

9 Aprile 2022

Lezione D NEFROLOGIA IN MEDICINA TERRITORIALE

Approccio globale e Gestione complessiva dei pazienti con ridotta funzionalità renale in presenza di ipertensione, cardiovasculopatie, diabete o semplicemente grandi anziani



UNIVERSITÀ
DEGLI STUDI
DI MILANO

LA STATALE



Fondazione IRCCS
Ca' Granda
Ospedale Maggiore
Policlinico

Sistema Socio Sanitario



Regione
Lombardia

Agenda

- **- Cosa accade quando il rene si ammala cenni sull'IRC : concetti generali.**
- **L'invecchiamento e la malattia renale: come leggere il decremento del GFR nel tempo.**
Quali segni di allarme? Quando inviare dal nefrologo?
- **Disidratazione, acidosi, alterazioni elettrolitiche** di interesse in medicina del territorio: il ruolo del rene, il ruolo dei farmaci.
- **Valutazione dei segni nefrologici e del loro significato clinico**
- **Insufficienza renale acuta**
- **Diabete e patologia renale**
- **Novità in nefroprotezione**

Acute kidney Injury: definition

Fast reduction of GFR associated with



Increased serum creatinine
and urea levels


Altered handling of water and electrolytes

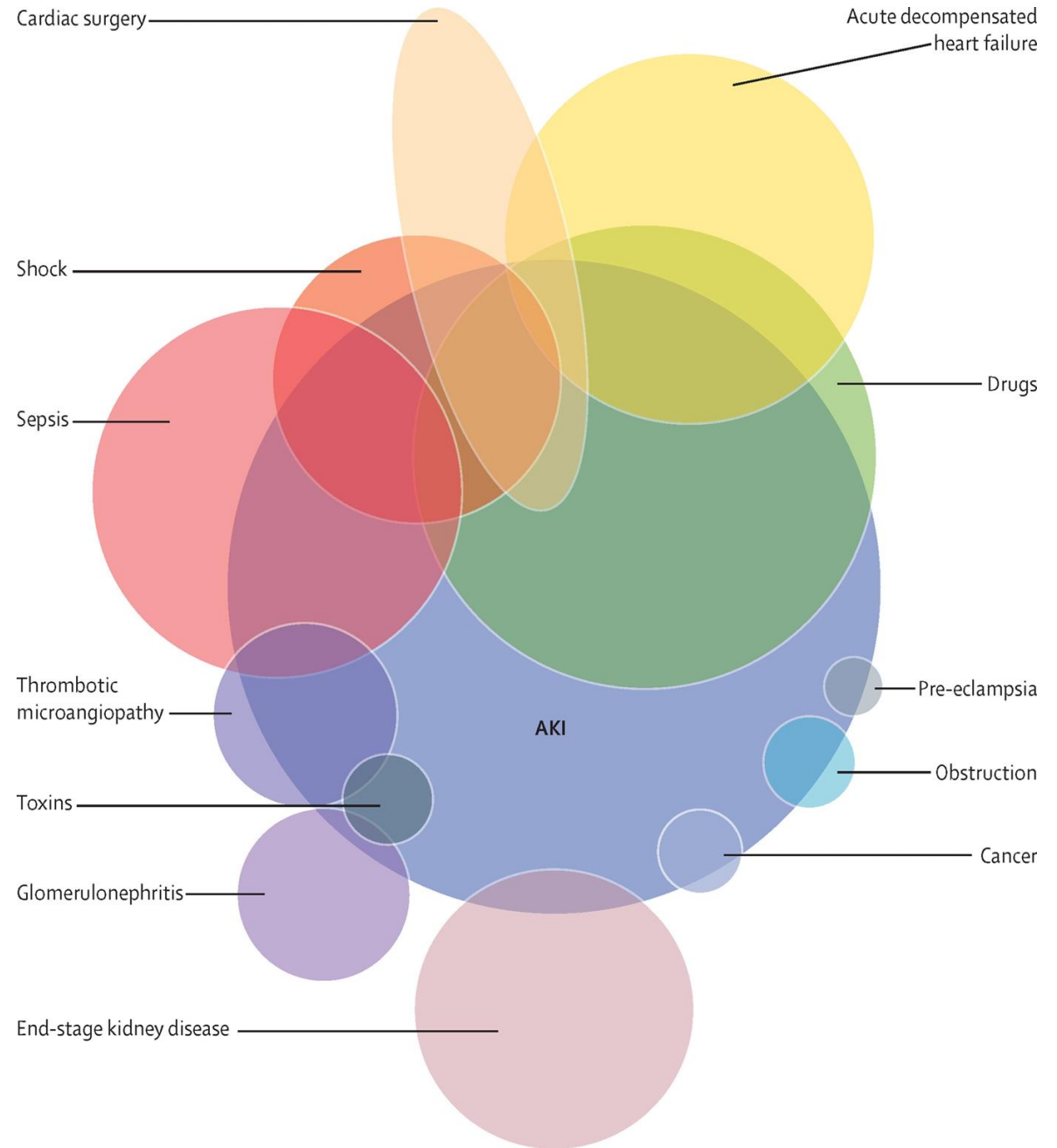
Changes in urine volume
(mostly oliguria/anuria)

