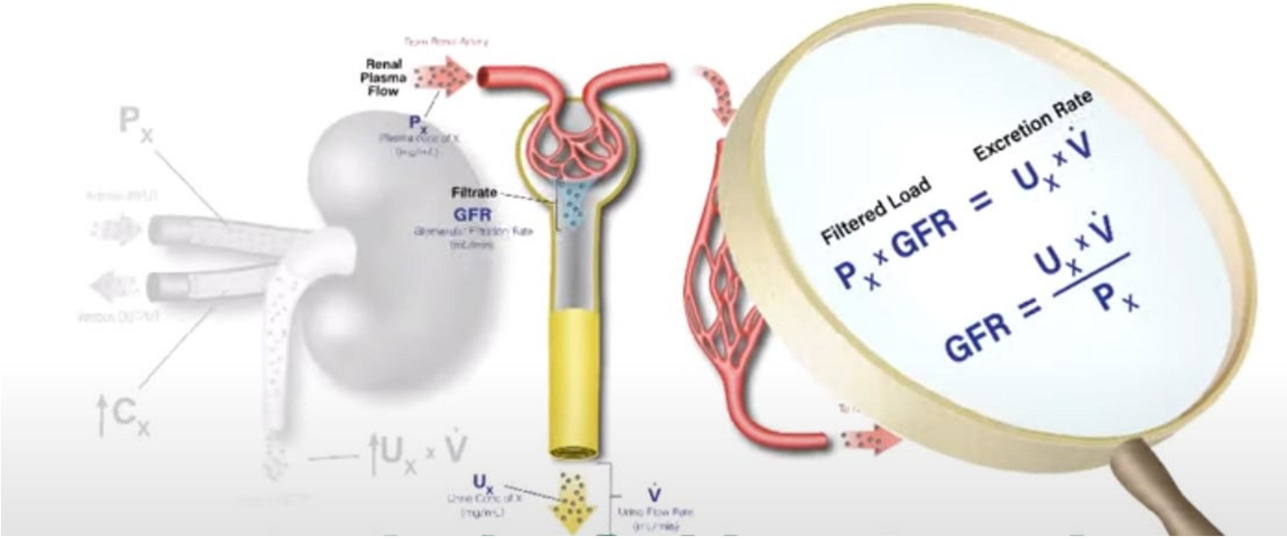
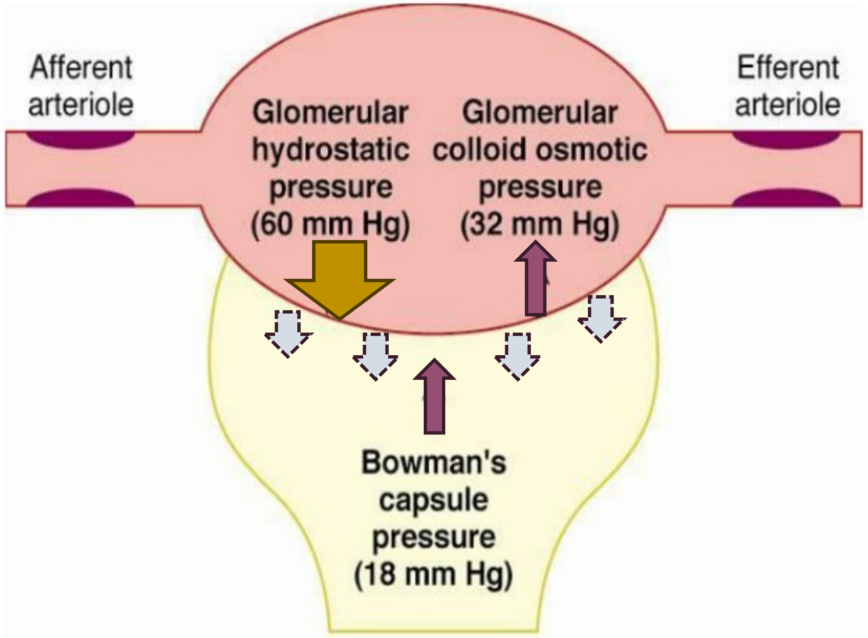
Spreading Knowledge – Improving Outcomes

