2012 Kidney Disease: Improving Global Outcomes consensus definition of acute kidney injury (AKI) has been very useful to classify patients and to compare the different studies of AKI [1]. However, this definition is based on urine output and serum creatinine levels that are suboptimal markers of renal function. It is known that serum creatinine depends not only on renal function, but also on muscular body mass, protein intake, hydration and medication. The other parameter

creatinine production rate [6]. Recent studies have shown that the KeGFR equation has better predictive performances for severe AKI and renal replacement therapy initiation than the MDRD equation and that it could also be predictive for AKI recovery [7, 8]. It has also been suggested that it could be helpful in drug dosage adaptation [9]. However, this is the first study comparing these formulae to direct GFR measurement in AKI.

The authors used the KeGFR and Jelliffe equation to esti-

Introduction

- The 2012 KDIGO consensus definition of AKI has been very useful to classify patients & to compare the different studies of AKI.
- This definition is based on **urine output & serum Cr** levels that are suboptimal markers of renal function.
- Serum Cr depends not only on renal function, but also on muscular body mass, pr intake, hydration & medication,...
- The other parameter is urine flow, which lacks sensitivity & specificity.

Luque Y. NDT. 2020

Introduction

- The **gold standard** of GFR assessment is direct measurement, wherein exogenous markers are administered (e.g., iohexol) & their clearance precisely quantified.
- However, the technical complexity, turnaround time, & cost make routine GFR measurement impractical.
- **Alternatively**, timed urine collections can be used for measurement of Cr clearance. The accuracy of such measurements is inconsistent.
- For these reasons, **GFR estimation equations** are widely used to guide treatment decisions in critically ill patients, despite well described limitations.



IF: 8.8
(2023)

REVIEW ARTICLE

Toward Equitable Kidney Function Estimation in Critical Care Practice: Guidance From the Society of Critical Care Medicine's Diversity, Equity, and Inclusion in Renal Clinical Practice Task Force

Miano, Todd A. PharmD, PhD, FCCM¹; Barreto, Erin F. PharmD, MSc, FCCM²; McNett, Molly PhD, RN, CNRN, FNCS, FAAN³; Martin, Niels MD, FACS, FCCM⁴; Sakhuja, Ankit MD, MBBS, FACP, FASN⁵; Andrews, Adair RN, MATD⁶; Basu, Rajit K. MD, MS, FCCM⁷; Ablordeppey, Enyo Ama MD, MPH, FACEP, FCCM⁸

Author Information

Critical Care Medicine 52(6):p 951-962, June 2024. | DOI: 10.1097/CCM.0000000000006237

