GFR Calculation

Hello everyone, welcome to our series exploring the connection between Chronic Kidney Disease and cardiovascular disease. In this video, we'll delve into one of the most crucial aspects of CKD diagnosis and management – the measurement of Glomerular Filtration Rate, or GFR.

One of the most important steps in identifying CKD is getting an accurate measurement of the GFR. The most precise way to measure GFR is to use an exogenous substance like inulin or iothalamate iodine isotopes, which are freely filtered and not reabsorbed or secreted in the kidney.

GFR is equal to the clearance of these substances over a given time. Despite being the most accurate measurement, exogenous substances are rarely used in clinical practice because this method is more expensive and time-intensive than using endogenous markers.

For decades, the gold standard for estimating GFR in clinic utilized serum creatinine levels. Creatinine is a natural byproduct of the breakdown of creatine in the body and is freely filtered in the glomerulus.

Creatinine is slightly secreted in the distal convoluted tubule, and this is accounted for in the GFR estimation formula. Problems can sometimes arise when a drug inhibits this secretion, which affects the accuracy of the GFR calculation.

Cystatin C is an alternative endogenous marker for estimating GFR. It is produced by all nucleated cells at a constant rate but is not secreted in the distal tubule like creatinine. Cystatin C levels are not influenced by protein intake or muscle mass, potentially providing a more reliable estimate of GFR for different groups of people.

Creatinine levels can be increased in patients with high protein intake, high muscle mass, or rhabdomyolysis. Cystatin C levels are generally as stable as creatinine but can be elevated in patients with advanced age, hyperthyroidism, or high-inflammatory states. Changes in serum creatinine or cystatin C must be noted, as they can impact GFR estimation. Additionally, cystatin C testing has become more cost-effective and widely available in recent years, and many insurance companies now cover it for use in clinical practice.

Factors Increasing Serum Creatinine (Sc) Levels	Factors Increasing Serum Cystatin C (CysC) Levels
High muscle mass	Advanced age
High protein intake	Inflammatory markers (C-reactive protein)
Rhabdomyolysis	Glucocorticoid therapy
	Hyperthyroidism
	Malignancy

Previous eGFR calculation formulas, such as those developed in the MDRD and CKD-EPI studies, included race as a surrogate marker to improve statistical precision. However, a clear biological explanation for the association between African American race and variations in GFR and serum creatinine concentration is still lacking.

MDRD	$GFR = 175 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$
CKD-EPI	$GFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times (1.018 \text{ if female}) \times (1.159 \text{ if African American})$

*S_{cr} is serum creatinine in mg/dL
κ is 0.7 for females and 0.9 for males
α is -0.329 for females and -0.411 for males
min indicates the minimum of S_{cr}/κ or 1
max indicates the maximum of S_{cr}/κ or 1

The 2009 CKD-EPI equation for GFR included an adjustment factor for race, but this introduced new inaccuracies and perpetuated disparities. The use of a race coefficient in the equation does not account for the diversity among self-identified African Americans. The adjustment was often applied based on appearance or social identity rather than specific genetic variations that might impact creatinine levels.

African-Americans with CKD often have poor outcomes regarding hypertension management, dialysis treatment, and access to kidney transplantation compared to other racial groups. Despite having a comparably low rate of CKD, African Americans with CKD experience an increased incidence of end-stage kidney disease compared to the general population. This disparity is partially because many black patients receive an inflated eGFR calculation due to the adjustment for race, which can impact their course of treatment.

The 2021 CKD-EPI guidelines are currently seen as the most accurate way to calculate eGFR and do not include an adjustment for race. The formulas were developed with the goal of providing a more accurate and equitable assessment of kidney function across different populations. This change is part of a broader effort to reduce racial inequities in healthcare.

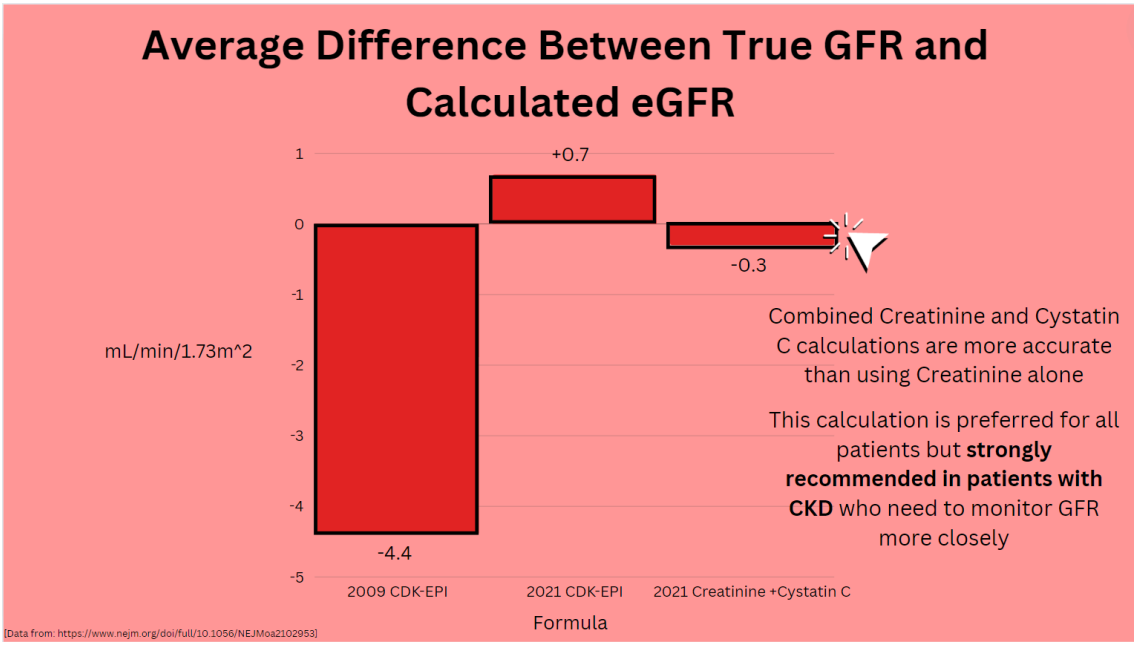
$$eGFR_{Cr} = 142 \times \min(S_{Cr}/\kappa)^{\alpha} \times \max(S_{Cr}/\kappa)^{-1.200} \times 0.9938^{age(years)}$$

