

Chronic Kidney Disease and Perioperative Complications

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”CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health.”

1. Kidney Disease: Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, p. S126.

Classification of CKD (CGA)¹

- Cause
- GFR category G1 – G5
 - G1 (normal) = $\text{GFR} \geq 90 \text{ mL/min/1.73m}^2$
 - G2 (mildly decreased) = $\text{GFR } 60 - 89 \text{ mL/min/1.73m}^2$
 - G3a (mildly – moderately decreased) = $\text{GFR } 45 - 59 \text{ mL/min/1.73m}^2$
 - G3b (moderately to severely decreased) = $\text{GFR } 30 - 44 \text{ mL/min/1.73m}^2$
 - G4 (severely decreased) = $\text{GFR } 15 - 29 \text{ mL/min/1.73m}^2$
 - G5 (kidney failure) = $\text{GFR} < 15 \text{ mL/min/1.73m}^2$
- Albuminuria category A1 – A3 (albumin to creatinine ratio, ACR)
 - A1 (normal to mildly increased): $< 30 \text{ mg/g}$ (or 3 mg/mmol)
 - A2 (moderately increased): $30 - 300 \text{ mg/g}$ (or $3 - 30 \text{ mg/mmol}$)
 - A3 (severely increased): $> 300 \text{ mg/g}$ (or 30 mg/mmol)

Global Incidence of CKD¹

- 850 million people worldwide (2021)
 - Diabetes: 420 million
 - Cancer: 42 million
- 1.4 million deaths in 2019
 - 11th leading cause of death
- Significant cause of disability
- Only ~ 10% at high risk know their status

Why should we care?

Outcomes Associated with CKD¹

- all-cause mortality
- cardiovascular events
 - myocardial infarction
 - stroke
 - heart failure
- kidney-specific outcomes
 - progression to kidney failure
 - AKI
- all-cause hospitalization
- incident atrial fibrillation

*For this indication, estimate of GFR should be based on cystatin C or cystatin C + creatinine

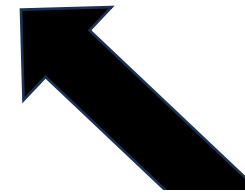
eGFR should NOT be based on race

But...how much is risk increased?

- 2024 KDIGO¹
 - Heat maps of relative risks
 - green = same risk
 - yellow → orange → red = significant risk
 - Matrix of eGFR v. albumin-creatinine ratio
 - Hazard ratio = relative risk of outcome v. control (1)

eGFR cr-cys

	Urine albumin-creatinine ratio, mg/g				Urine albumin-creatinine ratio, mg/g			
eGFRcr-cys	<10	10-29	30-299	300+	<10	10-29	30-299	300+
All-cause mortality: 11 cohorts								
105+					0.9	1.2	1.4	2.8
90-104	ref	1.3	1.5	2.0				
60-89	1.2	1.5	1.9	2.5				
45-59	1.7	2.2	2.5	3.3				
30-44	2.3	2.6	3.4	4.4				
<30	3.6	4.0	5.5	7.1				
Cardiovascular mortality: 11 cohorts								
105+					1.0	1.2	1.6	2.5
90-104	ref	1.3	1.5	2.0				
60-89	1.2	1.7	2.3	3.4				
45-59	1.9	2.7	3.2	4.6				
30-44	2.5	3.5	4.5	5.9				
<30	5.8	5.0	6.1	8.7				
Kidney failure with replacement therapy: 5 cohorts								
105+	0.6	0.8	2.3	10	0.9	1.2	1.7	3.7
90-104	ref	1.3	1.4	2.5				
60-89	5.8	13	25	73				
45-59	20	23	78	191				
30-44	111	261	343	580				
<30								
Acute kidney injury: 5 cohorts								
105+								
90-104								
60-89	1.6	2.5	2.9	5.3				
45-59	3.9	4.7	5.5	7.5				
30-44	5.8	7.0	8.4	10				
<30	11	12	12	21				
Hospitalization: 3 cohorts								
105+								
90-104								
60-89	1.1	1.2	1.3	1.6				
45-59	1.3	1.4	1.5	1.7				
30-44	1.5	1.5	1.6	2.1				
<30	1.8	2.0	2.1	3.0				
All-cause mortality: 10 cohorts								
105+					0.9	1.2	1.4	2.8
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30-44	2.3	2.6	3.4	4.4				
<30	3.6	4.0	5.5	7.1				
Stroke: 9 cohorts								
105+					1.0	1.2	1.6	2.5
90-104	ref	1.3	1.5	2.0				
60-89	1.2	1.7	2.3	3.4				
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45-59	3.9	4.7	5.5	7.5				
30-44	5.8	7.0	8.4	10				
<30	11	12	12	21				
Peripheral artery disease: 6 cohorts								
105+								
90-104								
60-89	1.1	1.2	1.3	1.6				
45-59	1.3	1.4	1.5	1.7				
30-44	1.5	1.5	1.6	2.1				
<30	1.8	2.0	2.1	3.0				



Urine albumin -
creatinine ratio

All mortality

MI

CV mortality

Stroke

Kidney failure

Heart failure

Little to no albuminuria!