Outline

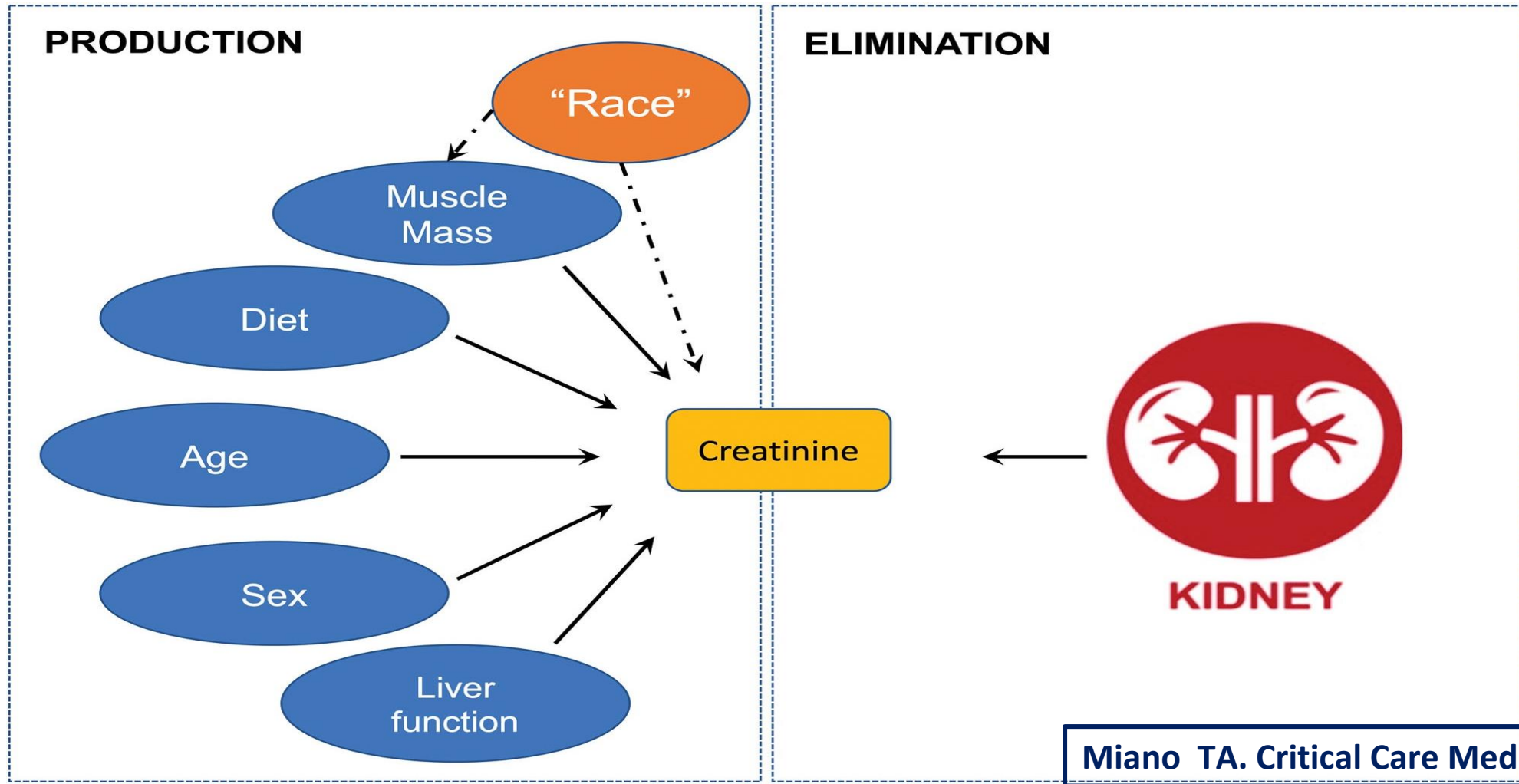
Images

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Cite



Nonrenal determinants of Cr & the role of race



Implications of GFR for Critical Care

1. GFR assessment is essential for drug dosing, as nearly **2/3** of medications used in hospitalized patients are renally eliminated.
2. Evaluation of the risk vs. benefit of treatment with nephrotoxins requires accurate GFR assessment. This latter role is especially important, given that **one in four** drugs used in hospitalized patients is potentially nephrotoxic.
3. Eligibility for organ transplantation & consideration for mechanical circulatory support.

Miano TA. Critical Care Medicine. 2024

IMPLICATIONS of GFR for CRITICAL CARE

1. GFR assessment is essential for drug dosing, as nearly **2/3** of medications used in hospitalized patients are renally eliminated.
2. Evaluation of the risk vs. benefit of treatment with nephrotoxins requires accurate GFR assessment. This latter role is especially important, given that **one in four** drugs used in hospitalized patients is potentially nephrotoxic.
3. Eligibility for organ transplantation & consideration for mechanical circulatory support.
4. Last, GFR assessment is important for the conduct of clinical trials, where baseline kidney function is frequently a criterion for enrollment. In trials of AKI therapeutics, GFR assessment plays a role in AKI phenotyping & the evaluation of renal recovery as a trial outcome

Miano TA. Critical Care Medicine. 2024

AKI Phenotyping

Tools

Functional biomarkers

Cystatin C
Pro-enkephalin
Serum creatinine

Tissue injury biomarkers

NGAL
IL-18
KIM-1
L-FABP
NAG
 α -/π-GST

Cycle-cell arrest markers

TIMP-2 × IGFBP-7 (Nephrocheck®)

GFR measurement or estimation?

Aims

- Risk stratification
- Prognosis
- Tissue injury
- Renal function
- Adapt drug dosage
- Early management

Luque Y. NDT. 2020

KeGFR



Outline



Images



Download

UP FRONT MATTERS

Retooling the Creatinine Clearance Equation to Estimate Kinetic GFR when the Plasma Creatinine Is Changing Acutely

Chen, Sheldon

Author Information

Journal of the American Society of Nephrology 24(6):p 877-888, June 2013. | DOI: 10.1681/ASN.2012070653

KeGFR

- Although KeGFR equations have previously been devised, they have not been widely practiced or taught.
- This is unfortunate because we need to continue the favorable trend of interpreting kidney function not in terms of plasma Cr but of **clearance**.
- In this regard, the clinical evaluation of CKD is more advanced, but the assessment of AKI & renal recovery can begin to catch up with the promulgation of **Cr kinetic formulae**.

KeGFR

- The earliest attempt at this was by:
 - Jelliffe and Jelliffe in 1972
 - Chiou and Hsu in 1975
 - Moran and Myers in 1985
 - Yashiro et al. in 2012
- Each may differ in their mathematical approach, algebraic or calculus based, but they are all essentially rooted in first principles of **Cr mass balance**.

Chen Sh. JASN. 2013

KeGFR

- To try to overcome the barriers to adoption, Dr. Chen has **reformulated** the core mathematical operations into a less intimidating & more pliable version at the bedside.

Chen Sh. JASN. 2013

KeGFR

$$KeGFR = \frac{SSP_{Cr} \times CrCl}{MeanP_{Cr}} \times \left(1 - \frac{24 \times \Delta P_{Cr}}{\Delta Time(h) \times Max\Delta P_{Cr}/Day} \right)$$

- SSP_{Cr} = Steady State Plasma Cr
- ΔPCr = PCr (end) – PCr (start)

Chen Sh. JASN. 2013



Nephrology Edition Contributing Author
Daniel Schwartz, MD, FRCPC



دوازدهمین سمینار سراسری انجمن علمی نفرولوژی ایران کلیه در شرایط کریتیکال

The 12th National Congress of the Iranian Society of Nephrology (NirSN)



▶ COVID-19

▶ General Calculators

▶ Nephrology

▶ Acute Kidney Injury

▶ Nephrolithiasis

▶ Pathology

▶ Chronic Kidney Disease

▶ PD

▶ Hemodialysis

▶ eGFR

▶ Fluids & Electrolytes

▶ Transplant

▶ Glomerulonephritis

▶ Hypertension

▶ AKI Clinical Trials

eGFR using CKD-EPI (Creatinine-Cystatin C) Equation (2021)
Calculate eGFR using the CKD-EPI (Creatinine-Cystatin C) Equation (2021)

Free Water Deficit

Contrast Nephropathy Post-PCI
Estimate risk of AKI after percutaneous coronary intervention

CRRT Dosing Calculator
Calculate desired dose of dialysate in CRRT

Dialysis Risk After Cardiac Surgery (Cleveland Clinic Score by Thakar)
Estimate risk of dialysis after cardiac surgery.