SEMINAR | VOLUME 394, ISSUE 10212, P1949-1964, NOVEMBER 23, 2019

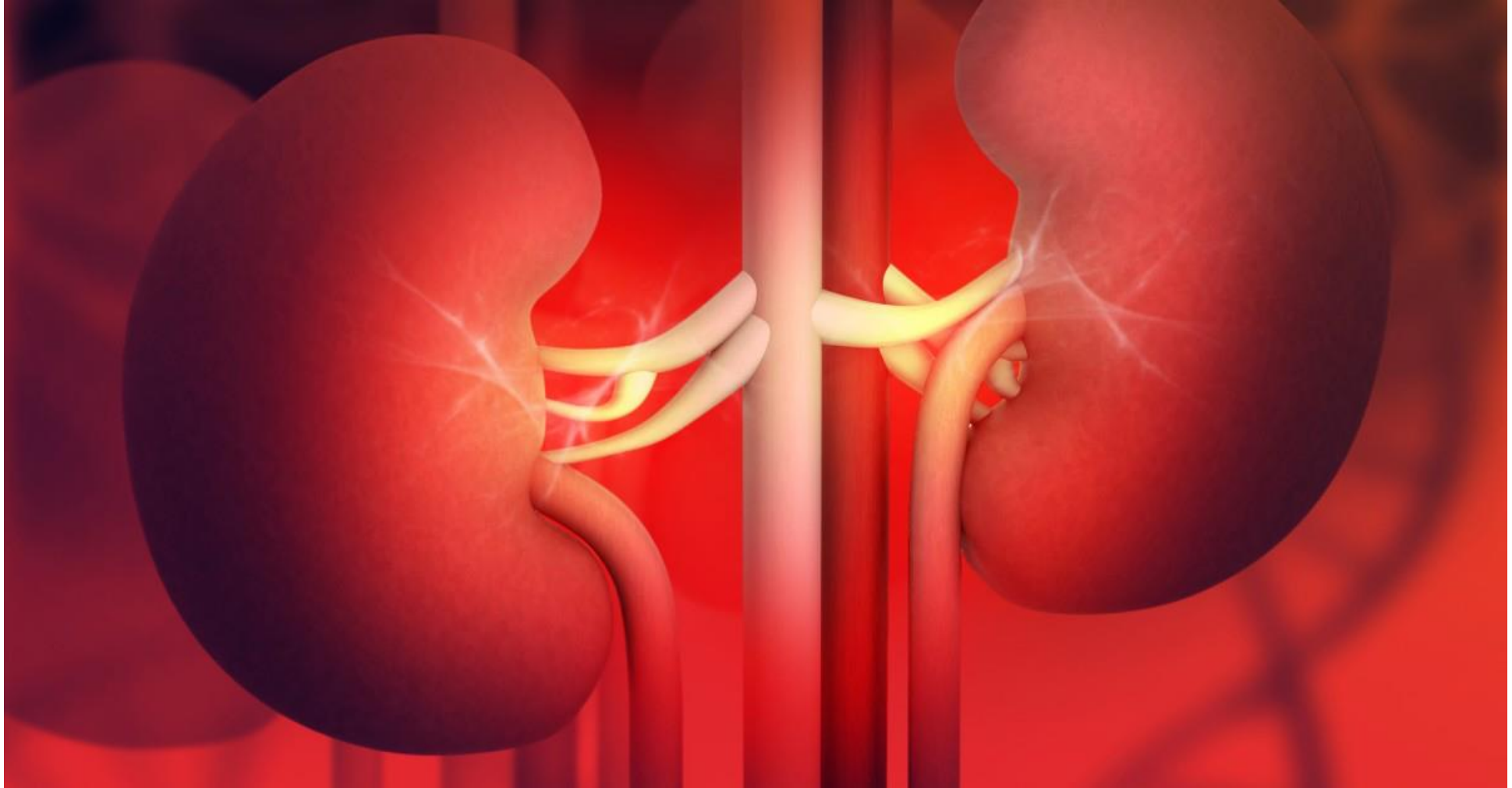
Acute kidney injury

Claudio Ronco, MD  Rinaldo Bellomo, MD  John A Kellum, MD

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Basal renal function → AKI

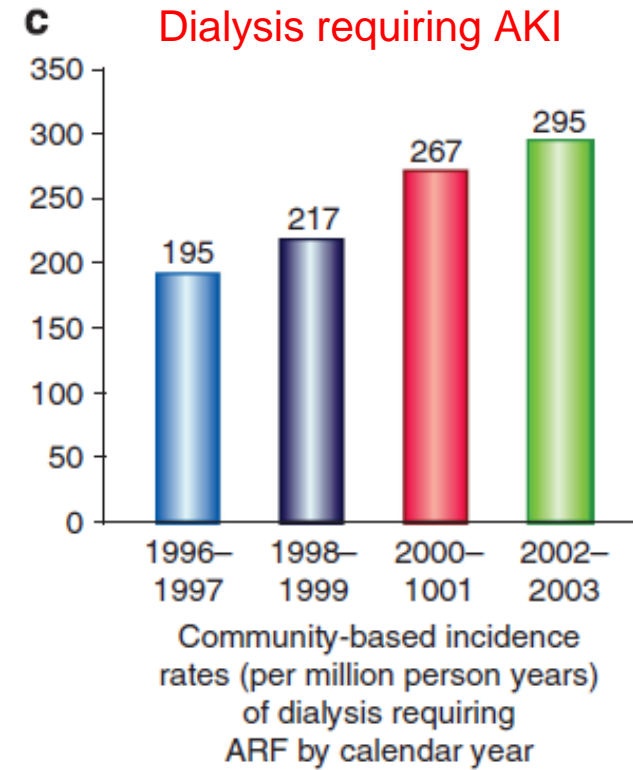
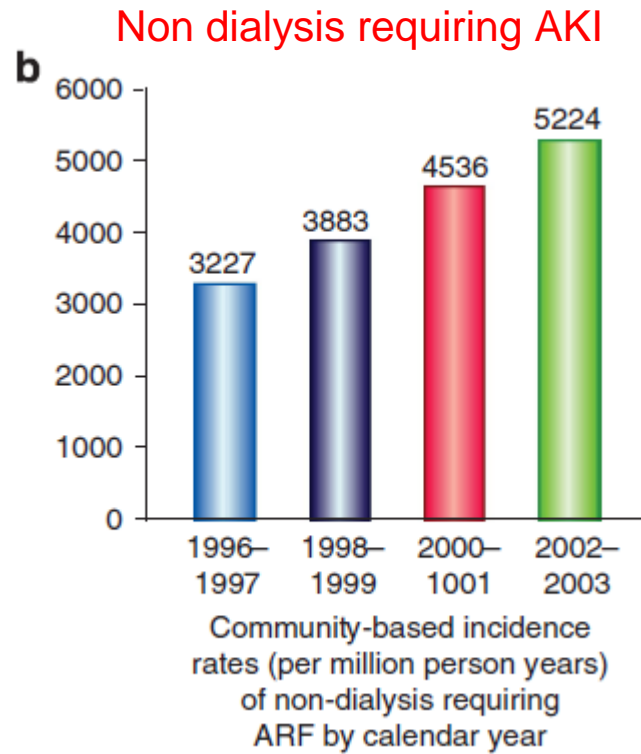


Acute Kidney Injury (AKI)

Comparison of RIFLE, AKIN and KDIGO Acute Kidney Injury Classifications

Classifications	RIFLE 2004	AKIN 2007	KDIGO 2012
Definition of AKI			
Staging			

Community-based incidence of nondialysis- and dialysis-requiring AKI in Northern California (USA) using administrative codes and creatinine-based definitions



Domanda 1.

Dopo un episodio di insufficienza renale acuta con ripristino completo della funzione renale basale:

- 1) Il paziente può definirsi guarito
- 2) Il paziente è a maggior rischio di sviluppare insufficienza renale cronica
- 3) Il paziente deve essere seguito nei successive 3 mesi con stretto follow up

An iceberg floating in the ocean. The tip of the iceberg is above the water surface, and the much larger part is submerged below. The word 'AKI' is written in red on the tip. Four text boxes are overlaid on the image, providing information about AKI.

AKI

Impatta il 10-15% di tutti i ricoveri.
In terapia intensiva può incidere
oltre il 50%

E' un fattore di rischio
per mortalità a breve e lungo
termine,

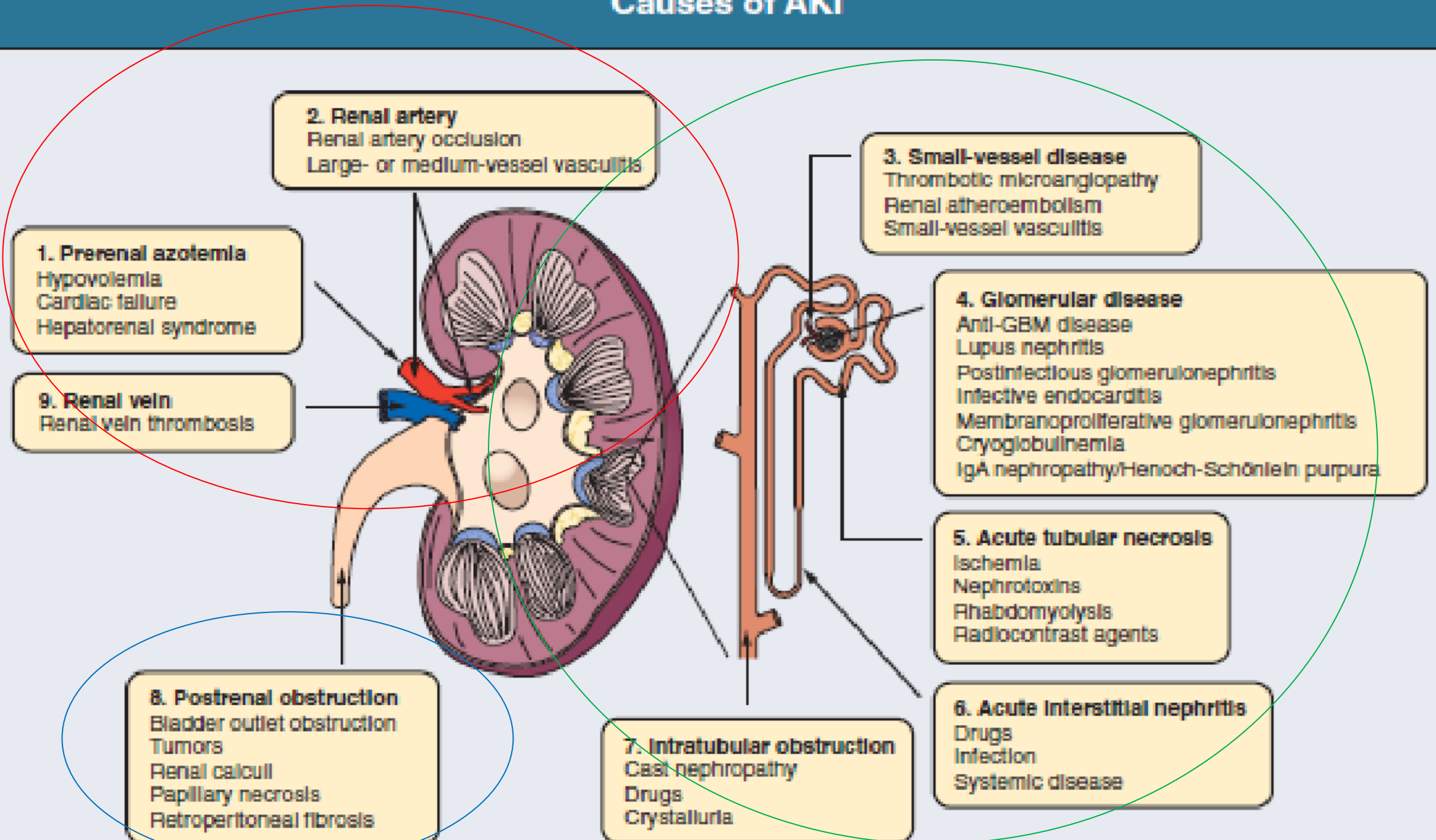
Aumenta i rischi a lungo
termine per lo sviluppo di
comorbidità, con aumento dei
costi sanitari e degenze
ospedaliere prolungate