AKI

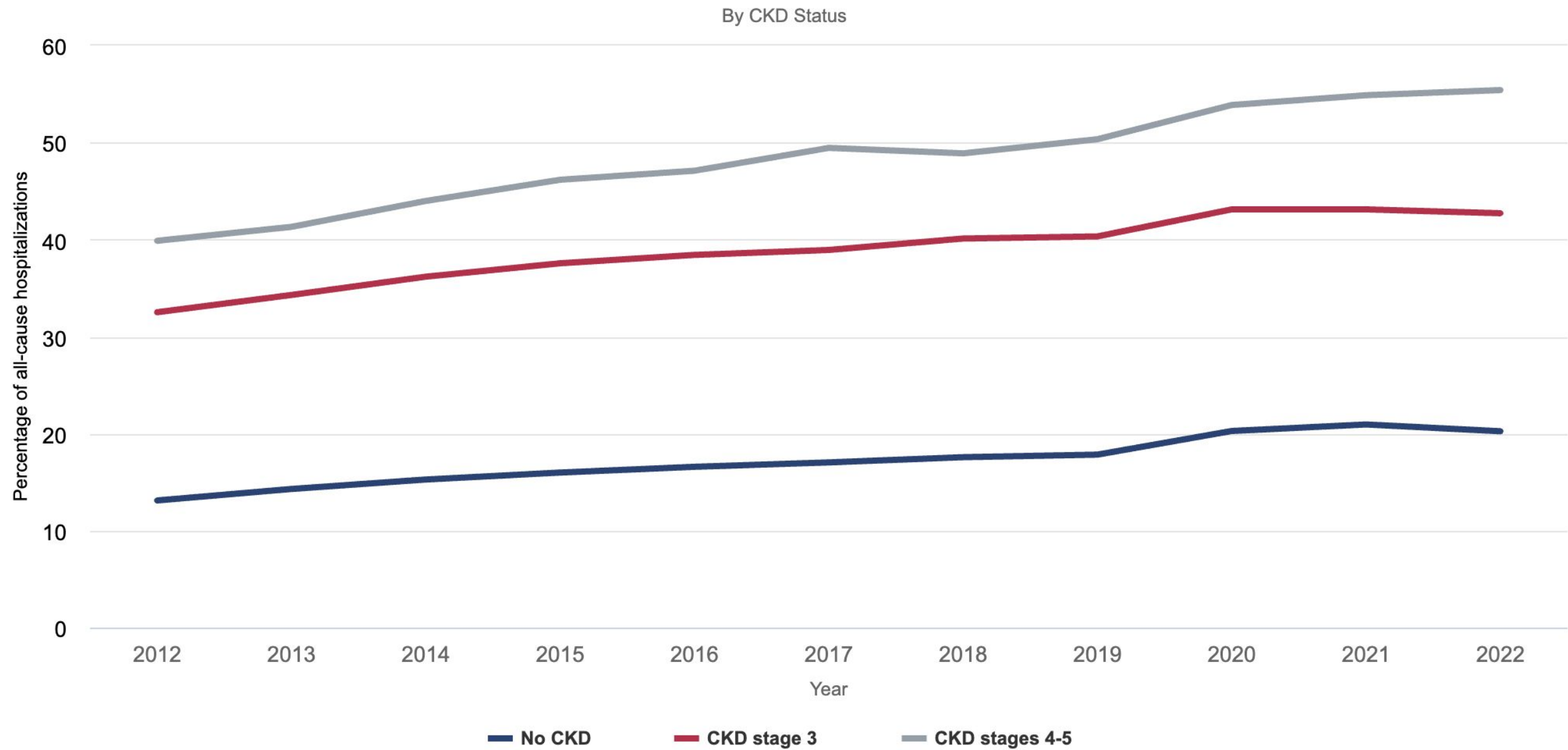
A-fib

Hospitalization

PAD

- Stage 3a eGFR ONLY --> albuminuria)
 - All cause mortality 1.7 □ 2.2
 - CV mortality 1.9 □ 2.7
 - MI 1.6 □ 1.9
 - Stroke 1.6 □ 1.7
 - **Kidney failure 5.8 □ 13**
 - AKI 3.9 □ 4.7
 - **Peripheral arterial disease 2.5 □ 3.7**
 - Hospitalization 1.3 □ 1.4

Figure 4.2a Percentage of all-cause hospitalizations with acute kidney injury in older adults, 2012-2022



Data Source: 2024 United States Renal Data System Annual Data Report

Perioperative Risks

- Mortality, CV mortality
- Stroke
- AKI
- Hospitalization
- Other
 - Infection
 - Transfusion
 - Deep vein thrombosis

CKD & Incidence of Perioperative Complications²

- Elective <inpatient> surgery, adults
- Large EMR database
- CKD = ICD-9 code 585 (eGFR (Cockcroft-Gault formula**) < 60, albuminuria)
- 80,000 total patient records; 43% had CKD
- ~ 16,000 matched pairs: no CKD - CKD

ALL stages (3-5)

CKD & Incidence of Perioperative Complications²

- ~ 74% GA, 26% RA
- ~62% of surgeries < 2 hrs
- ~ 80%: Ortho, GI, neuro, other

Key Findings: Overall Rate of AEs²

No CKD

CKD

•1.7% (OR 1)

•4.4% (OR 3.5)

•Hgb < 8.5 g/dL: 8.3% (OR 4.2)

•K > 5.5 mmol/L: 26% (OR 17.9!)