Dialysis Risk After Cardiac Surgery (Mehta)
Estimate the risk of dialysis after cardiac surgery (Mehta model)

Elevated serum creatinine or hyperkalemia after ACEi/ARB
Estimate risk of elevated serum creatinine or hyperkalemia after ACEi or ARB initiation

Fractional Excretion of Sodium
Differentiate pre-renal AKI from ATN.

Fractional Excretion of Urea
Identify a pre-renal state in patients using diuretics

KDIGO AKI Staging
Classification in acute kidney injury (AKI)

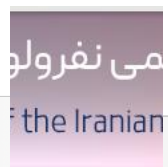
KDIGO Clinical Practice Guideline for Acute Kidney Injury
Sponsored

Kinetic eGFR (KeGFR)
Estimate GFR when creatinine is changing acutely (either rising or falling)

Mayo AKI Risk after Primary Total Hip Arthroplasty
Estimate perioperative risk of acute kidney injury

McMahon Rhabdomyolysis Risk Score
Predict the risk of severe acute kidney injury or mortality in patients with rhabdomyolysis

NCDR AKI and Dialysis Risk after PCI
Estimate risk of AKI and dialysis after PCI



< Back

Kinetic eGFR (KeGFR)

< Back

< Back

Kinetic eGFR (KeGFR)

Hide Results



Questions

Steady State Plasma Creatinine? Unanswered >

Creatinine Clearance or eGFR at baseline? Unanswered >

Creatine at 1st Time Point? Unanswered >

Creatinine at 2nd Time Point? Unanswered >

Time Interval Between Two Creatinine Values? Unanswered >

Question

Steady State

Answer

Ent

More Information

Baseline creatinine

Questions

Steady State Plasma Creatinine? 1 mg/dL >

Creatinine Clearance or eGFR at baseline? 76 ml/min >

Creatine at 1st Time Point? 2 mg/dL >

Creatinine at 2nd Time Point? 3.2 mg/dL >

Time Interval Between Two Creatinine Values? 24 Hours >

Questions

Steady State Plasma Creatinine? 1 mg/dL >

Creatinine Clearance or eGFR at baseline? 76 ml/min >

Creatine at 1st Time Point? 2 mg/dL >

Creatinine at 2nd Time Point? 3.2 mg/dL >

Time Interval Between Two Creatinine Values? 48 Hours >

Results

Kinetic eGFR

17.5 ml/min

5.8 ml/min

Nephrol Dial Transplant (2020) 35: 1886–1893
 doi: 10.1093/ndt/gfz178
 Advance Access publication 16 September 2019

ORIGINAL ARTICLE

Estimating glomerular filtration rate in patients with acute kidney injury: a prospective multicenter study of diagnostic accuracy

Karyne Pelletier¹, Jean-Philippe Lafrance², Louise Roy³, Mathieu Charest⁴, Marie-Claire Bélanger⁵, Jean-François Cailhier³, Martin Albert¹, Anatolie Duca¹, Naoual Elftouh² and Josée Bouchard¹

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⁵Department of Biochemistry, Centre Hospitalier de l'Université de Montréal, Faculty of Medicine, Université de Montréal, Montreal, QC, Canada

Downloaded from <https://ac>

Methods

- The authors used the **KeGFR & Jelliffe** equations to estimate GFR in **119** adult AKI patients, mostly from the ICU (63%).
- It is the **first** to evaluate these equations compared with a validated GFR measurement in the AKI setting.
- They included a majority of moderate AKI patients (71% of Stage 1 AKI), & oliguric patients were excluded.
- GFR radioisotopic measurement was performed 24 h after inclusion in the majority of cases with a single **99mTcDTPA** intravenous bolus.

Pelletier K. NDT. 2020

Conclusion

- The Jelliffe & KeGFR equations had **good correlations** with mGFR; however, they had wide limits of agreement.
- Both equations performed better in patients with **severe CKD**, & KeGFR performed better in **older patients**.