E' un fattore di rischio per la
progressione verso la CKD e l'ESRD,
fino all'avvio di RRT

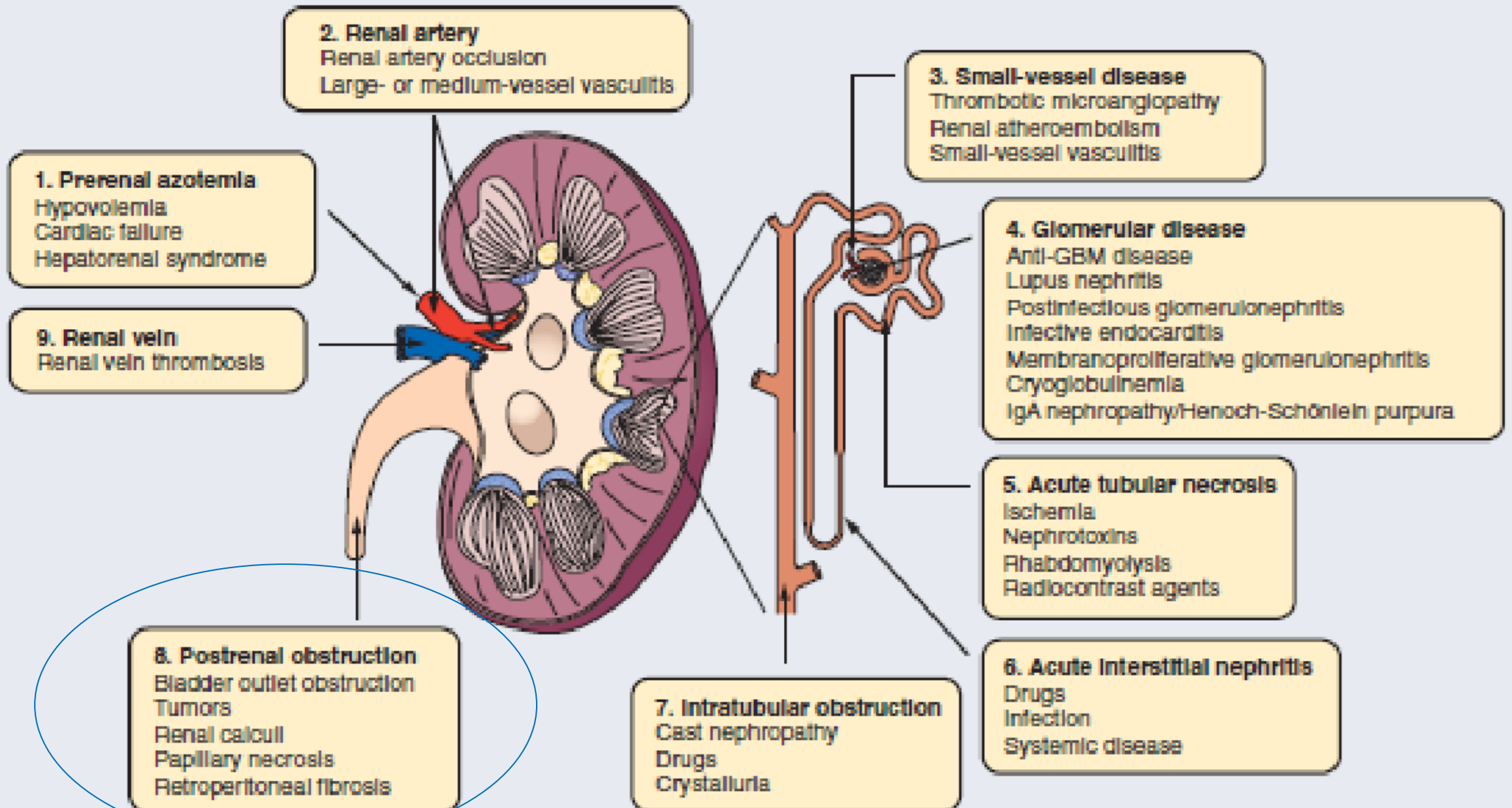
Risk factors for AKI

- Old or very young age
- Preexisting CKD
- Heart diseases
- Diabetes
- Liver diseases
- Sepsis
- Drugs (NSAID, ACE-I, ARB, Aminoglyc, CNI, etc.)

Causes of AKI



Causes of AKI



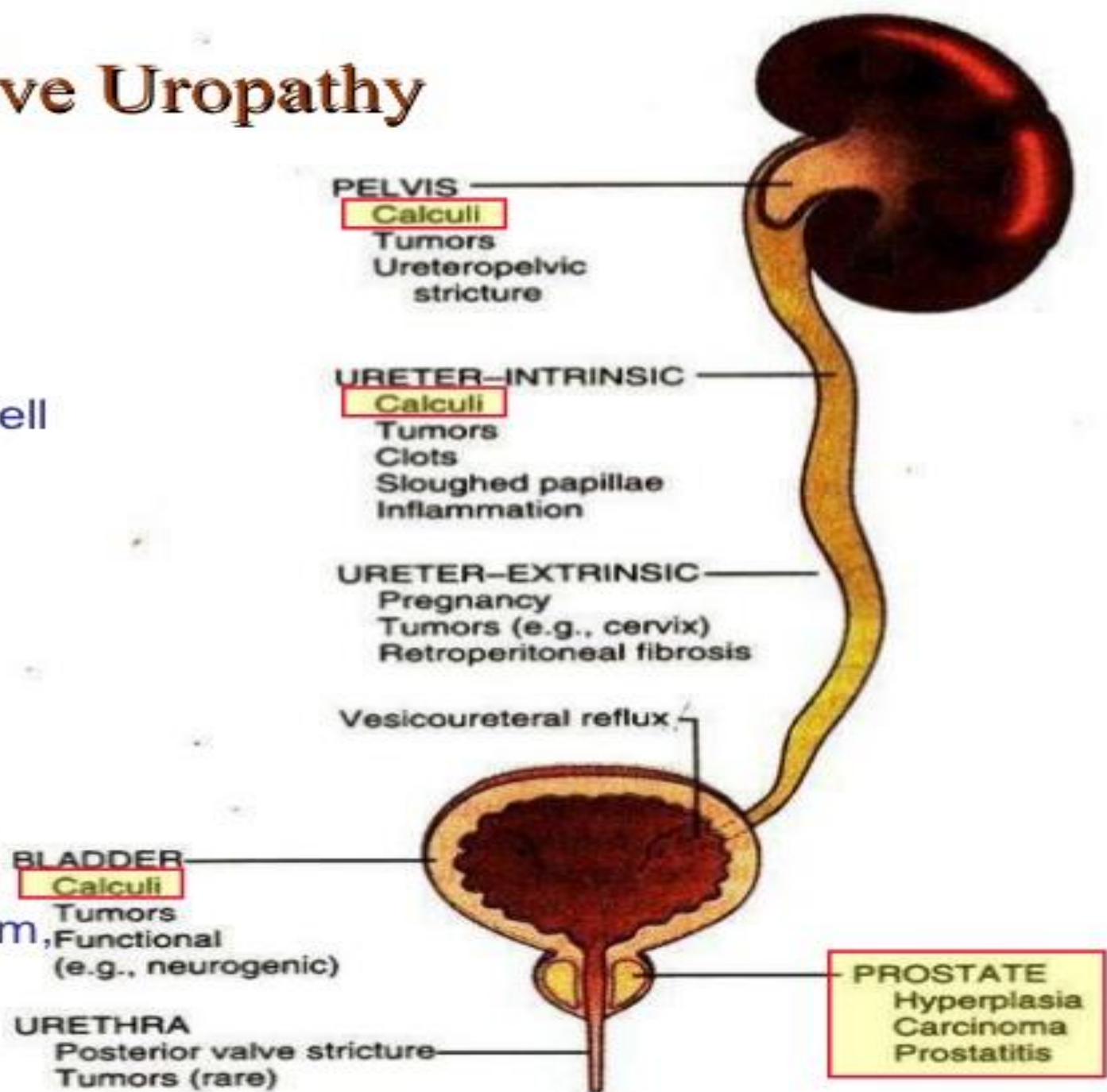
Causes of Obstructive Uropathy

- INTRINSIC:

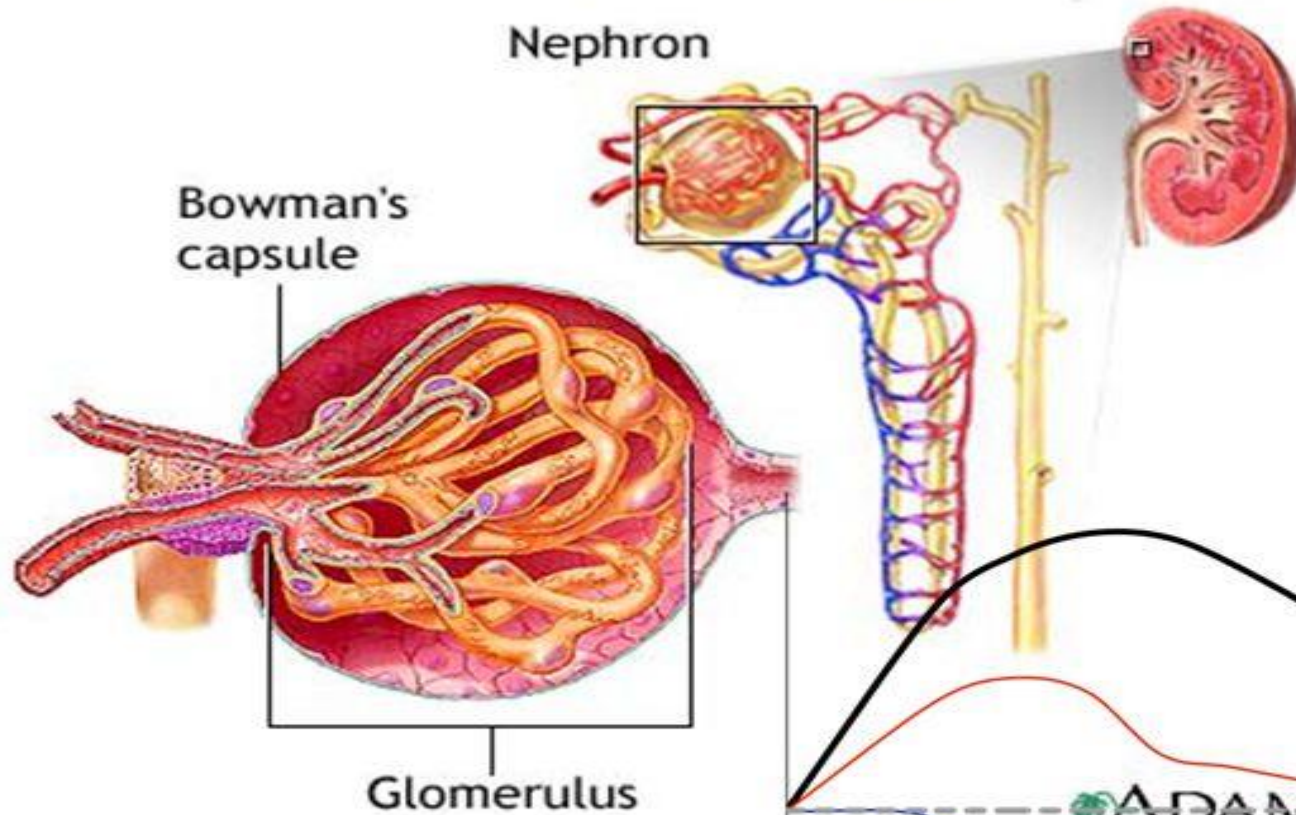
- **Calculi - Lithiasis**
- Strictures – congenital, inflammatory
- Tumors – Transitional cell Ca.
- Blood clots – UTI, Glomerulonephritis

- EXTRINSIC:

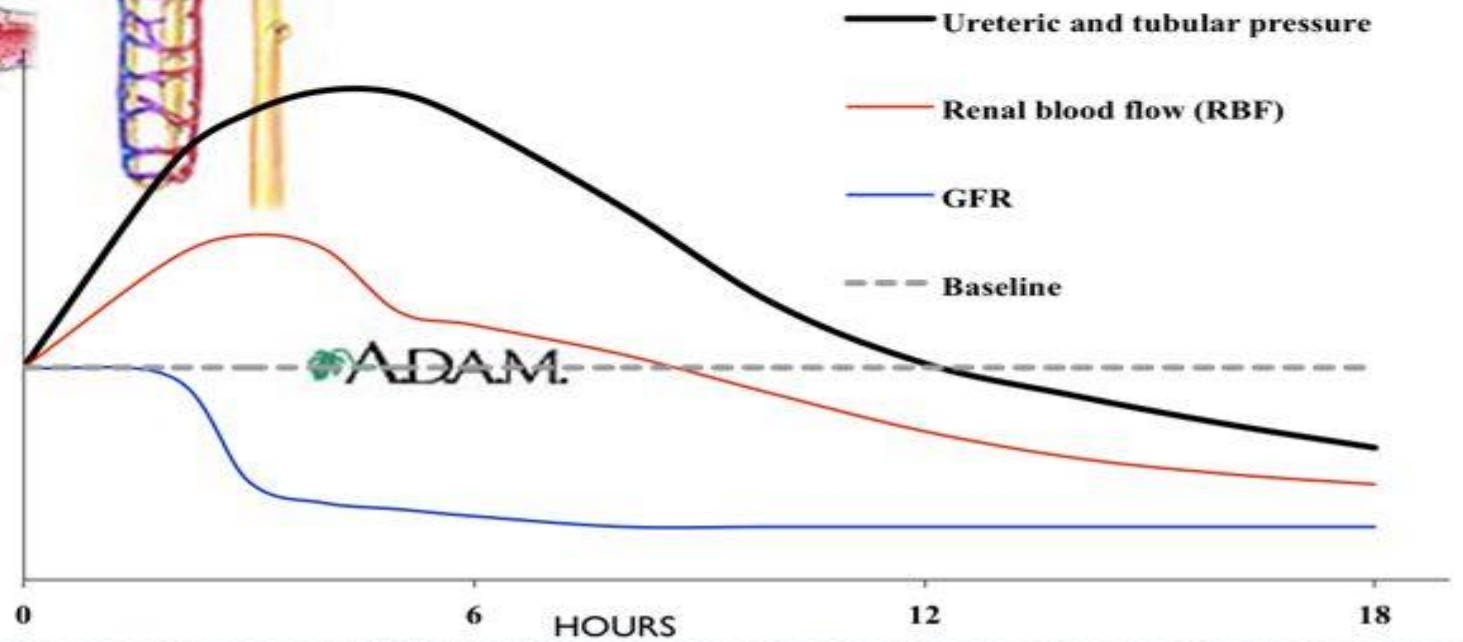
- Pregnancy
- Inflammation- PID, peritonitis, diverticulitis, salphingitis.
- Tumors: **Prostate**, rectum, bladder, ovaries etc.