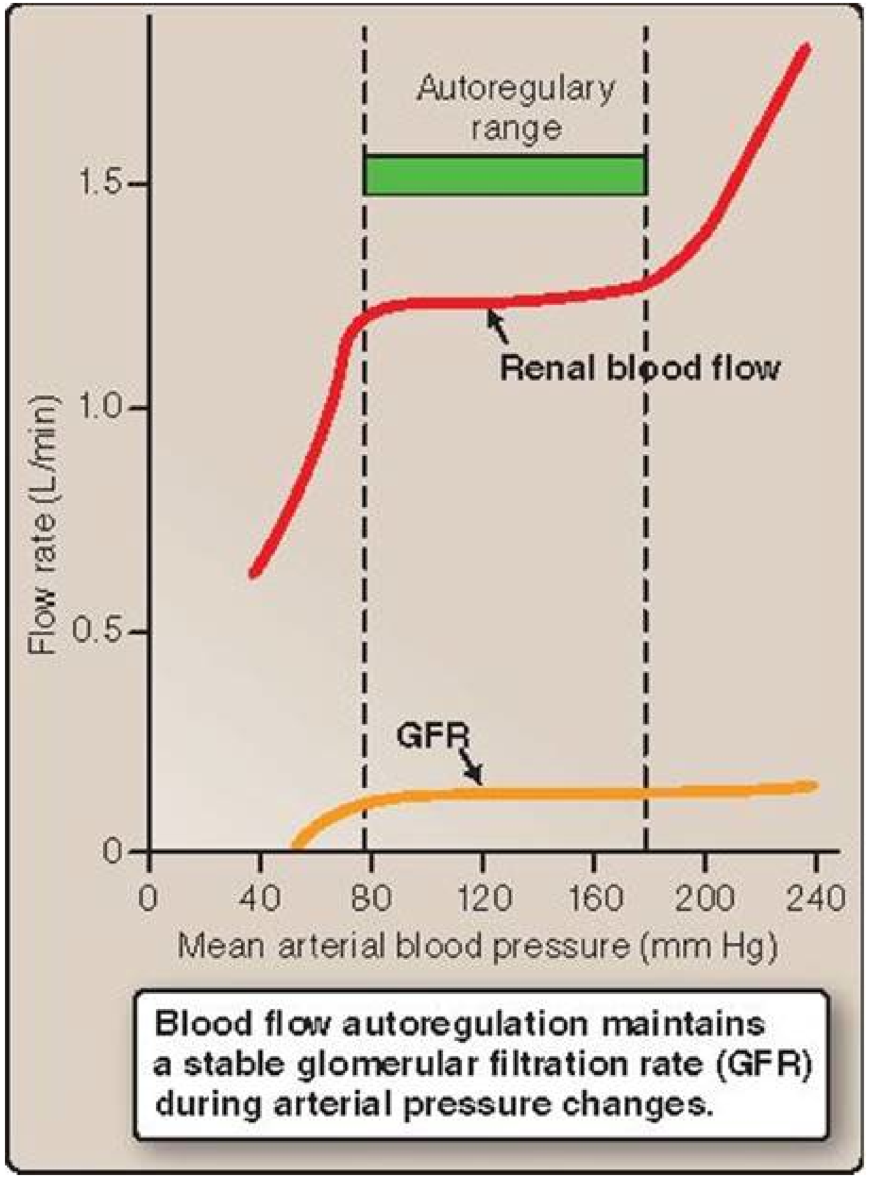


Renal Clearance in the ICU

Determinants of Glomerular Filtration Rate

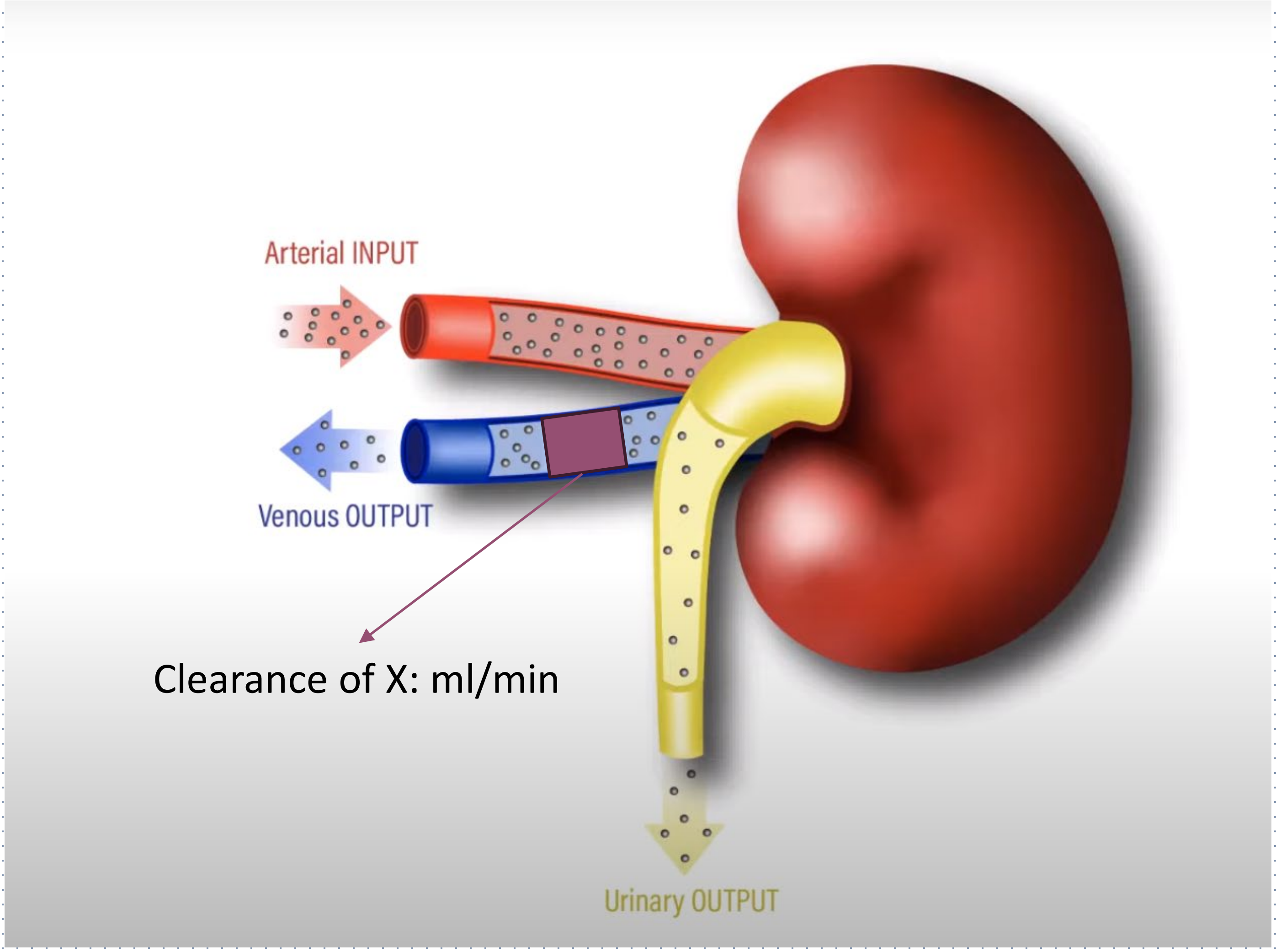


Net Filtration Pressure	=	Glomerular Hydrostatic Pressure	-	Bowman's Capsule Pressure	-	Glomerular Oncotic Pressure
10 mm Hg		**60 mm Hg**		**18 mm Hg**		**32 mm Hg**



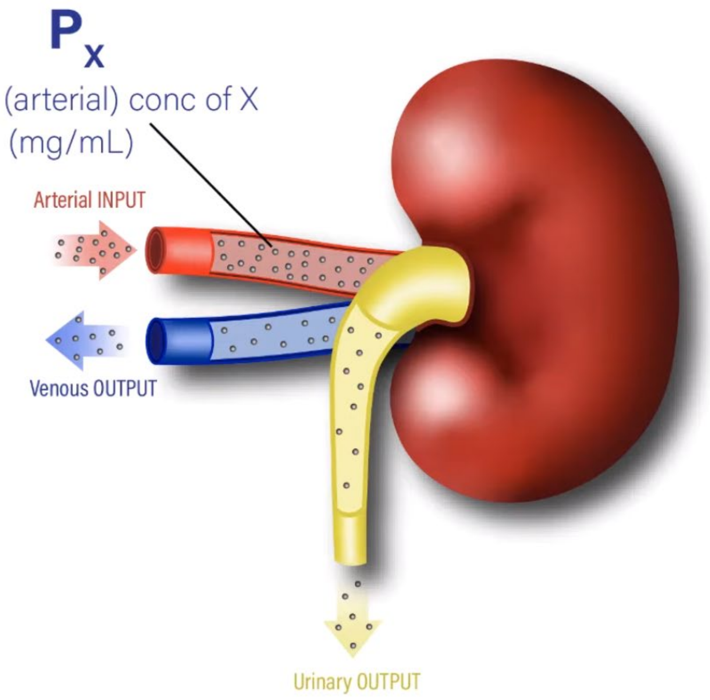
Blood Flow Autoregulation

What is Renal Clearance?