Pelletier K. NDT. 2020


Volume 144, Issue 6

June 2020



RESEARCH ARTICLES | MAY 05 2020

Using Kinetic eGFR for Drug Dosing in AKI: Concordance between Kinetic eGFR, Cockcroft-Gault Estimated Creatinine Clearance, and MDRD eGFR for Drug Dosing Categories in a Pilot Study Cohort

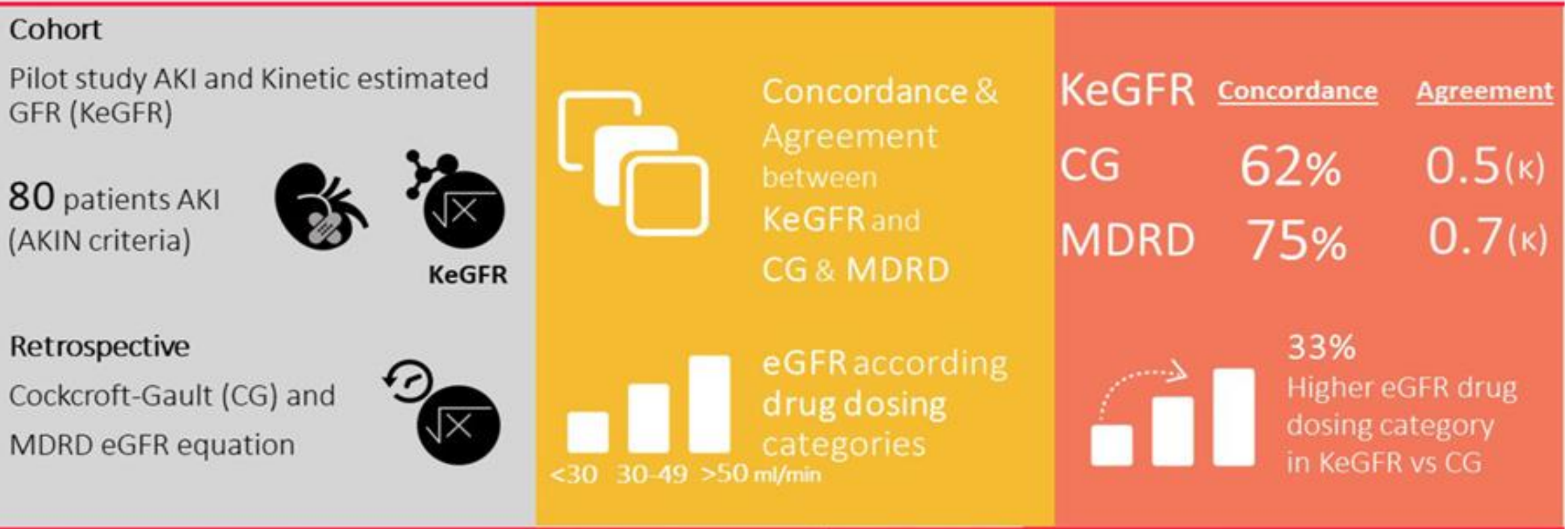
Subject Area:  Nephrology

Manohar Bairy  

Nephron (2020) 144 (6): 299–303.

Concordance of Kinetic eGFR for drug dosing in AKI vs. Cockcroft-Gault & MDRD

Nephron



Conclusions: In AKI, compared to CG, using KeGFR may affect drug dosing significantly by changing the eGFR category. Further studies of KeGFR for drug dosing will need therapeutic drug monitoring and pharmacokinetic studies for validation.

Bairy M: Using Kinetic eGFR for Drug Dosing in AKI: Concordance between Kinetic eGFR, Cockcroft-Gault Estimated Creatinine Clearance, and MDRD eGFR for Drug Dosing Categories in a Pilot Study Cohort. Nephron DOI: 10.1159/000507260

Visual Abstract by Aldo Rodrigo Jimenez Vega @aldorodrigo

Bairy M.Nephron. 2020

Conclusions

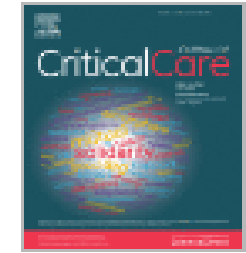
- In AKI, compared to CGeCrCL, using KeGFR may affect drug dosing **significantly** by changing the eGFR category.
- Further studies of KeGFR for drug dosing will need therapeutic drug monitoring & pharmacokinetic studies for validation.

Bairy M. Nephron. 2020





Journal of Critical Care

Volume 75, June 2023, 154276



Diagnosing acute kidney injury ahead of time in critically ill septic patients using kinetic estimated glomerular filtration rate

Lada Lijović^{a, b}  , Stipe Pelajić^b, Fatime Hawchar^c, Ivaylo Minev^d,
Beatriz Helena Cermaria Soares da Silva^{e, f}, Alessandra Angelucci^g, Ari Ercole^h,
Harm-Jan de Grooth^a, Patrick Thorat^a, Tomislav Radočaj^b, Paul Elbers^a

Methods

- Retrospective analysis on **septic ICU** patients who developed AKI.
- The reference standard for AKI was KDIGO classification.
- Prediction of AKI was based on stages defined by **KeGFR & UO**.
- Classifications were compared by:
 - Length of ICU stay (LOS)
 - Need for RRT
 - 28-day mortality.
- Predictive performance & time between prediction & diagnosis were calculated.

Lijovic L. J of Cri Care. 2023

Results

- Of 2492 patients in the cohort, **62.0%** were diagnosed with AKI by KDIGO & **68.5%** by KeGFR criteria.
- Disease stages had agreement of kappa = 0.77, with KeGFR sensitivity 93.2%, specificity 73.0% & accuracy 85.7%.
- Median time to recognition of AKI Stage 1 was 13.2 h **faster** for KeGFR, & 7.5 h & 5.0 h for Stages 2 & 3.
- **Outcomes** revealed a slight difference in LOS & 28-day mortality for Stage 1.