Key Findings: In-Hospital Mortality²

No CKD

CKD

•0.4% (OR 1)

•2.1% (OR 5.5)

Key Findings: Non-Infectious Complications²

No CKD

CKD

- Stroke: 0.8% (OR 1)
- Others: 0%

- Stroke 1.4% (OR 2.2)
- Others: 0.2% (ns)

Key Findings: Infectious Complications² (septicemia, pneumonia, cellulitis)

No CKD

CKD

•0.1 – 0.2%

•0.3 - 0.4% (OR 4.4 - 5.9)

Key Findings: ICU Admission²

No CKD

CKD

•2%

•4.5% (OR 3.2)

What about patients with ESRD?

Major non-cardiac surgery³

- A total of 8% (272 /3398 pts) experienced:
 - Death w/in 30 days - 5.3%
 - Acute MI w/in 30 days – 3.3%
 - Death from CV causes – 0.9%
- 86% associated with urgent procedures
- Highest incidence with transplant, ortho, vasc. surgeries

What about patients with ESRD?

Elective surgeries (all types) under GA⁴

- All cause mortality
 - 0 - 7.7% in pts with no CKD
 - 0 – 19.3% in pts with ESRD
 - OR across studies: 4 – 10.8
- Largest increase in RR
 - Orthopedics – OR 10.7
 - General surgery – OR 6.7
 - Cardiac – OR 4.2

Secondary Analysis: VISION & POISE-2⁵

- 45 y or older, nonurgent, noncardiac inpatient surgeries
- Research questions
 - Is there a relationship b/w preop eGFR (2021 equation**) and perioperative cardiac events?
 - How does eGFR compare to other predictors: age, sex, Hgb, comorbidities, surgery type?

Secondary Analysis: VISION & POISE-2⁵

- Lower eGFR □ higher risk of cardiac events & death
- The threshold & effect size varied by age & gender
 - **For younger patients, the inflection point was at eGFR of ~ 85 ml/min!! in VISION
- Men = 1.4 times higher risk
- Example (VISION) @ eGFR 60 adjusted relative risks:
 - 50 y.o. female: 2.8; 65 y.o. female = 1.4
 - 50 y.o. male: 3.1; 65 y.o. male = 1.5

Secondary Analysis: VISION & POISE-2⁵

- Preoperative eGFR was the STRONGEST predictor of perioperative cardiac events
- Stronger than type of surgery, age, gender, preoperative Hgb, and history of CV disease!
- In existing prediction models, it would be more beneficial to use eGFR [continuous variable] v. the binary variable [CKD - no CKD]

CKD and Other Postoperative Complications (*slightly more messy evidence*)

- Septicemia, stroke, pneumonia
 - significantly increased (OR 1.3-1.8) after non-urological surgery [claims database analysis]⁶
- DVT and blood transfusions
 - significantly increased after elective hip & knee surgery [meta-analysis]⁷

CKD and Perioperative Acute Kidney Injury (PO-AKI)



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Acute kidney injury (AKI) is “.... an abrupt decrease in kidney function that includes, but is not limited to, acute renal failure.”

- KDIGO

Post-operative acute kidney injury (PO-AKI) is when KDIGO criteria are met within 7 days of an operative procedure.

- Acute Disease Quality Initiative & Perioperative Quality Initiative

“Acute Renal Failure”

**Risk
Injury
Failure
Loss
End-stage**

RIFLE

Urine Output (UO) Criteria

Increased or GFR decreases	UO <0.5 ml/kg/hr x 6 hr
Increased Cr x 1.5 or GFR decreases $>50\%$	UO <0.5 ml/kg/hr x 12 hr
Increased Cr x 3 or GFR decreases $>75\%$	UO <0.5 ml/kg/hr x 24 hr
Failure	UO <0.5 ml/kg/hr x 12 hr
Loss	UO <0.5 ml/kg/hr x 24 hr