The volume of plasma that is completely cleared of a substance by the kidney per unit time

Input = Output

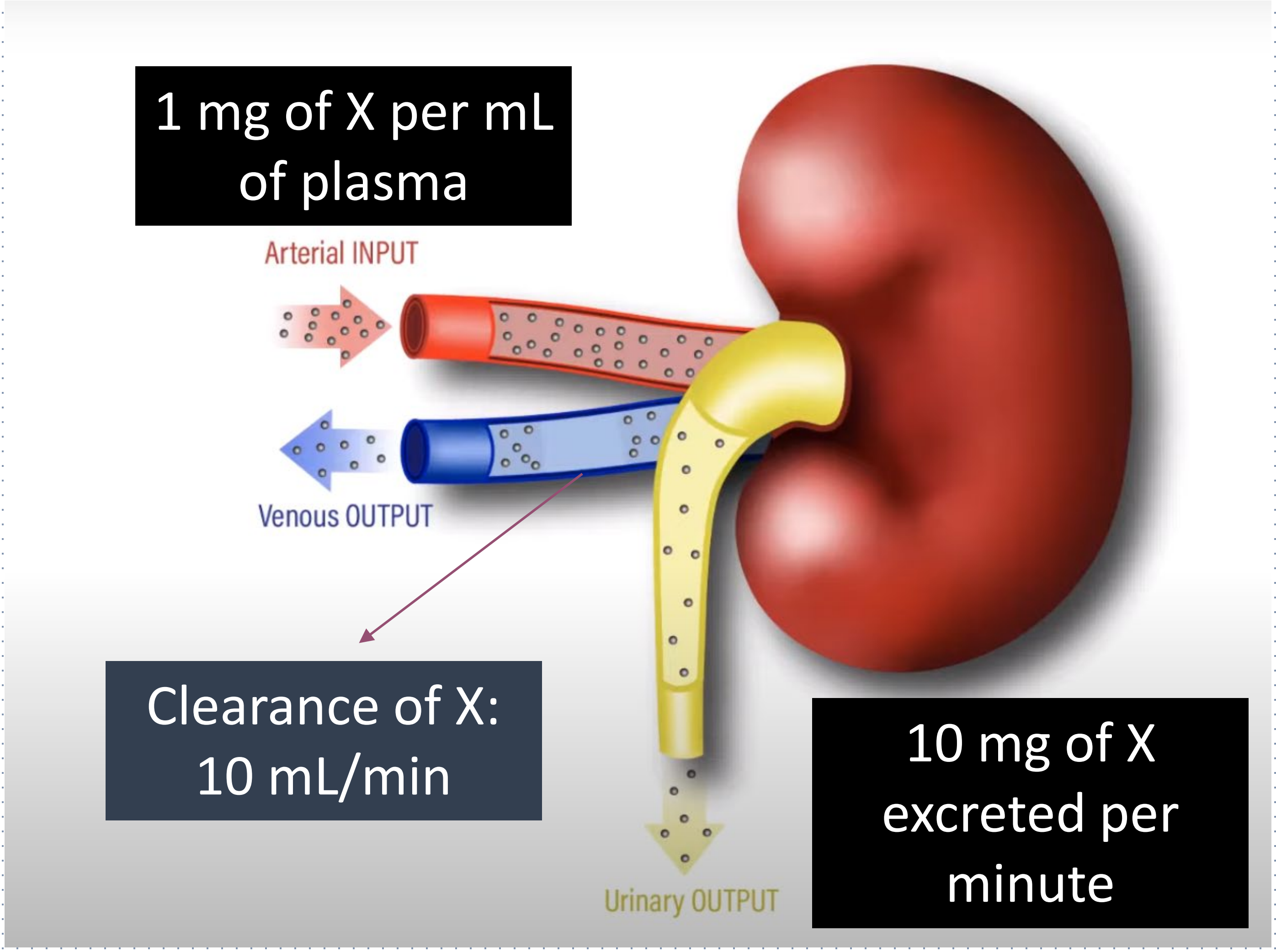


Entering Kidneys — **Leaving Kidneys**

Arterial INPUT = Venous OUTPUT + Urinary OUTPUT

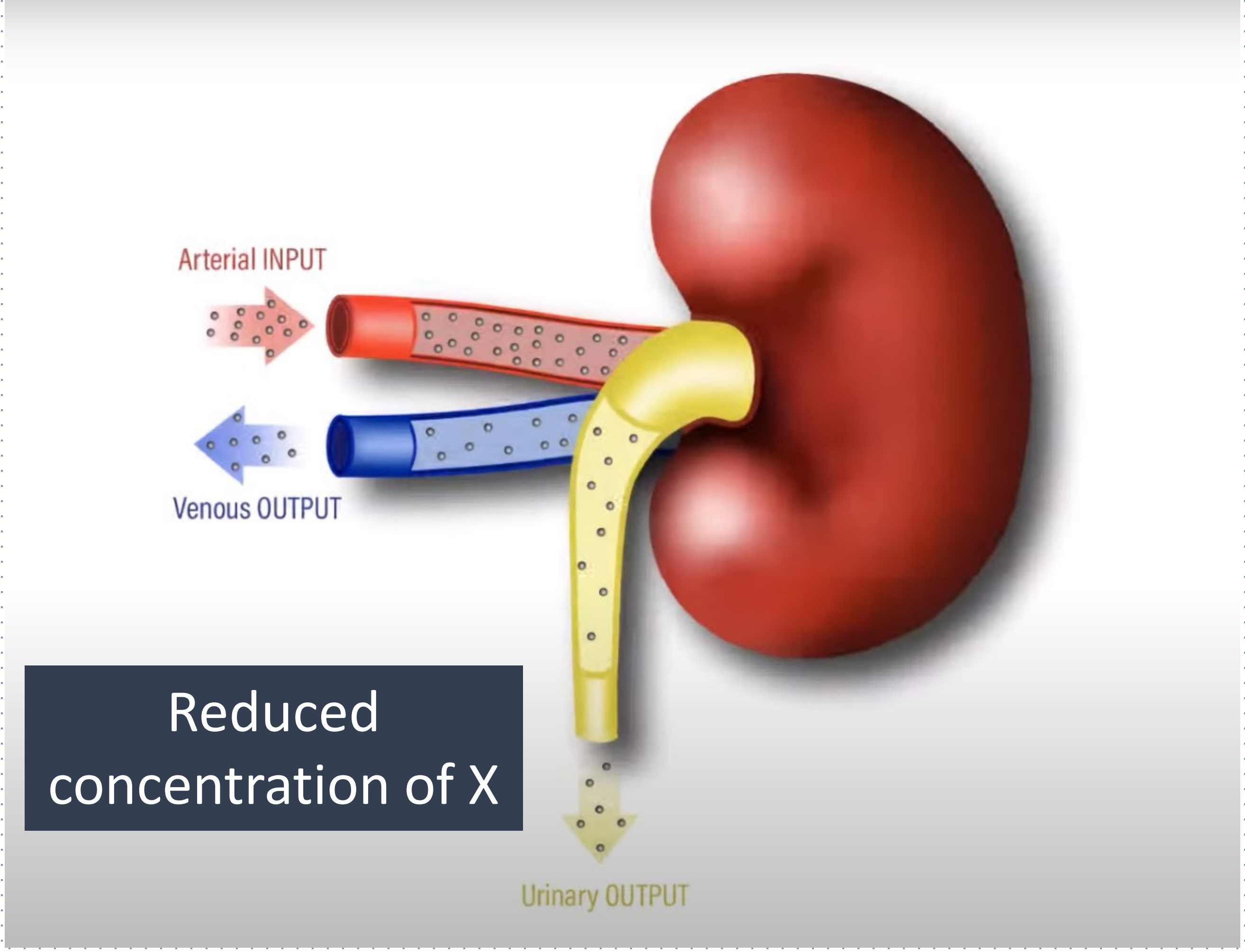
Assuming the kidney neither produce or metabolize substance X