Lijovic L. J of Cri Care. 2023

Highlights

- Classical estimations of GFR are not reliable for patients with non-steady state Cr levels
- In non-steady state Cr levels, KeGFR offers **time advantage** to diagnosis
- Performance of KeGFR in patient recognition, staging & outcome prediction is **similar** to KDIGO
- KeGFR may shift the actionable window for preventing & mitigating renal insufficiency

Lijovic L. J of Cri Care. 2023

Shortened CrCl

COMMENTARY

Measuring glomerular filtration rate in acute kidney injury: Yes, but not yet

Bruce A Molitoris*

See related research by Pickering *et al*, <http://ccforum.com/content/16/3/R107>

Abstract

Acute kidney injury has become a major focus for nephrologists and critical care physicians. The development of structural biomarkers is proceeding, but the results to date have been disappointing. The use of a shortened creatinine clearance as a functional acute kidney injury biomarker is not new but has not been compared with that of other diagnostic approaches. A rapid, repeatable, and accurate measured glomerular filtration rate would be the gold standard for a functional biomarker and is not far off.

technique with clinical utility has not been developed. Reduction in the GFR, secondary to kidney injury, is the hallmark of AKI and results in increased levels of blood urea nitrogen (BUN) and serum creatinine. Unfortunately, the rates of increase in BUN and serum creatinine do not parallel the fall in GFR in a time frame that is clinically useful. In addition, since both creatinine production from muscle and GFR determine the serum creatinine level, using serum creatinine as an indicator of GFR is highly patient-specific and often problematic or even misleading. These issues have been described elsewhere [3].

Achieving the ability to rapidly and accurately measure

Shortened CrCl

- Rosenthal & colleagues used a 2-hour CrCl in **stable** patients & found an acceptable & repeatable correlation with the 24-hour CrCl.
- The accuracy & utility of a shortened collection in unstable patients were **questioned** by 2 studies conducted in patients with AKI.

Molitoris BA. Crit Care. 2012

Shortened CrCl

- This **limitation** may relate to:
 - Reduced production of Cr in sepsis
 - Increased production of Cr with trauma
 - Increased metabolism including the use of glucocorticoids
 - The changing of GFRs during the collection periods.
- Until such studies are conducted, confidence for using a CrCl may be limited.

Molitoris BA. Crit Care. 2012

4 hour CrCl for monitoring renal function in critically ill patients

- Pickering & colleagues set out to determine the clinical utility of a **4-hour (CrCl)**, compared with plasma Cr, for diagnosing AKI.
- CrCl increased the likelihood of diagnosing AKI; a decreasing CrCl correlated with increased kidney injury severity, death, or dialysis; & the CrCl was **most helpful** when patients began with a serum Cr in the normal range.
- The study was a **small pilot study**.

Pickering JW, et al. Crit Care 2012



Measured versus estimated creatinine clearance in critically ill patients with acute kidney injury: an observational study

Sara Kadivarian¹, Fatemeh Heydarpour², Hasanali Karimpour³, Foroud Shahbazi¹

¹Department of Clinical Pharmacy, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah; ²Social Development and Health Promotion Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah; ³Department of Anesthesia, School of Medicine, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran

Background: Acute kidney injury (AKI) commonly occurs in critically ill patients. Estimation of renal function and antibiotics dose adjustment in patients with AKI is a challenging issue.

Methods: Urinary creatinine clearance was measured in a 6-hour urine collection from patients

Original Article

Measured versus eCrCl in critically ill patients with AKI: Methods

- Urinary CrCl was measured in a **6-hour urine** collection from patients with AKI.
- The correlations between different formulas including the **modified CG, MDRD, CKD-EPI, Jelliffe, kinetic GFR, Brater, & Chiou** formulas were considered.
- The pattern of the prescribed antimicrobial agents was also compared with the patterns in the available resources.

Kadivarian S. ACC. 2022

Measured versus eCrCl in critically ill patients with AKI: Results

- **Ninety-five** patients with AKI
- Mean age : 63.11 ± 17.58 ys old.
- The most patients (77.89%) were in stage 1 of AKI according to the AKIN criteria, followed by stage 2 (14.73%) & stage 3 (7.36).
- None of the formulations had a high or very high correlation with the measured CrCl.
- In stage 1, **Chiou** ($r=0.26$), & in stage 2 & 3, **kinetic-GFR** ($r=0.76$ & $r=0.37$) had the highest correlation coefficient.
- Antibiotic over- & under-dosing were frequently observed in the study.

Kadivarian S. ACC. 2022

Measured versus eCrCl in critically ill patients with AKI: Conclusions

- None of the static methods can predict the measured CrCl in the critically ill patients.
- The dynamic methods such as **kinetic-GFR** can be helpful for patients who do not receive diuretics & vasopressors.

Kadivarian S. ACC. 2022



CJASN[®]

Clinical Journal of the American Society of Nephrology



[Clin J Am Soc Nephrol](#). 2023 Aug; 18(8): 1080–1088.