Stage 1

Stage 2

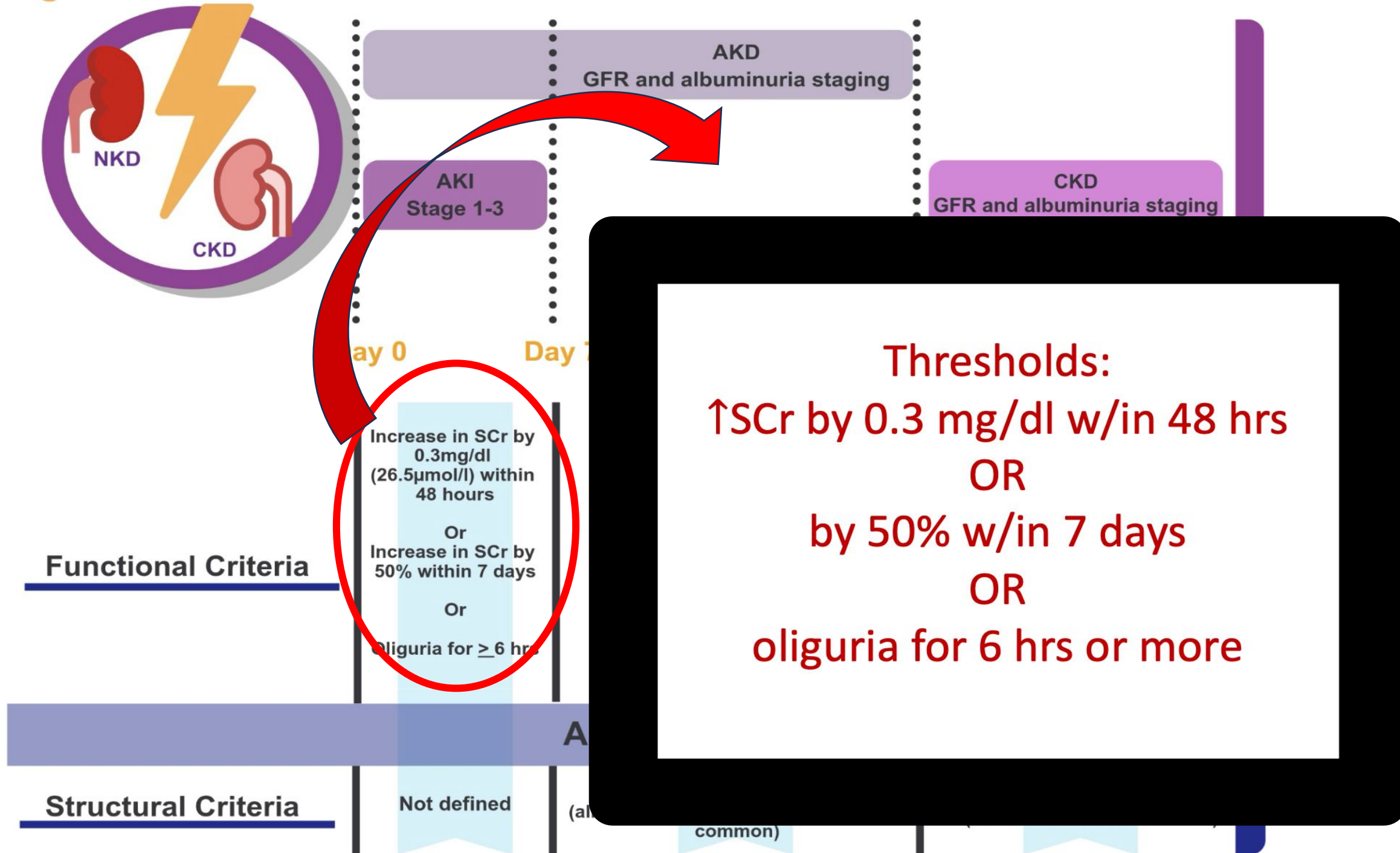
Stage 3

Patients who receive renal replacement therapy (RRT) are considered to have met the criteria for stage 3 irrespective of the stage that they are in at the time of commencement of RRT.