Renal Clearance of X



Every one minute, there will be 10 mL of plasma completely devoid of substance X

Renal Clearance of X



Reduced concentration of X

Renal Clearance Formula

$$P_x \, X \, Cx = Ux \, X \, \dot{V}$$

$$C_x = \frac{U_x \, X \, \dot{V}}{P_x}$$

U_x : Urinary concentration of X (mg/mL)

V : Urinary volume (mL/min)

P_x : Plasma concentration of X (mg/mL)

C_x : Clearance rate of X (mL/min)

Renal Clearance Formula

$$C_x = \frac{U_x \, X \, \dot{V}}{P_x}$$

$$C_x = \frac{10 \, mg/mL \; X \; 1 \, \dot{m}L}{1 \, mg/mL}$$

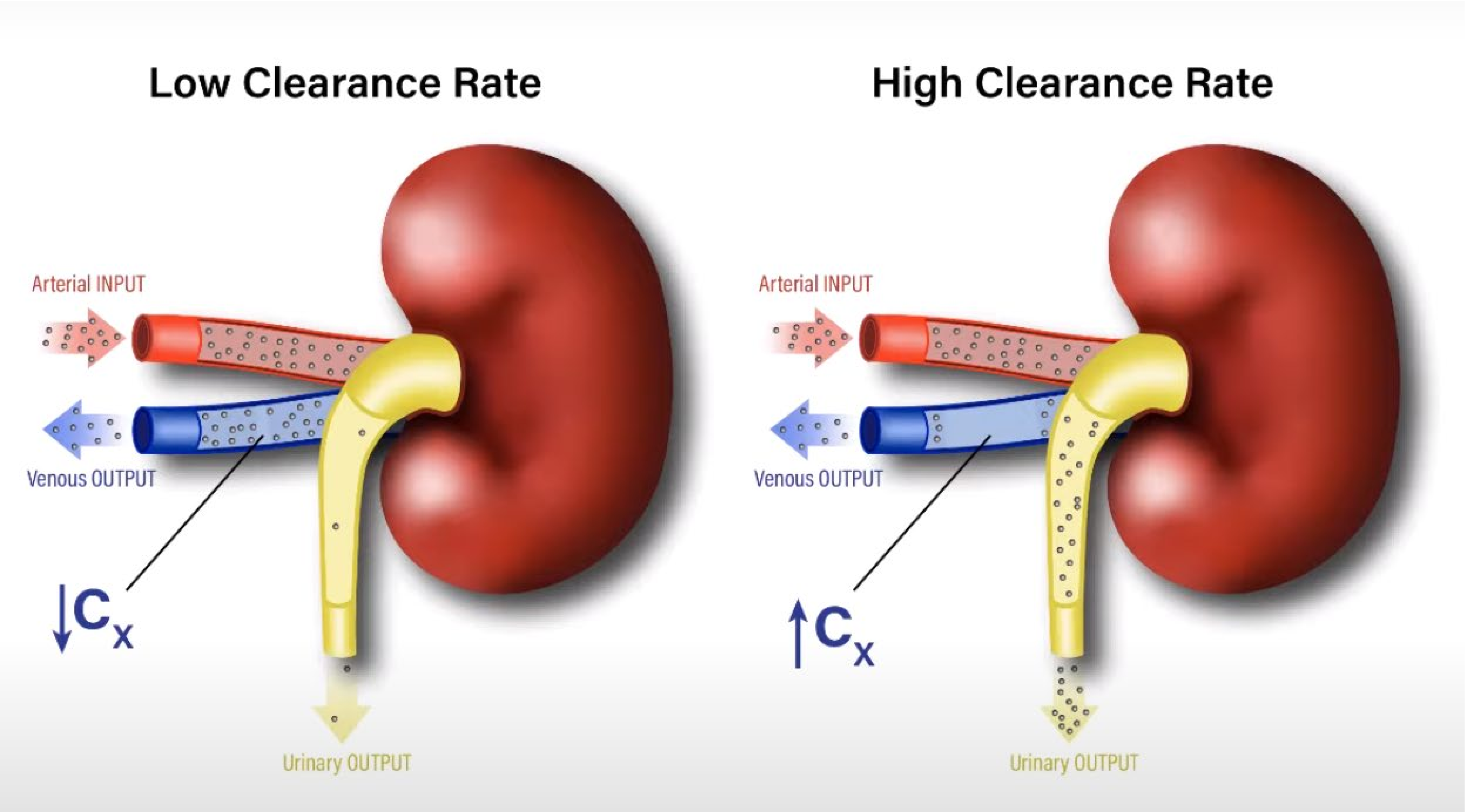
U_x : Urinary concentration of X (mg/mL)

V: Urinary volume (mL/min)