PMCID: PMC10564345

Published online 2023 Feb 1. doi: [10.2215/CJN.000000000000101](https://doi.org/10.2215/CJN.000000000000101)

PMID: [36723347](https://pubmed.ncbi.nlm.nih.gov/36723347/)

Medication Management in the Critically Ill Patient with Acute Kidney Injury

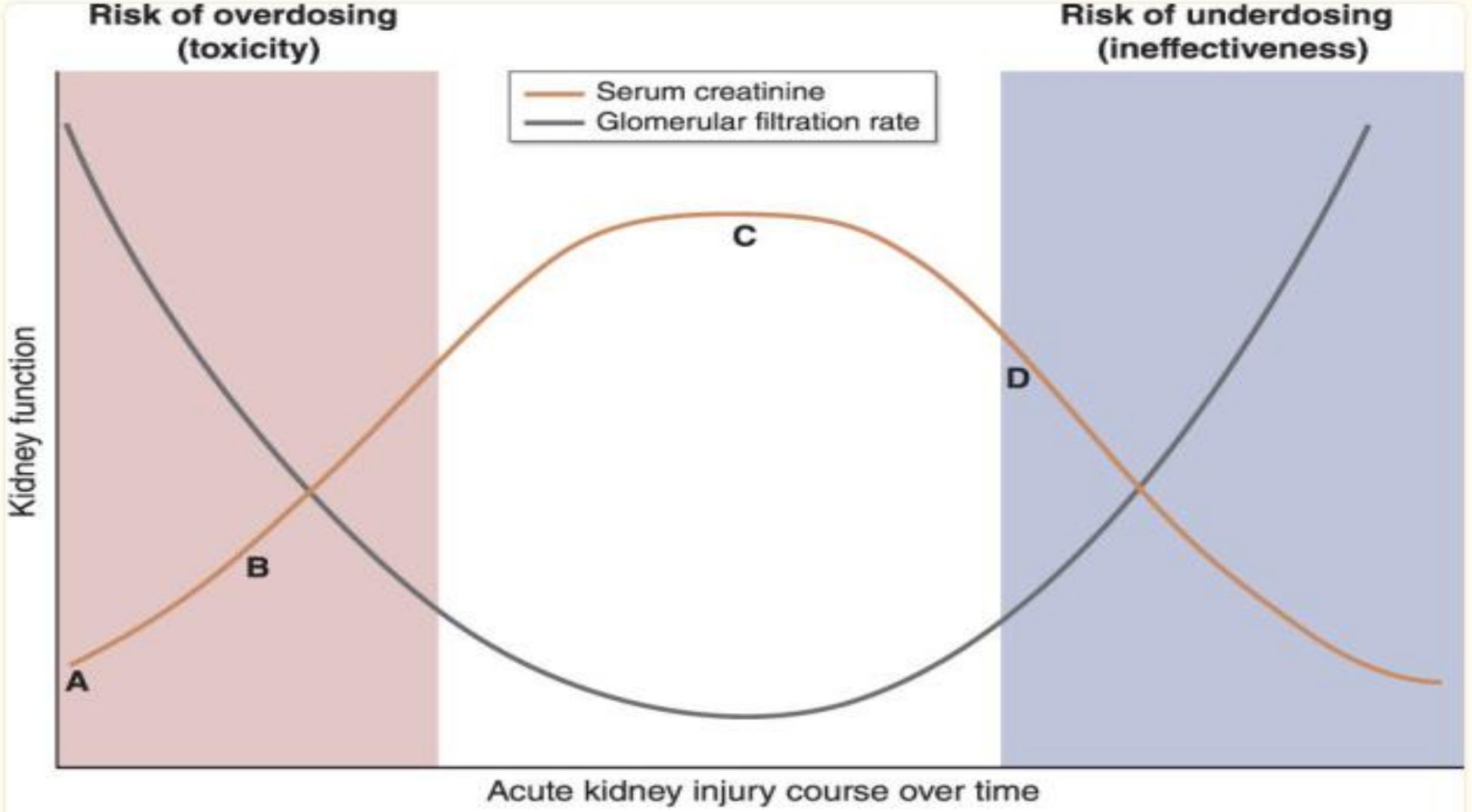
[Michael L. Behal](#),^{1, 2} [Alexander H. Flannery](#),^{1, 2} and [Erin F. Barreto](#)^{✉ 3}

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Abstract

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AKI occurs frequently in critically ill patients. Patients with AKI, including those who require KRT, experience multiple pharmacokinetic and pharmacodynamic perturbations that dynamically influence medication effectiveness and safety. Patients with AKI may experience both subtherapeutic drug concentrations, which lead to ineffective therapy, and suprathreshold drug concentrations, which increase the risk for toxicity. In critically ill patients with AKI not requiring KRT, conventional GFR estimation equations, especially those based on serum creatinine, have



Impact of dynamic AKI course on medication dosing in the critically ill patients

A
 SCr 0.7 mg/dl
 eGFR 94 ml/min
 True GFR ~90 ml/min
 Assessment: Similar

B
 SCr 1.0 mg/dl
 eGFR 66 ml/min
 True GFR ~30 ml/min
 Assessment: Potential overdose, toxicity

C
 SCr 2.5 mg/dl
 eGFR 26 ml/min
 True GFR ~25 ml/min
 Assessment: Similar

D
 SCr 2.0 mg/dl
 eGFR 33 ml/min
 True GFR ~60 ml/min
 Assessment: Potential underdose, ineffective

Behal ML. CJASN, 2023

Medication Management in AKI

- Cr exhibits a 48–72 hours **lag time...**
- The so-called **“creatinine-blind”** period...