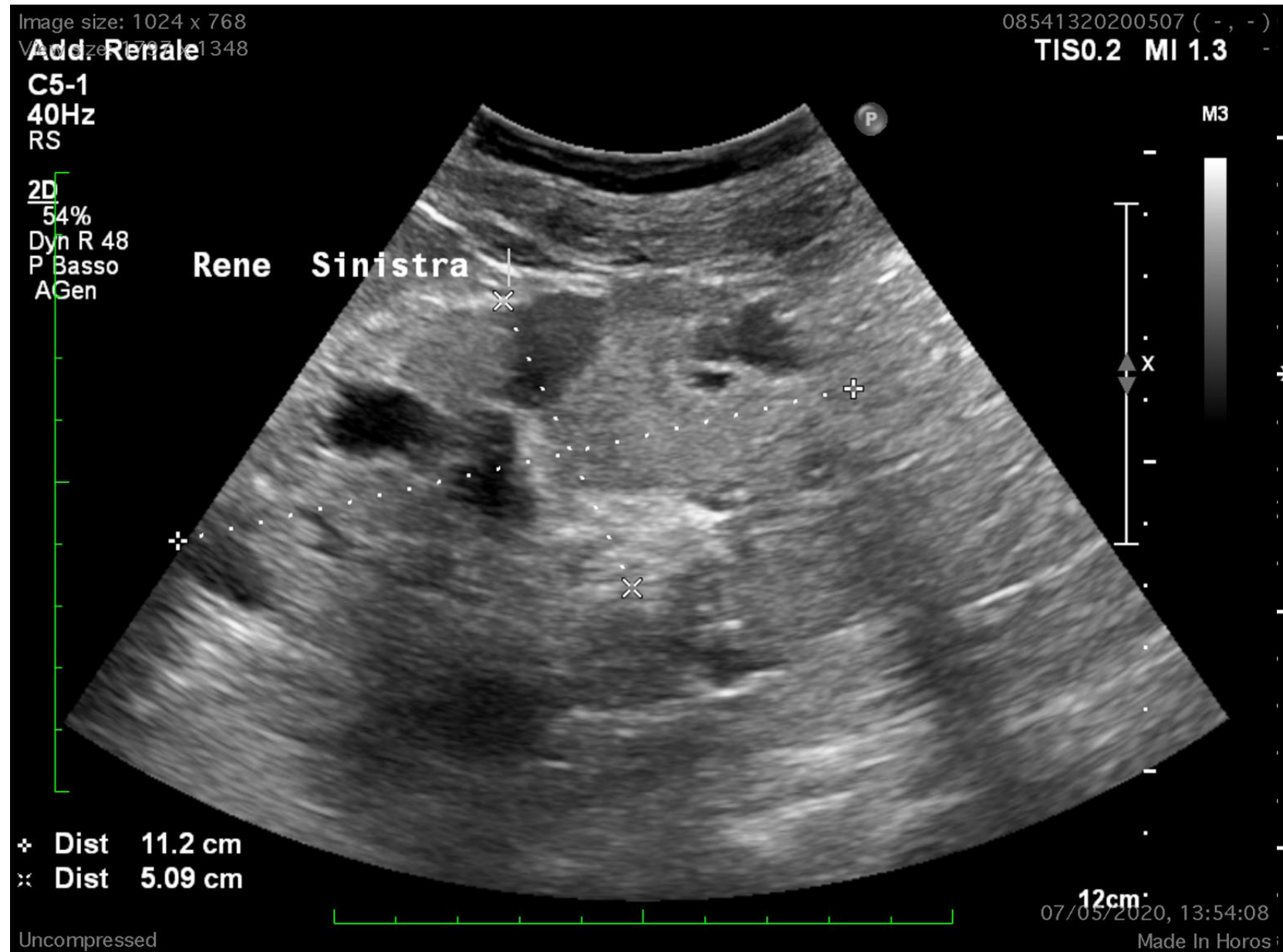
Pathophysiology



Obstructive Uropathy
Obstructive Nephropathy



Ultrasound has a first line role in AKI differential diagnosis!