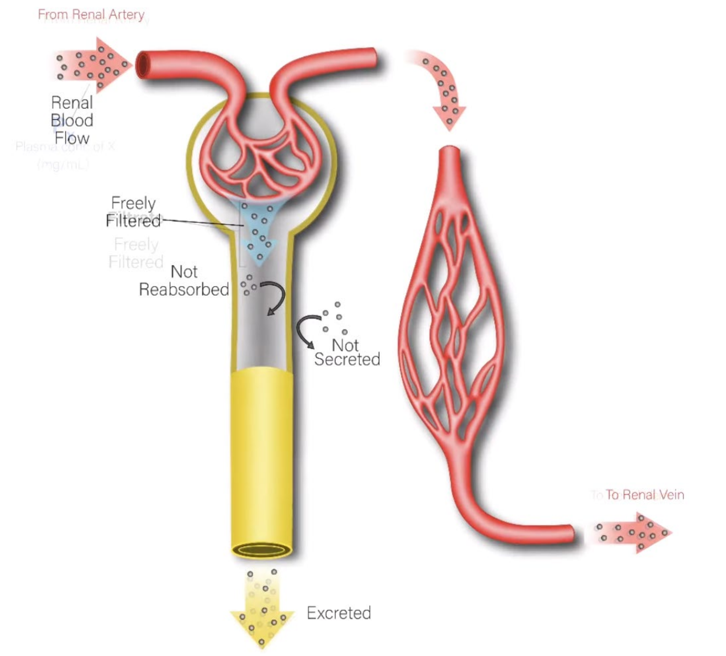
P_x : Plasma concentration of X (mg/mL)

C_x : Clearance rate of X (mL/min)

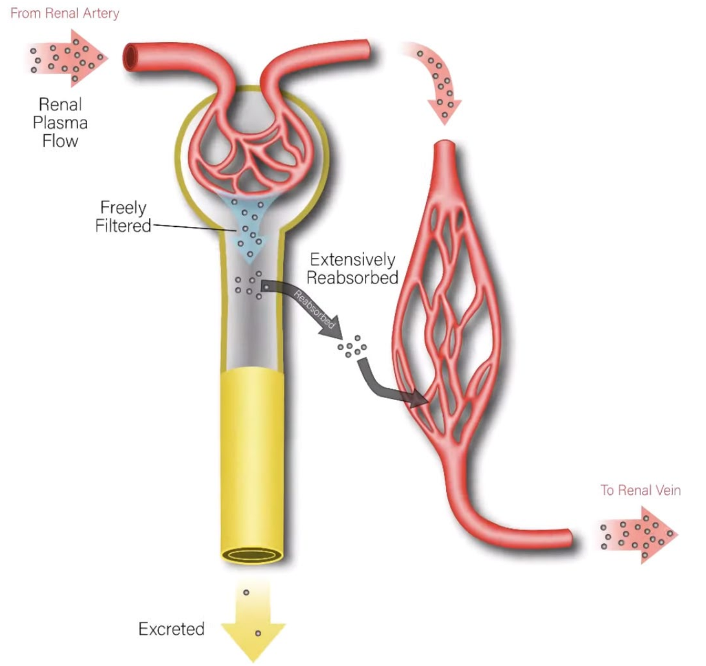
Renal Clearance Rate



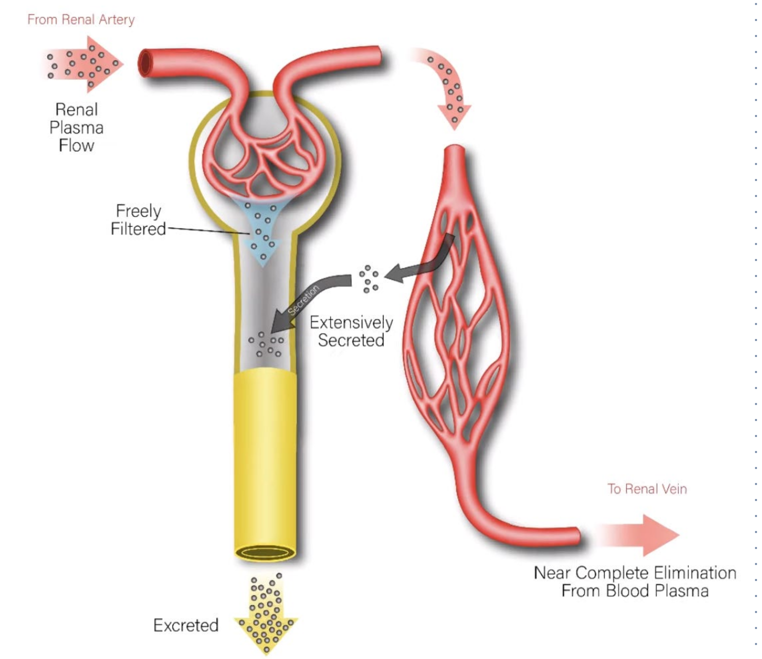
What Determines Renal Clearance Rates?



Moderate Clearance Rate
Creatinine



Low Clearance Rate
Glucose/Inulin



High Clearance Rate
Para-aminohippuric Acid

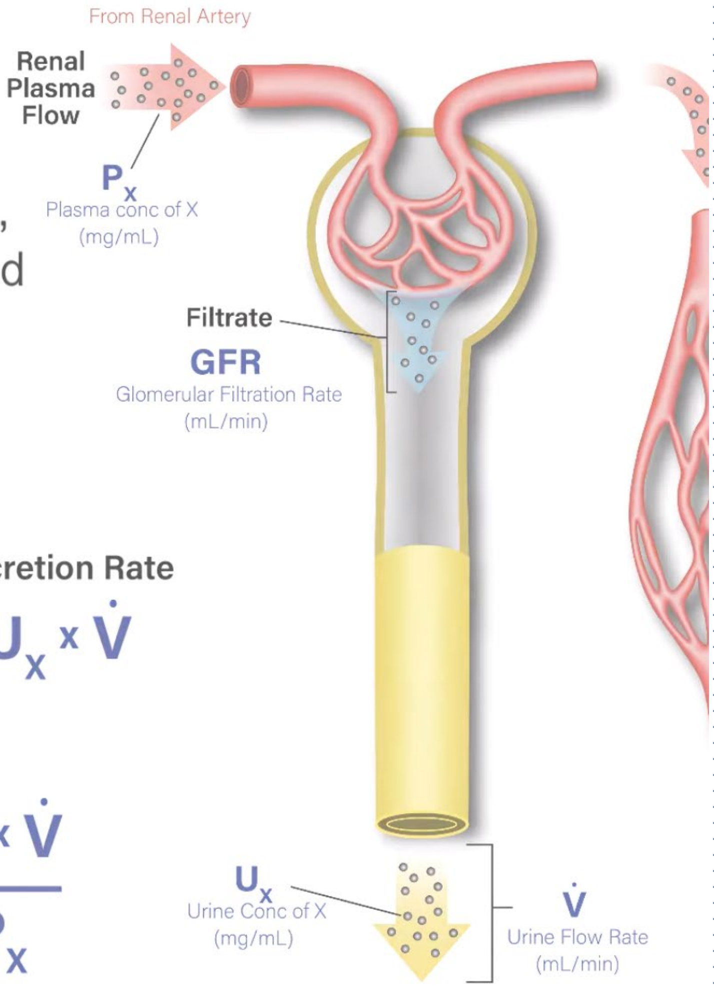
Glomerular Filtration Rate

IF: Freely filtered, neither reabsorbed nor secreted

THEN:

Filtered Load		Excretion Rate
$P_X \times GFR$	=	$U_X \times \dot{V}$

$$GFR = \frac{U_X \times \dot{V}}{P_X}$$



Factors Affecting Estimating GFR in ICU setting

Fluctuations of serum creatinine over time:
- Non-steady state

Fluid balance variations:
- Under or over estimation of creatinine level

Fluctuating renal hemodynamics:
- Augmented renal clearance

Change in oncotic pressure due to low albumin
- Increased filtration rate

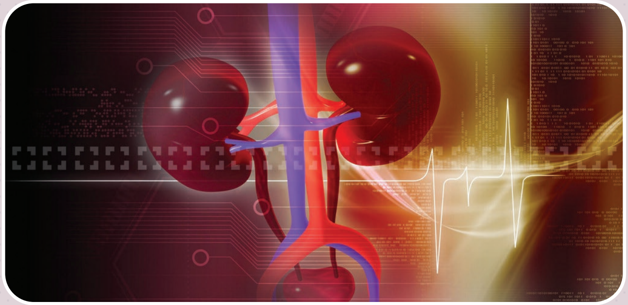
Commonly used creatinine-based equations are flawed in the critical care setting. Ideal methods like inulin clearance become impractical in an ICU setup

24-h urine collection is not practical

Both overdosing and underdosing are problems when GFR could not be estimated close to accuracy

Estimation of CrCl

Steady State Chronic Renal Failure



Cockcroft-Gault Formula

(140 – Age in years) × Body weight in kg/72 × Serum creatinine in mg/dl x 0.85 if female

The 4-variable MDRD

$186 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ if female

The 6-variable MDRD

$170 \times (\text{serum creatinine})^{-0.999} \times (\text{age})^{-0.176} \times (\text{BUN})^{-0.170} \times (\text{Alb}) + 0.318$

Inaccurate estimation of GFR in a non-steady state (AKI and critically ill patients)

Jelliffe's Equation

Relatively accurate estimation of GFR in a non-steady state as in AKI requires timed urine collections, which is not always practically possible in a critically ill patient, To overcome this, Jelliffe introduced an equation in 2002:

Estimated GFR = {(Volume of distribution × (Serum creatinine on day 1 – Serum creatinine on day 2)) + Creatinine production} 100/1,440/Average serum creatinine

Creatinine production

[29.305 – (0.203 × age)] × weight × [1.037 – (0.0338 × average Cr)] × correction for gender (0.85 for males and 0.765 for females).

Dynamic changes in creatinine

Creatinine is a hydrosoluble substance and its concentration changes with fluctuations in total body water

? Fluid balance variation

Volume of distribution: 0.4× weight (kg) × 10.
Body weight is defined as initial hospital admission weight.

When sCr rises, sCr on Day 2 is used instead of average sCr.

Modified Jelliffe's Equation

Relatively accurate estimation of GFR in a non-steady state as in AKI requires timed urine collections, which is not always practically possible in a critically ill patient, To overcome this, Jelliffe introduced an equation in 2002:

Estimated GFR = {(Volume of distribution × (Adjusted serum creatinine on day 1 − Adjusted serum creatinine on day 2)) + Creatinine production} 100/1,440/Average serum creatinine

Creatinine production mg/day

[29.305 − (0.203 × age)] × weight in kg × [1.037 − (0.0338 × average Cr)] × correction for gender (0.85 for males and 0.765 for females).

Dynamic changes in creatinine

Adjusted Creatinine for Fluid Balance

Adjusted creatinine=sCr × correction factor
Correction factor=[hospital admission weight (kg) ×0.6 + ∑ (daily fluid balance)]/hospital admission weight × 0.6.

Volume of distribution: 0.6× weight (kg) × 10.
Body weight is defined as initial hospital admission weight.

When sCr rises, sCr on Day 2 is used instead of average sCr.

Chronic kidney disease-epidemiology (CKD-EPI) equation in critically ill patients

CKD-EPI GFR = 141 x min(serum creatinine/k,1)$^{\alpha}$ x max(serum creatinine/k,1)$^{-1.209}$ x 0.993^{age} x 1.018(if female) x (1.159 if black)

Where k is 0.7 for females and 0.9 for male patients
a is −0.329 for female patients and −0.411 for male patients
min indicates the minimum of creatinine/k or 1
max indicates the maximum of creatinine/k or 1)

Needs to be further validated in clinical settings

Cystatin C

Cystatin C is a non-glycosylated protein produced by all nucleated cells at a constant rate.

Its constant rate of production, low molecular weight of 13 kDa, and positive charge at physiological pH makes it a suitable marker for glomerular filtration.

It is reabsorbed and almost completely catabolized in the proximal tubule.

It is found in relatively high concentrations in many body fluids, especially in the seminal fluid, cerebrospinal fluid, and synovial fluid

It has extreme sensitivity to small changes in GFR and higher diagnostic accuracy than creatinine in estimating GFR

Its concentration is least affected by infections, malignancies, steroid therapy, inflammatory disorders, and muscle mass (no adjustment with age or gender)

Estimating GFR from Cystatin C

Grubb's equation: GFR = $83.93 \times \text{Cystatin C}^{-1.676}$

Crit Care. 2005; 9(2):