Approach to medication dosing in critically ill patients with AKI with or without the use of KRT

Consider benefit of medication given the indication vs. risks of systemic toxicity



Recommend appropriate first dose



Consult primary literature, package inserts, tertiary references



AKI (no KRT)



Rapid recovery expected (<24 h?)

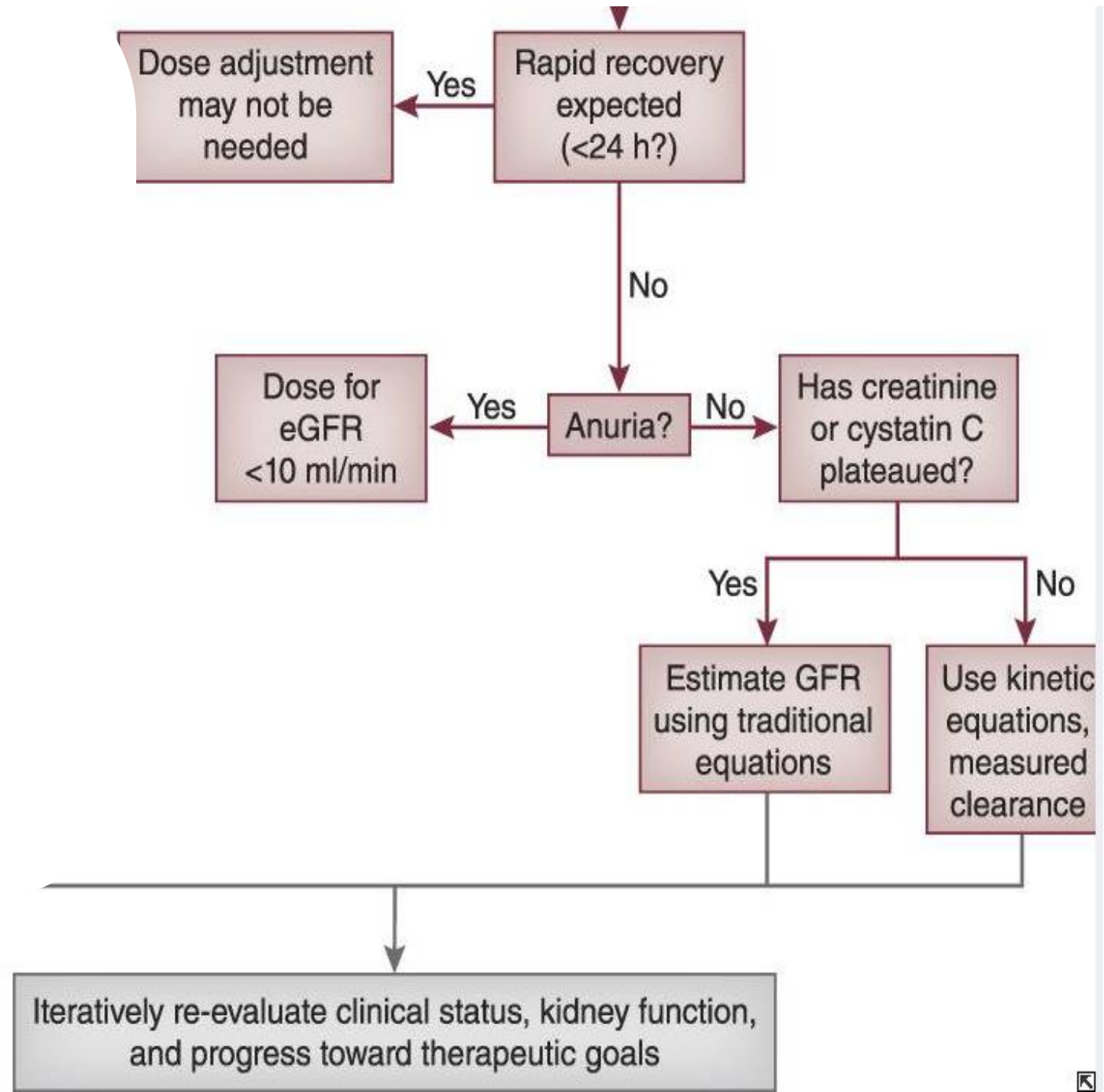
Yes

Dose adjustment may not be needed

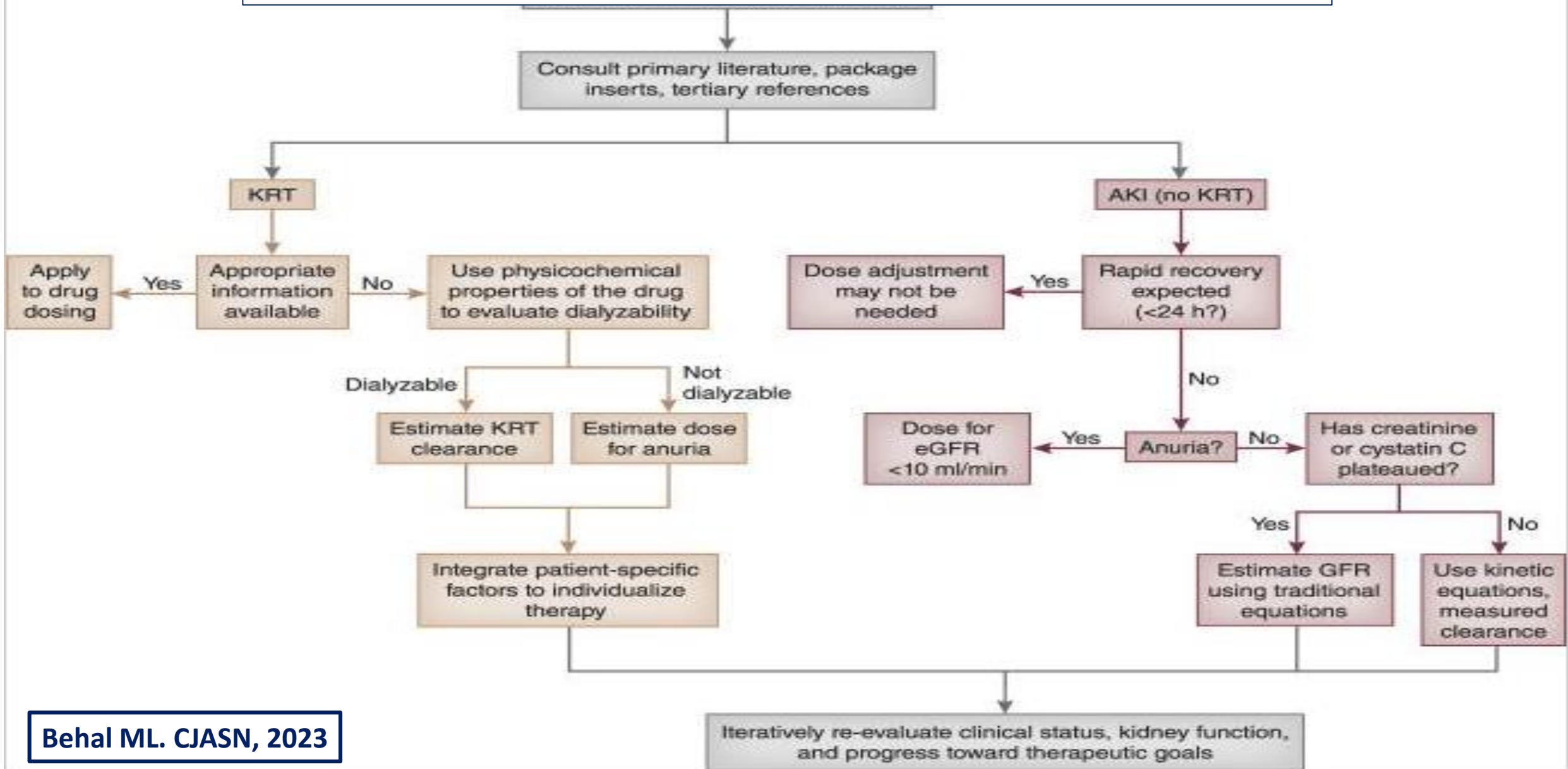


Approach to medication dosing in critically ill patients with AKI with or without the use of KRT