S_{Cr} *is serum creatinine in mg/dL (minimum SCr/ is 1.0)*
κ *= 0.7 (females) or 0.9 (males)*
α *= -0.241 (female) or -0.302 (male)*
Results are multiplied by 1.018 for women

$$eGFR_{Cr-Cys} = 135 \times \min(S_{Cr}/\kappa)^{\alpha} \times \max(S_{Cr}/\kappa)^{-0.544} \times \min(S_{Cys}/0.8)^{-0.323} \times \max(S_{Cr}/\kappa)^{-0.778} 0.9961^{age(years)}$$

[Multiply by 0.963 if female]
where:
S_{cr} *= standardized serum creatinine in mg/dL*
κ *= 0.7 (females) or 0.9 (males)*
α *= -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*
S_{cys} *= standardized serum cystatin C in mg/L*

While both equations are widely accepted in clinical practice, **the equation utilizing both creatinine and cystatin C shows greater accuracy and is preferred in patients with end-stage renal disease**, where small changes in eGFR can impact the course of treatment. eGFR calculations utilizing creatinine alone are sufficient to monitor patients with adequate kidney function, but its use is decreasing as cystatin C testing becomes more available.



The European Kidney Function Consortium updated its GFR calculation in 2021. It uses only creatinine and has a more thorough adjustment for age, but does not differentiate for race . Overall, it shows comparable accuracy to the 2021 CKD-EPI formula.

$$eGFR = 107.3\, x \left(\frac{S_{Cr}}{Q}\right)^{-0.322} \quad if\ serum\ creatinine < Q$$

$$eGFR = 107.3\, x \left(\frac{S_{Cr}}{Q}\right)^{-1.132} \quad if\ serum\ creatinine > Q$$

$$S_{Cr} = serum\ creatinine$$

Q = 80μmol/L (0.90mg/dL) for males > age 25 and 62μmol/L (0.70 mg/dL) for females > age 25

For men aged 18-25, $\ln(Q) = 3.200 + 0.259 \times Age - 0.543 \times \ln(Age) - 0.00763 \times Age^2 + 0.0000790 \times Age^3$

For women aged 18-25, $\ln(Q) = 3.080 + 0.177 \times Age - 0.223 \times \ln(Age) - 0.00596 \times Age^2 + 0.0000686 \times Age^3$

Multiply the total by $0.990^{(age-40)}$ if over age 40

Calculating an accurate eGFR using the 2021 CKD-EPI equation can vastly improve patient outcomes by improving diagnosis and preventing unnecessary medical interventions, which can put strain on the healthcare system. For many patients, the relatively small inaccuracy still present in the most updated creatinine GFR calculation may not change their CKD categorization. However, the more accurate combined Creatinine/Cystatin C calculation has the potential to improve care, particularly for vulnerable populations and those with severely compromised kidney function.

Thanks for watching. Don't forget to follow for more videos on CKD and its management. See you next time!

Vocabulary:

- **Creatinine:** A byproduct of creatine breakdown in muscle fibers that is used as an endogenous marker for kidney function
- **Cystatin C:** A protein produced by all nucleated cells at a constant rate which is used as an alternative endogenous marker of kidney function
- **Rhabdomyolysis:** A condition where rapid muscle breakdown causes a massive release of muscle proteins, electrolytes, and other cellular contents into the bloodstream
- **Glucocorticoid therapy:** Glucocorticoids are a subtype of corticosteroid drugs that are primarily used to treat autoimmune or inflammatory conditions

References:

Ahmed, S. et al. (2020). *Examining the potential impact of race multiplier utilization in estimated glomerular filtration rate calculation on African-American care outcomes*. Journal of General Internal Medicine, 36 (2), 464-471.

Atiquzzaman, M. et al. (2024). *Implications of Implementing the 2021 CKD-EPI Equation Without Race on Managing Patients With Kidney Disease in British Columbia, Canada.* Kidney International Reports, 9 (4), 830-842.

CKD-EPI Creatinine Equation (2021). (2024, March 8). National Kidney Foundation. https://www.kidney.org/content/ckd-epi-creatinine-equation-2021

eGFR using CKD-EPI (Creatinine-Cystatin C) Equation (2021). (n.d.). https://reference.medscape.com/calculator/863/egfr-using-ckd-epi-creatinine-cystatin-c-equation-2021

Inker, L. et al. (2021). *New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race.* New England Journal of Medicine, 385, 1737-1749.

Ma, Y. et al, (2023). Validation of the European Kidney Function Consortium Equation in Chinese Adult Population: An Equation Standing on the Shoulders of Predecessors. Nephron, 148 (2), 63-73.

Merchant, P. et al. (2023). *The new GFR equations: How will eliminating the race coefficient affect Black patients?* Cleveland Clinic Journal of Medicine, November 2023, 90 (11) 685-691.

Mohottige, D. et al. (2023). *Use of Race in Kidney Function Estimation: Lessons Learned and the Path Toward Health Justice.* Annual Review of Medicine, 27 (74), 385-400.