Add. Renale

TIS0.1

MI 1.3

C5-1

32Hz

RS

Rene Destra

2D

57%

R din. 48

P Basso

AGen



M3

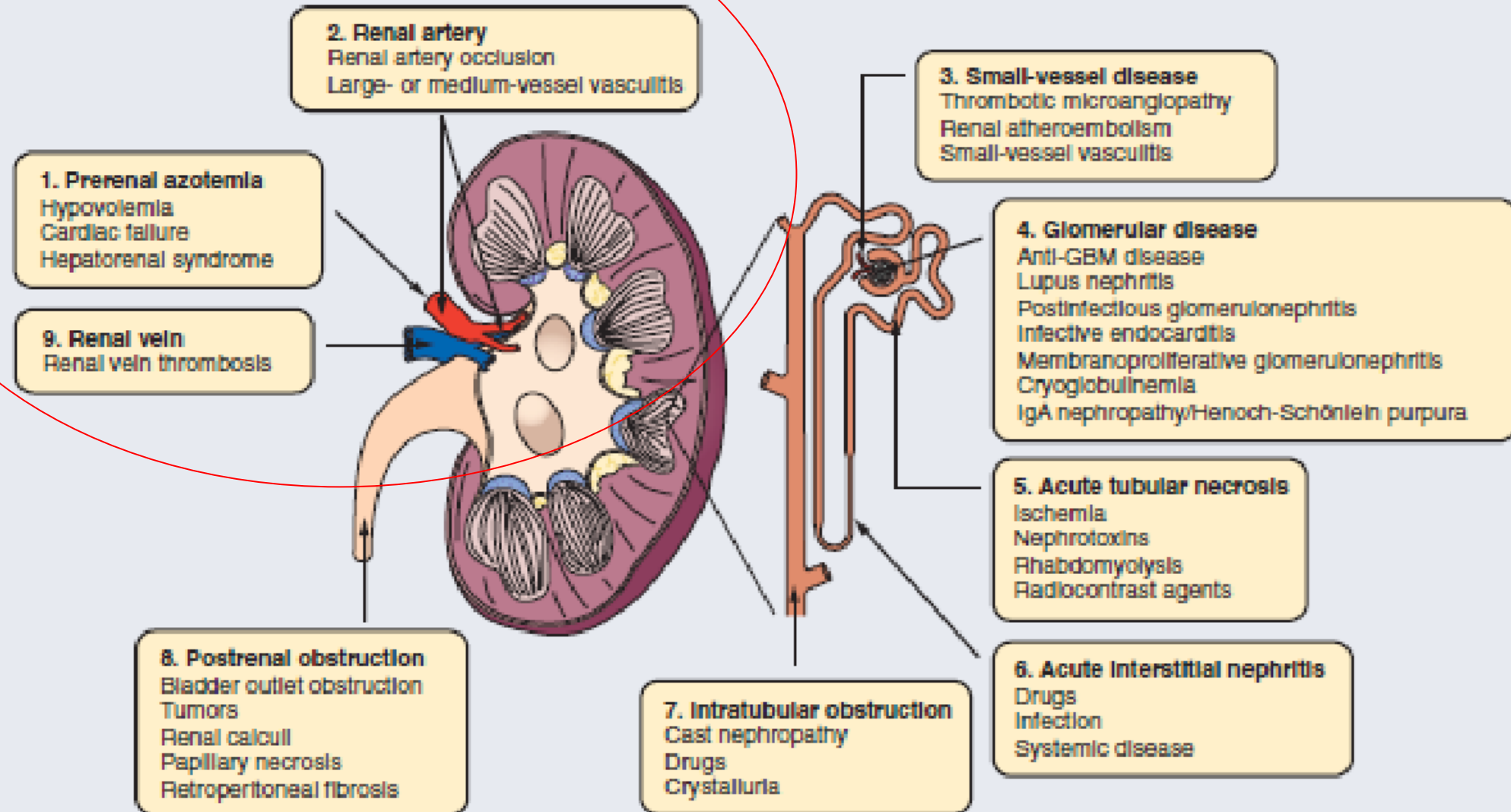


16cm

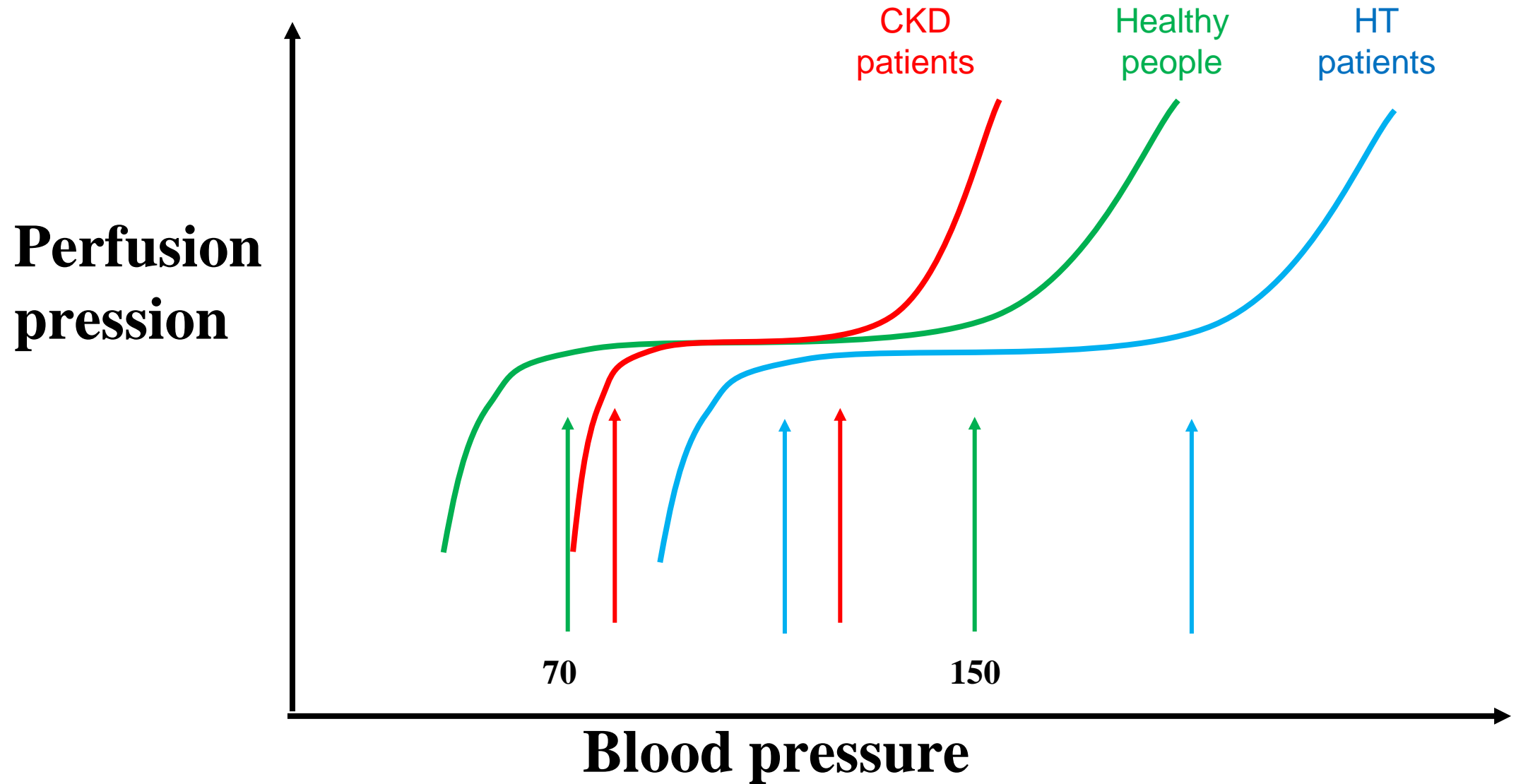
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Causes of AKI