PMCID: PMC1175926

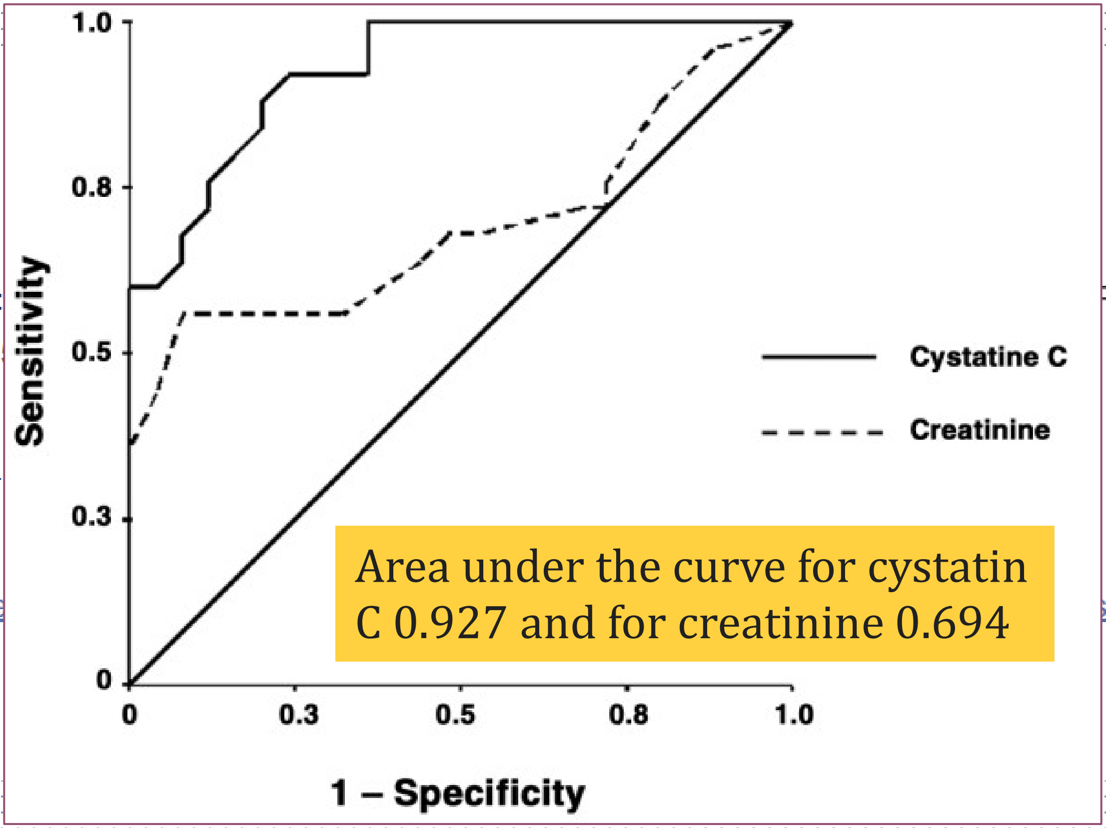
Published online 200

PMID: 15774046

Serum cystatin ... in critically ill patients

Patricia Villa,[1] Manue ...[2]

▸ Author information



Area under the curve for cystatin C 0.927 and for creatinine 0.694

Nephrol Dial Transplant (2010) 25: 102–107
doi: 10.1093/ndt/gfp392
Advance Access publication 13 August 2009

Comparison of methods for estimating glomerular filtration rate in critically ill patients with acute kidney injury

Josée Bouchard[1], Etienne Macedo[1], Sharon Soroko[1], Glenn M. Chertow[2], Jonathan Himmelfarb[3], Talat Alp Ikizler[4], Emil P. Paganini[5] and Ravindra L. Mehta[1] DM, FACP, FASN. Program to Improve Care in Acute Renal Disease (PICARD)

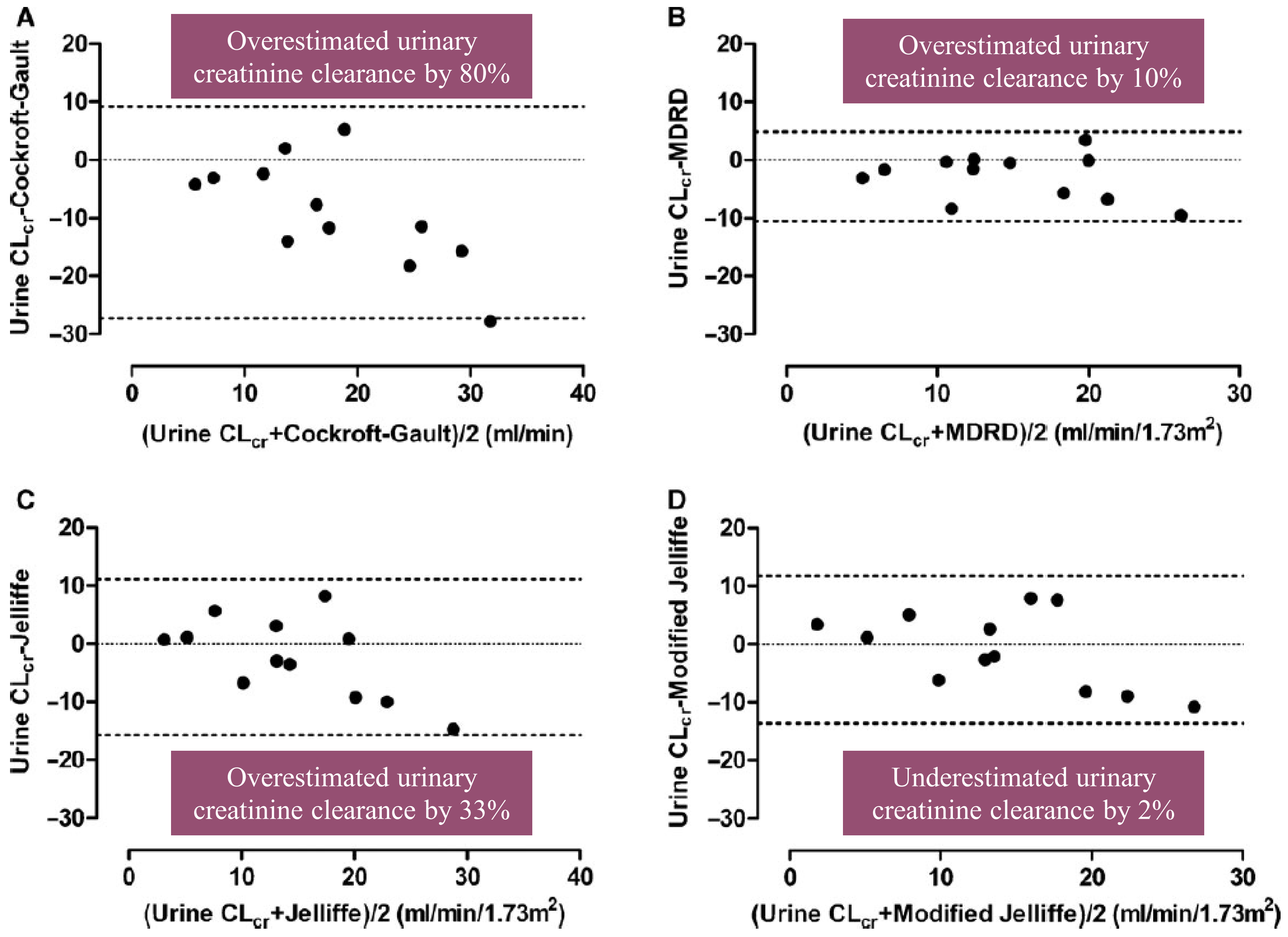


Fig. 1. Bland–Altman method between urine creatinine clearance and glomerular filtration rate estimated by the Cockcroft–Gault (A; mL/min), MDRD (B; mL/min/1.73 m^2), Jelliffe (C; mL/min/1.73 m^2) and Modified Jelliffe (D; mL/min/1.73 m^2) equations.