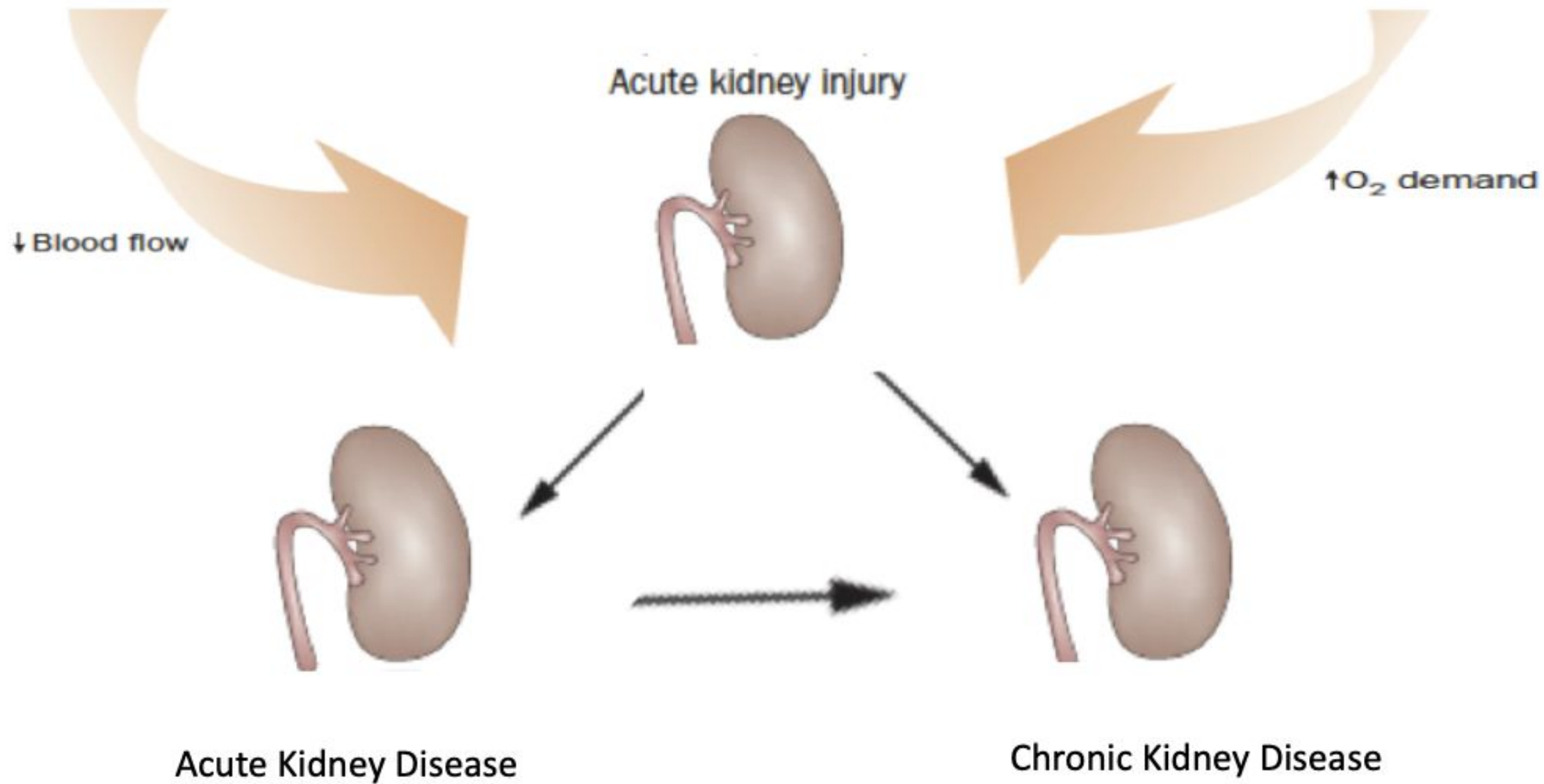


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WE ARE THE UNCOMMON.



Stage	Serum creatinine	Urine Output
1	1.5 to 1.9 X baseline or ≥ 0.3 mg/dl increase	<0.5 ml/kg/hr for 6 to 12 hrs
2	2 to 2.9 X baseline	<0.5 ml/kg/hr for ≥ 12 hrs
3	3 X baseline or ≥ 4.0 mg/dl or initiation of RRT	<0.3 ml/kg/hr for ≥ 24 hrs or anuria for ≥ 12 hours