AUTOREGULATION of renal blood flow

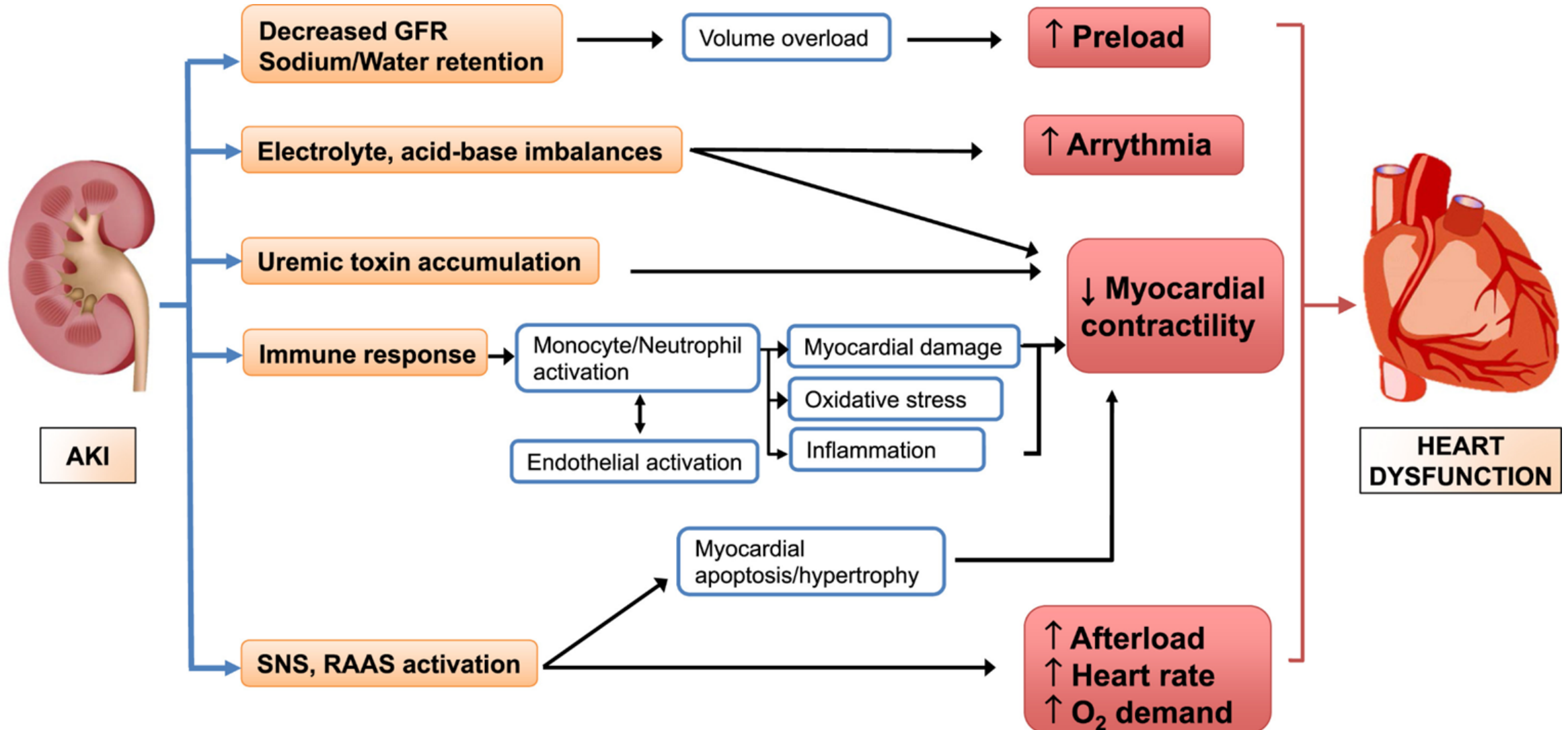


**Hemodynamic
Renal functional
changes**

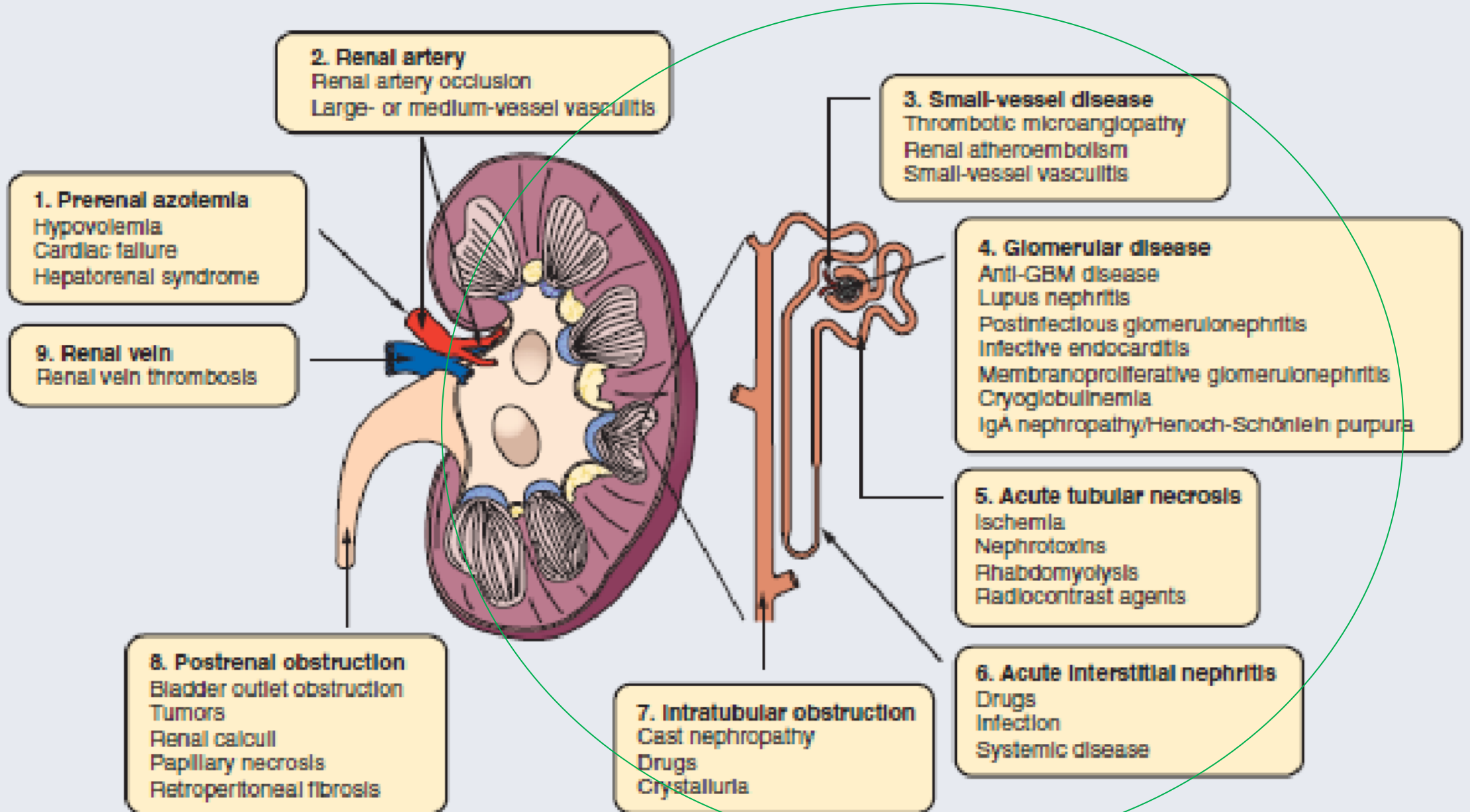


**Renal
Parenchymal
damage**
(tubular, interstitial,
glomerular)

CROSS TALK CARDIO RENALE



Causes of AKI



Factors which can induce an AKI: exogenous and endogenous factors

• Exogenous factors

- Antimicrobial drugs
- Chemotherapy
- Contrast media
- Heavy Metals
- NSAID
- solvents, herbicides, poisons, etc

• Endogenous factors

- Light chains
- Myoglobin
- Hemoglobin
- Bilirubin
- Uric acid
- Oxalate
- Hypercalcemia
- Chemokines
- Coagulatory alter.
- Immuno-mediated mechanisms

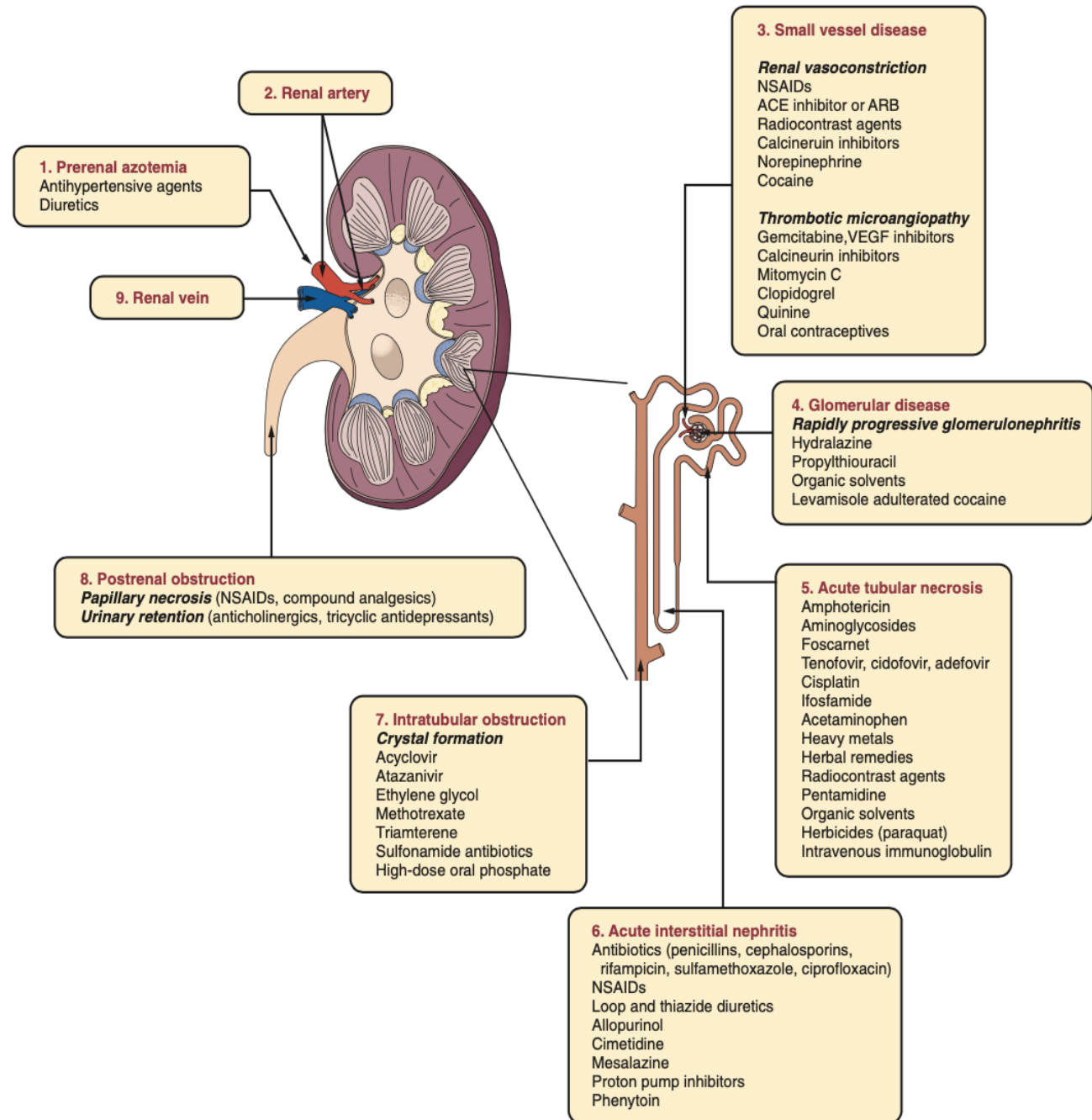


Fig. 66.8 Common nephrotoxic agents leading to acute kidney injury. ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blocker; NSAIDs, nonsteroidal antiinflammatory drugs.