Bouchard J, et al. Nephrol Dial Transplant. 2010 Jan;25(1):102-7.

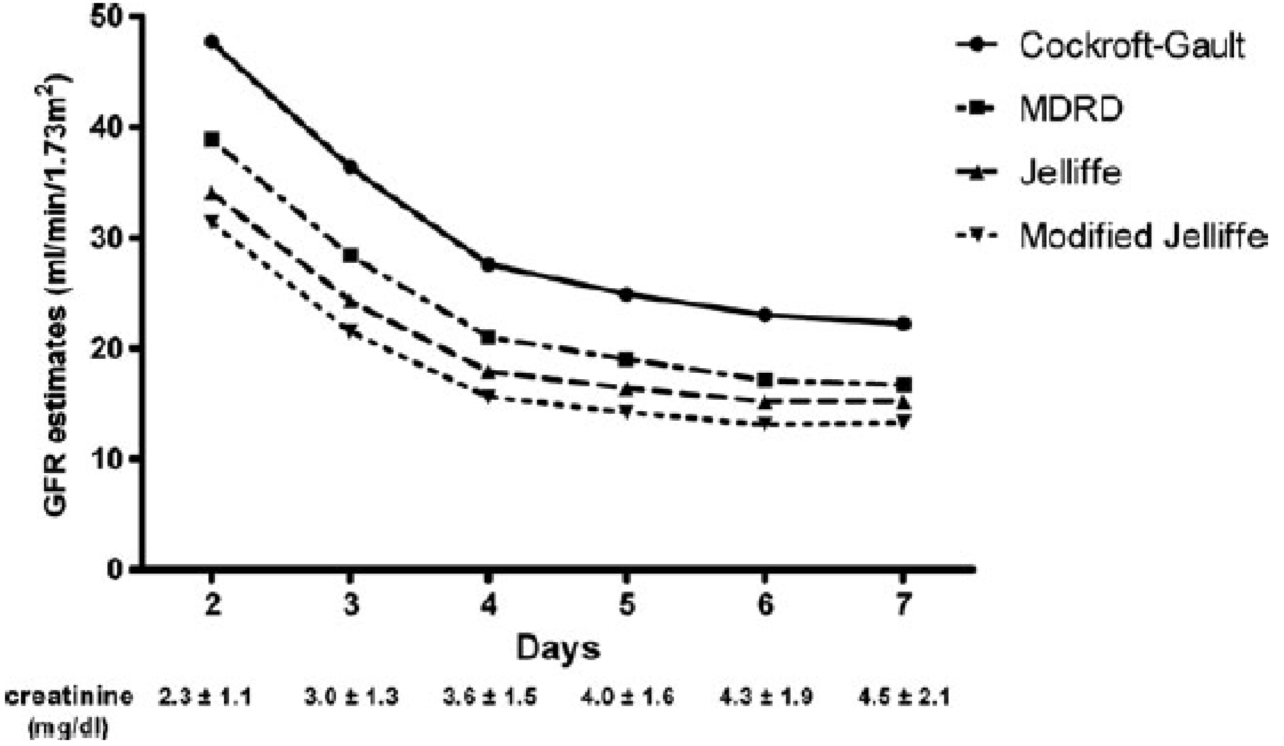


Fig. 2. GFR estimates by Cockcroft–Gault*, MDRD, Jelliffe and Modified Jelliffe equations.

The relative overestimation in Cockcroft–Gault GFR compared to Modified Jelliffe GFR estimates was higher at AKI diagnosis (16.3 mL/min) and decreased as kidney function declined over time (8.9 mL/min).

Bouchard J, et al. Nephrol Dial Transplant. 2010 Jan;25(1):102-7.

Augmented Renal Clearance

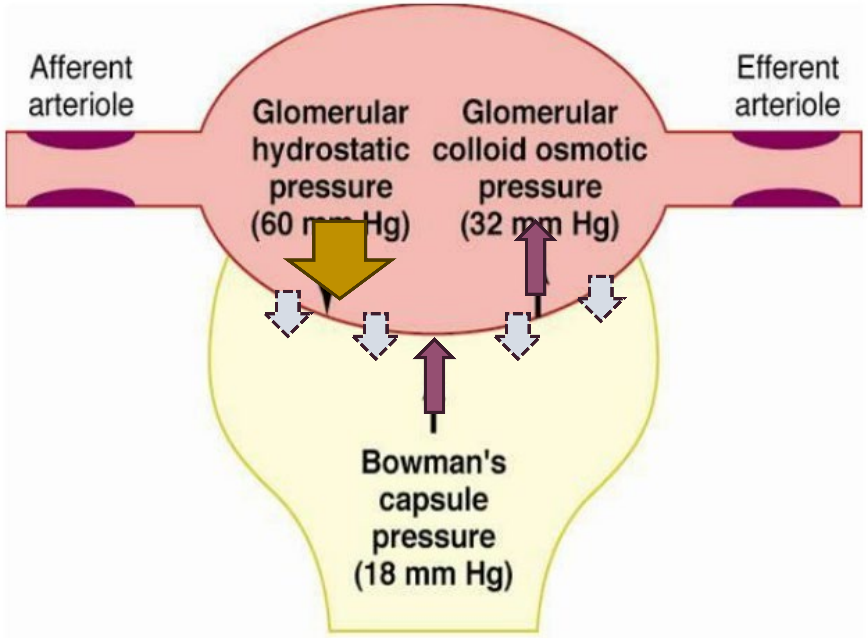
ARC is defined as estimated GFR > 130 ml/min

Demonstrated in patients with traumatic brain injury, burns, sepsis, surgery, and in ICU patients

- Younger patients
- Lower Acute Physiology And Chronic Health Evaluation (APACHE) II scores
- Higher diastolic blood pressures
- Higher urine output on the first morning of admission to the ICU

Cytokine release from acute injury, the innate immune and inflammatory responses to trauma, and aggressive fluid resuscitation may promote increased organ blood flow and enhanced excretory function.

Determinants of Glomerular Filtration Rate



Net Filtration Pressure	=	↑ Glomerular Hydrostatic Pressure	-	Bowman's Capsule Pressure	-	↓ Glomerular Oncotic Pressure
		Epinephrine Fluid resuscitation				Low albumin

In Summary

The issue of ARC should be considered to avoid improper dosing of drugs.

Cockcroft-Gault and 4-variable MDRD equations should better be avoided in ICU setup.

These methods could be employed in this order to estimate renal function and to provide instant and accurate results.

Cystatin C	Modified Jelliffe's	Jelliffe's	6-variable MDRD equations