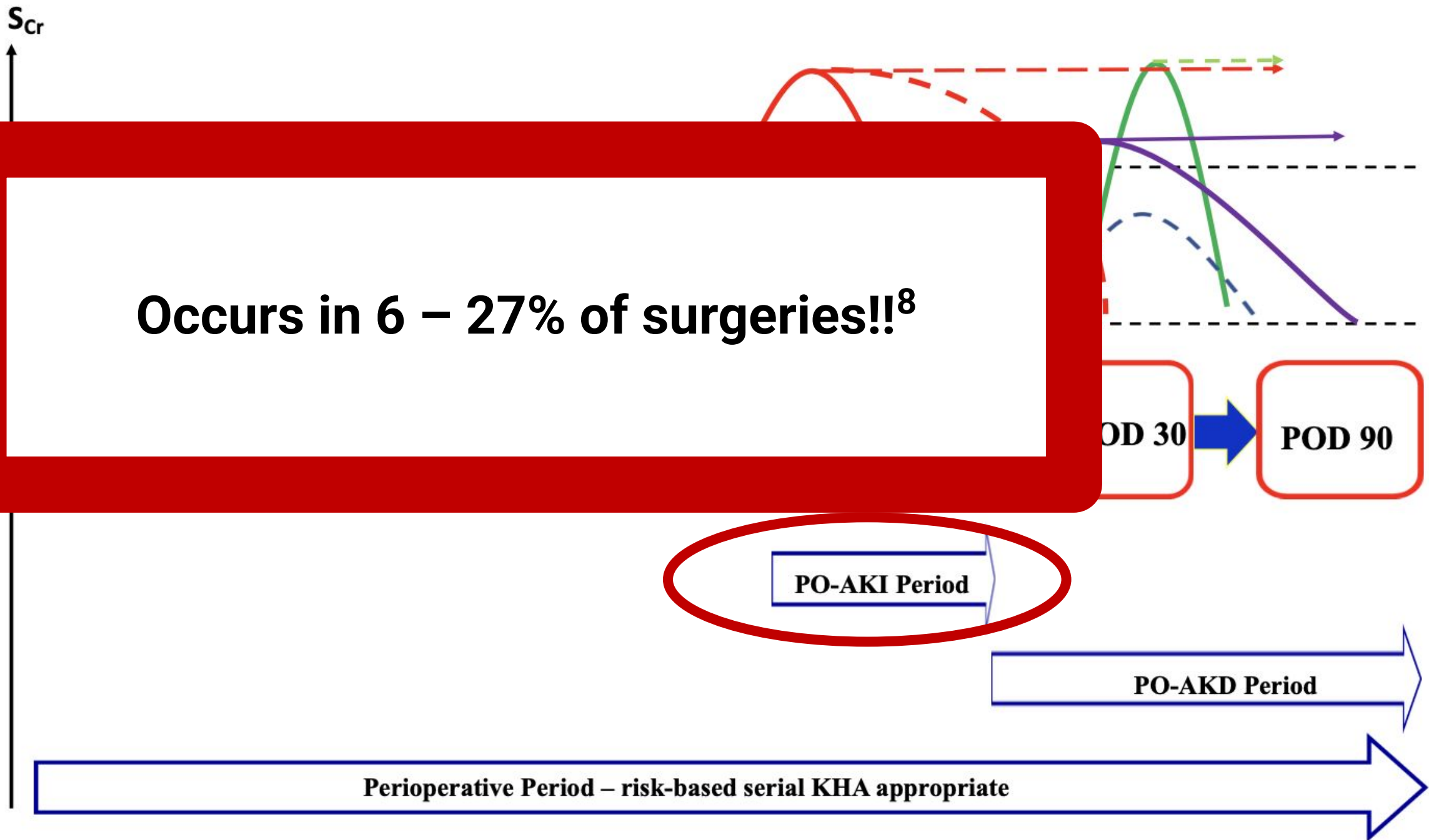


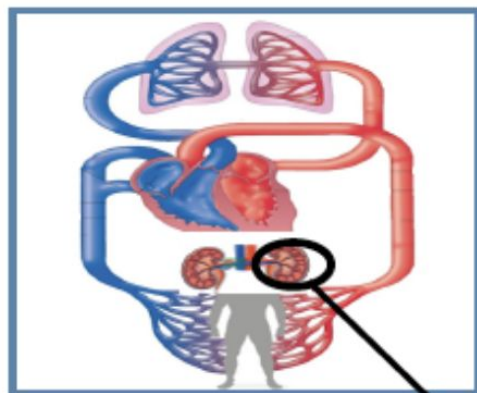
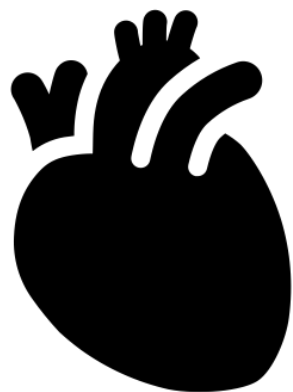
Acute kidney diseases (AKD): abnormalities of kidney function and/or structure with implications for health, with a duration of ≤ 3 months

- KDIGO

Post-operative acute kidney DISEASE (PO-AKD): KDIGO criteria for AKI are still met > 7 days after an operative procedure

- Acute Disease Quality Initiative & Perioperative Quality Initiative





Effect of CPB Circuit
Low Cardiac Output
Blood Pressure
Venous Pressure
Preload/Volume
Anemia/Hemolysis
Ischemia/Reperfusion

Hemodynamic Perturbations

Figure 1



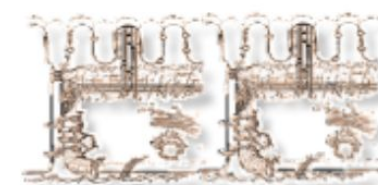
Emboli
Arterial Obstruction
Venous Congestion

Mechanical Factors

Some surgeries are far worse than others of course.....

Inflammation/Immunity

Inflammation
Oxidant Stress
Complement Activation
Toxins / Drugs
Contrast Media



PO-AKI: Preoperative Risk Factors⁹

- Pre-existing kidney dysfunction
- Diabetes
- Cardiac dysfunction
- Age
- Sepsis
- Hypovolemia
- Hepatic failure
- Crush injury
- Exposure to nephrotoxins

PO-AKI: Intraoperative Risk Factors⁹

- Hypovolemia
- Renal ischemia
- Inflammation
- Increased intra-abdominal pressure
- Decreased cardiac output
- Vasodilation
- Exposure to nephrotoxins
- Embolism

PO-AKI: Postoperative Risk Factors⁹ (new ones only)

- Urinary obstruction
- Acute lung injury
- Mechanical ventilation

In addition to increasing risk of □ CKD

- PO-AKI = sentinel event!⁸
- PO-AKI & complications¹⁰
 - 5-fold increase in mortality (overall for cardiac/non-cardiac)
 - Even minor increases in sCr (not reaching AKI criteria) □
2-fold increase in mortality
 - More severe AKI □ greater increase in risk
 - Substantial increase in hospital LOS
 - Impact more pronounced in the non-cardiac surgery population

CONSENSUS STATEMENT

OPEN



Postoperative acute kidney injury
in adult non-cardiac surgery: joint
consensus report of the Acute Disease
Quality Initiative and PeriOperative
Quality Initiative

Take-Home Points

- CKD, any stage, is an independent risk factor for serious perioperative complications after noncardiac surgeries
- Preoperative eGFR is a strong predictor of CV risk, especially in younger patients
- The risk of all complications is higher, but varies across surgery types and patient populations
- CKD is a risk factor for PO-AKI and PO-AKD, which further increase the risks of perioperative complications

Mitigation Strategies

What can WE do?