Behal ML. CJASN, 2023



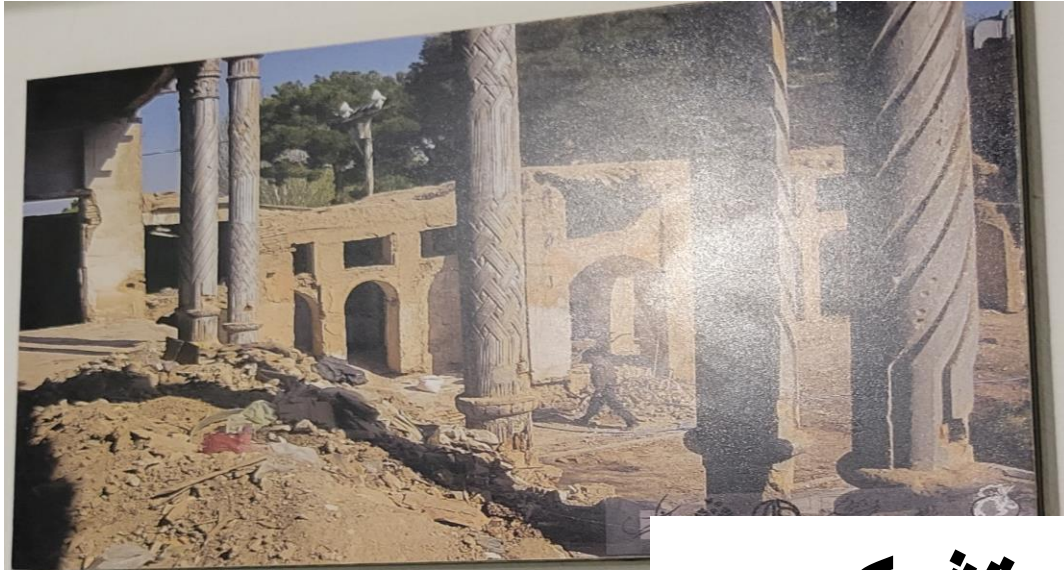
Approach to medication dosing in critically ill patients with AKI with or without the use of KRT



Conclusion

Today, the **direct measurement of GFR** in AKI is performed in clinical research, not in routine practice, but in the future, if technically feasible, & if a therapeutic intervention becomes available, it may be required at the early infra-clinic phase.

Luque Y. NDT. 2020



از توجه شما متشکرم