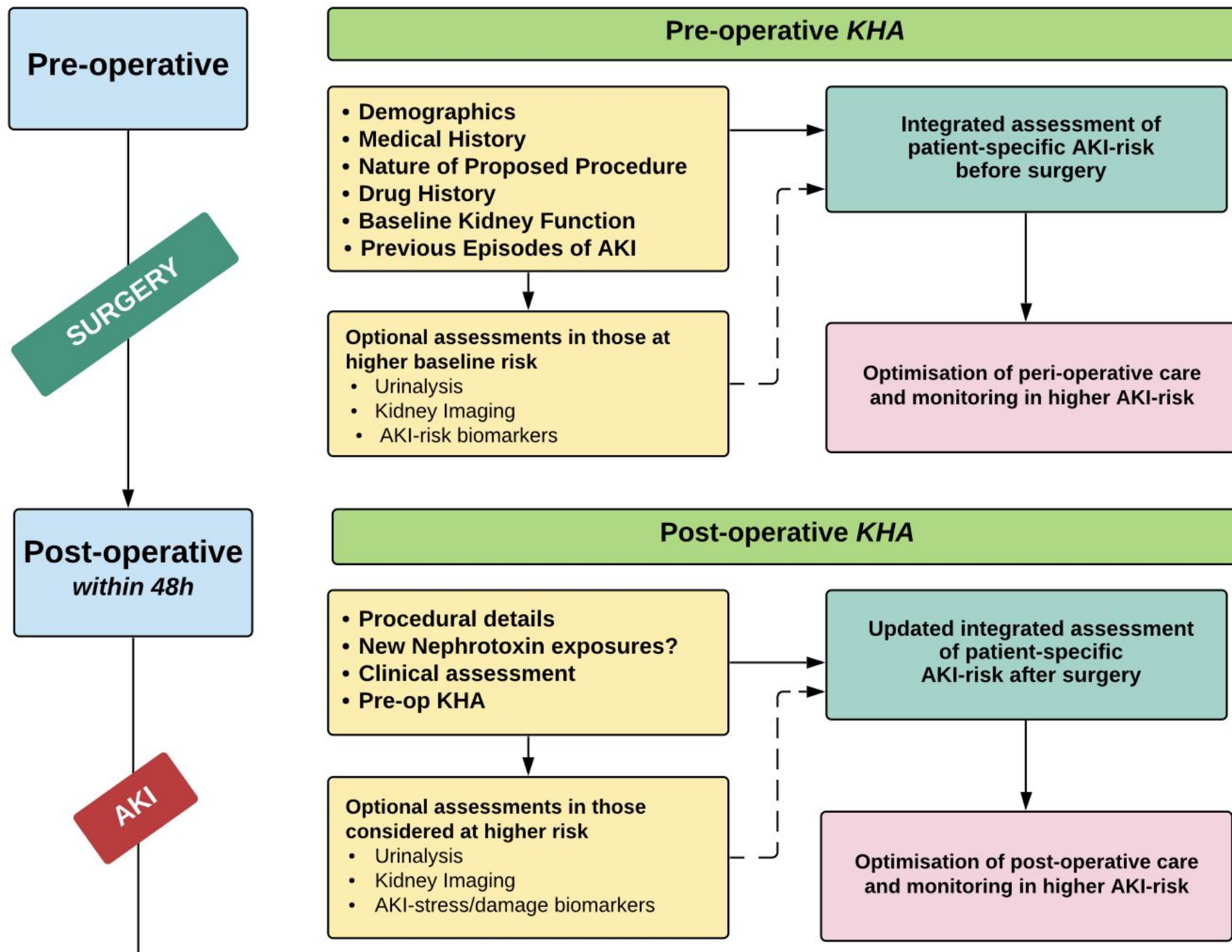
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Preoperative Evaluation

- Indications for preoperative screening (serum creatinine, urinalysis)
 - Diabetes
 - Hypertension
 - Heart disease
 - Other kidney disorders
 - History of AKI
 - Older age
- High degree of suspicion – esp. if high-risk surgeries
 - Abnormal blood sugar/pre-diabetes
 - Abnormal blood pressure
 - Meds with renal side effects - NSAIDs, diuretics, ACEIs, ARBs, contrast, mycins, herbal medications (bucha leaves, juniper berries, uva ursi, parsley), other toxins



Kidney Health Assessment (KHA) = ABCD⁹

- **A**KI history
- **B**lood pressure
- **C**KD/**C**reatinine
- **D**rugs/**D**ipstick

CKD Prognosis Consortium¹

Consider discontinuing the following medications 48-72 hrs before surgery:

Medication	Rationale
ACEi/ARBs	Hypotension, AKI
Diuretics	Volume depletion, AKI
SGLT2is*	Ketoacidosis
Metformin	Lactic acidosis
Aminoglycosides	ATN/AKI
NSAIDs	AKI/acute interstitial nephritis

Preoperative Interventions

- Establish euvolemia
- What about multimodal analgesia (NSAIDs??)
- Establish normoglycemia? What target?

Intraoperative Management: Monitoring

Consider the following (risks v. costs v. benefits)

- 5-lead ECG
- BP monitoring (frequency, non-invasive v. invasive)
- Glucose monitoring
- Hgb assessment

Intraoperative Management: Techniques

- Volatile agents v. TIVA?
 - All volatile agents are acceptable
 - Few studies allow inclusion of patients with CKD
- Regional anesthesia v. general?
 - Regional anesthesia may have advantages
 - Tight hemodynamic management during neuraxial
- If ESRD: drug adjustments

Intraoperative Management: IV Fluids⁸

- Increased risk of PO-AKI:
 - 0.9% saline
 - Starch-based colloids
 - ERAS (fluid restriction + NSAIDs)
- Decreased risk of PO-AKI (maybe)
 - Goal-directed therapy
- Isotonic crystalloids for maint.
- Albumin if colloids needed (cost v. benefit)
- Avoid blood transfusions if possible

Intraoperative Management

- Hemodynamic targets⁸
 - Absolute MAP at least 60-70 mmHg
 - Relative MAP within 30% from baseline
 - If GDT: target MAP of 65 mmHg or greater
- Mechanical ventilation target
 - TV of 6 mL/kg PBW (each 1 mL/kg increased odds of AKI by 5%)¹¹
- Avoid nephrotoxins if possible

Postoperative Care

- Extended monitoring
- Aggressive BP treatment⁸
 - Get and KEEP BP "close" to baseline
 - ? How close to baseline? One trial: 10% X FOUR HOURS
- Aggressive glucose management: $< 180 \text{ mg/dL}$ ⁸
- Restart medications (timing controversial)¹

Postoperative Oral Opioids¹² (one example regimen ****always use with caution****)

- Hydromorphone
 - Normal GFR: 2-4 mg q 4 - 6 hr
 - Stage 4 CKD: 1 mg q 6 hr
 - Stage 5 CKD: 0.5 mg q 6 hr
- Oxycodone
 - Normal GFR: 10-30 mg q 4 - 6 hr
 - Stage 4 CKD: 5 mg q 6 – 8 hr
 - Stage 5 CKD: 2.5 - 5 mg q 8 - 12 hr

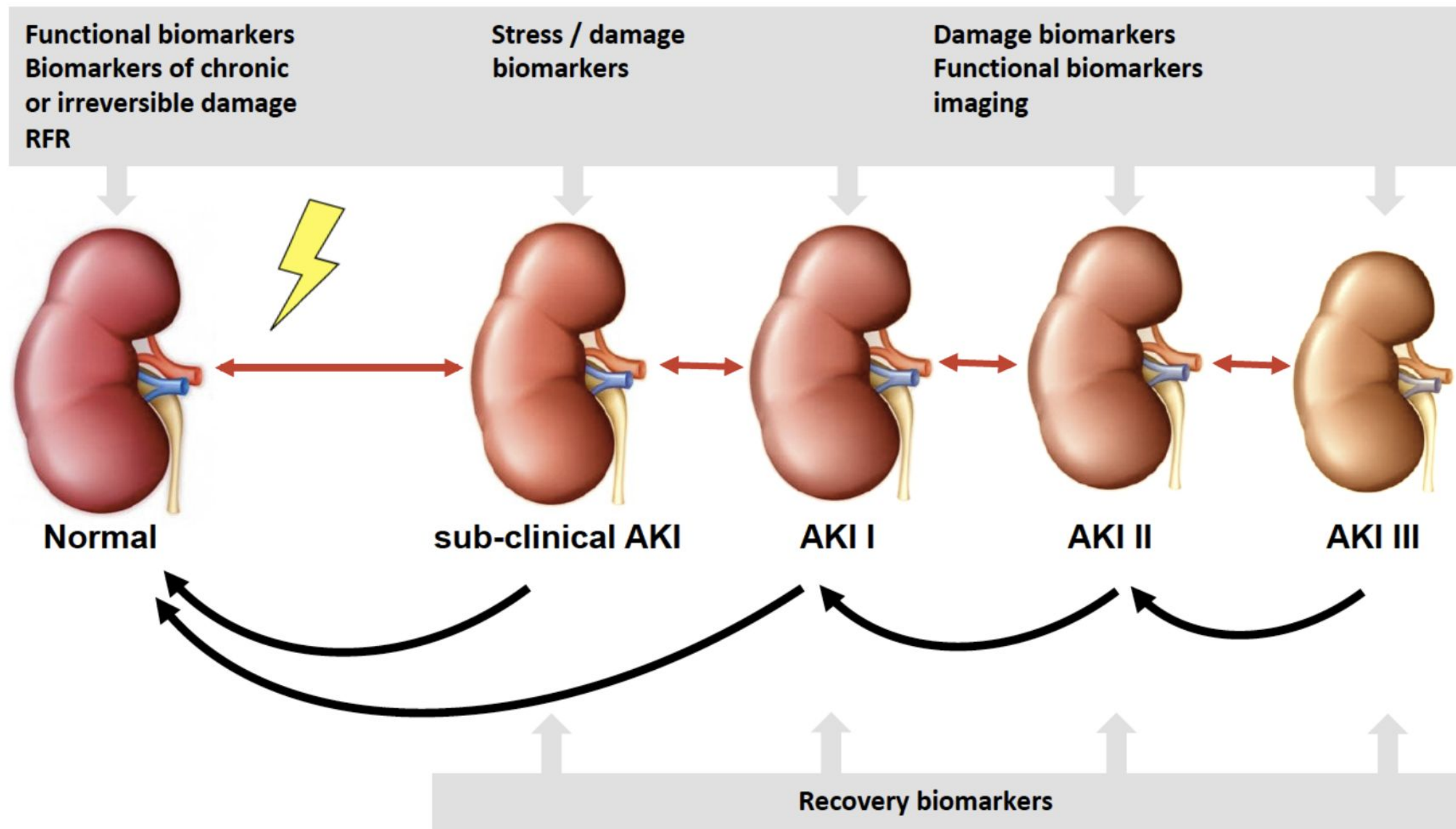
A scenic landscape at sunset. In the foreground, the dark silhouette of a large pine tree with many needles dominates the left and right sides. The sun is a bright, glowing orb on the horizon, partially obscured by the tree's trunk. The sky is a mix of orange, yellow, and blue, with some wispy clouds. In the background, there are dark, silhouetted mountains.

On the horizon??

More sensitive mechanisms to detect AKI?

Novel Biomarkers

- Neutrophil gelatinase-associated lipocalin (NGAL)
- Kidney injury molecule-1 (KIM-1)
- Cystatin C
- Tissue inhibitor of metalloproteinases-2 (TIMP-2)
- Insulin-like growth factor binding protein-7 (IGFBP-7)
- NephroCheck (TIMP-2 & IGFBP-7) combo – FDA approved





Questions??

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