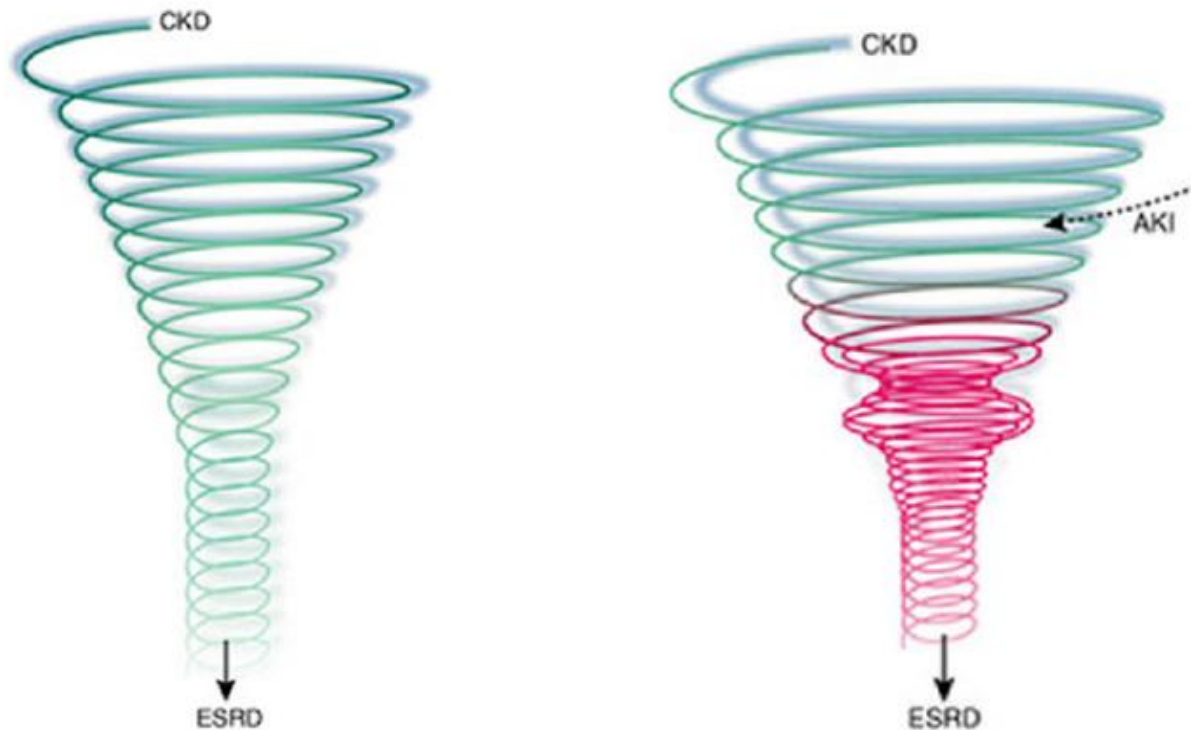


**HOW ACUTE KIDNEY INJURY
MAY PREDISPOSE TO
CHRONIC KIDNEY DISEASE???**

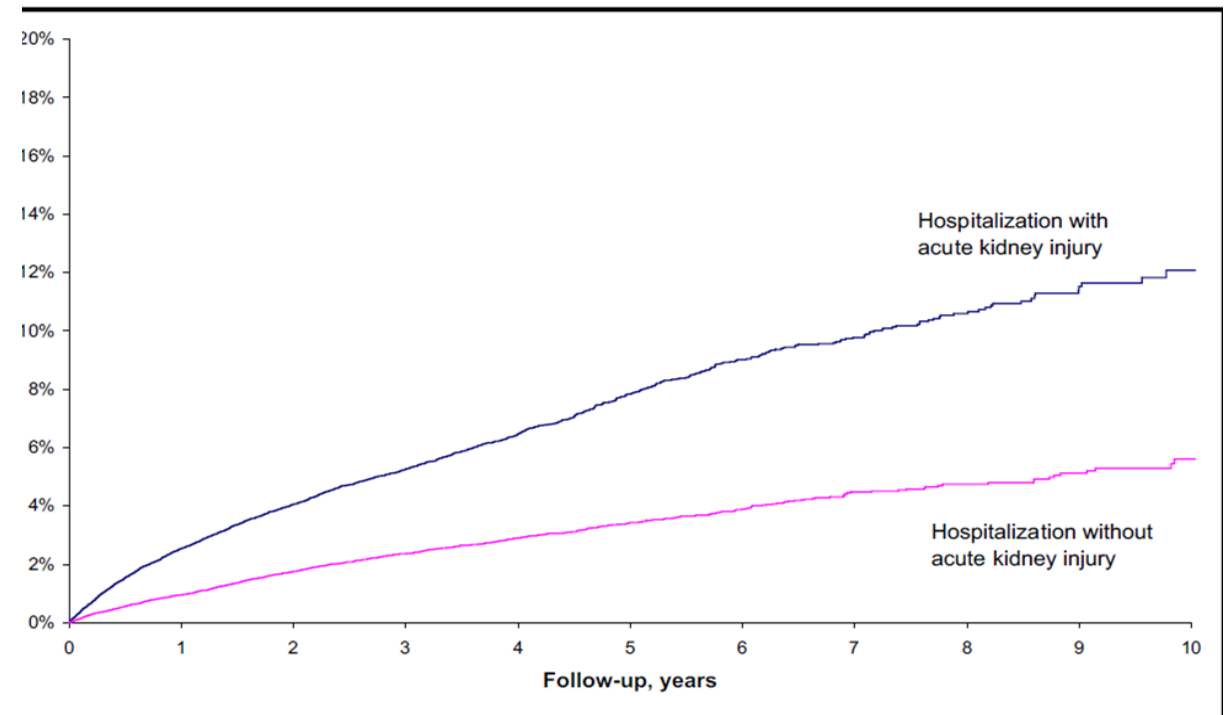
What are the clinical complications of AKI?

Risk of Chronic Dialysis and Death Following Acute Kidney Injury

Ron Wald, MDCM,^{a,b} Robert R. Quinn, MD,^c Neill K. Adhikari, MDCM,^d Karen E. Burns, MD,^{b,e} Jan O. Friedrich, MD,^{b,e} Amit X. Garg, MD,^f Ziv Harel, MD,^a Michelle A. Hladunewich, MD,^{d,g} Jin Luo, MD,^h Muhammad Mamdani, PharmD,^{b,i} Jeffrey Perl, MD,^{a,b} Joel G. Rav, MD^{b,j}; for the University of Toronto Acute Kidney Injury Research Group



In a population based study of hospitalised patients with severe AKI-requiring dialysis, **the risk of new ESRD was increased by three-fold.**



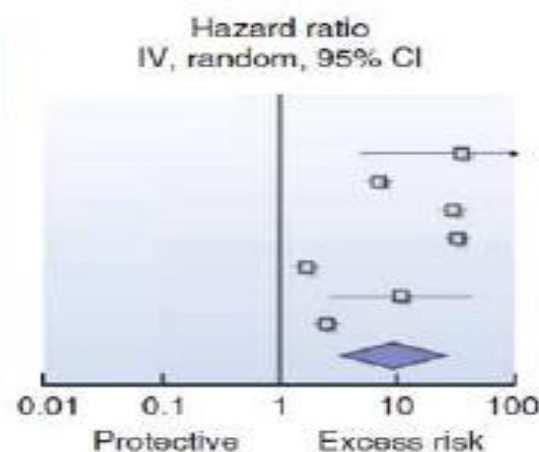
Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis

Steven G. Coca^{1,2,3}, Swathi Singanamala^{1,3} and Chirag R. Parikh^{1,2}

a

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Weiss <i>et al.</i> (13)	10.0	32.79 (4.30–249.77)
Amdur <i>et al.</i> (22)	15.5	6.64 (5.05–8.74)
Lo <i>et al.</i> (11)	15.5	28.08 (21.01–37.53)
James <i>et al.</i> (16)	15.6	29.99 (24.32–36.99)
James <i>et al.</i> (15,23)	15.5	1.60 (1.20–2.14)
Ando <i>et al.</i> (19)	12.4	9.91 (2.48–39.63)
Ishani <i>et al.</i> (21)	15.6	2.33 (1.83–2.96)
Total (95% CI)	100.0	8.82 (3.05–25.48)

Heterogeneity: $\tau^2 = 1.87$; $\chi^2 = 446.89$, d.f. = 6 ($P < 0.00001$);
 $I^2 = 99\%$. Test for overall effect: $Z = 4.02$ ($P < 0.0001$)

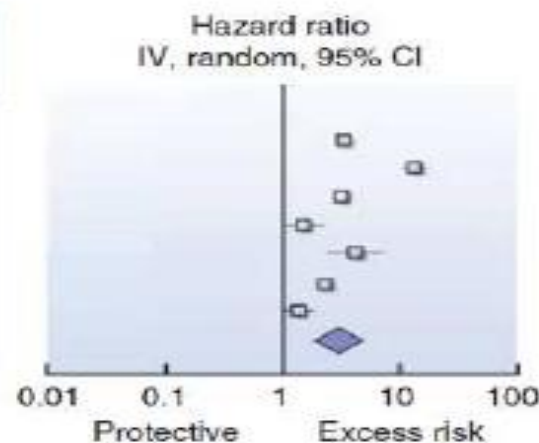


Il rischio di progredire verso una CKD e' aumentato di 10 volte

b

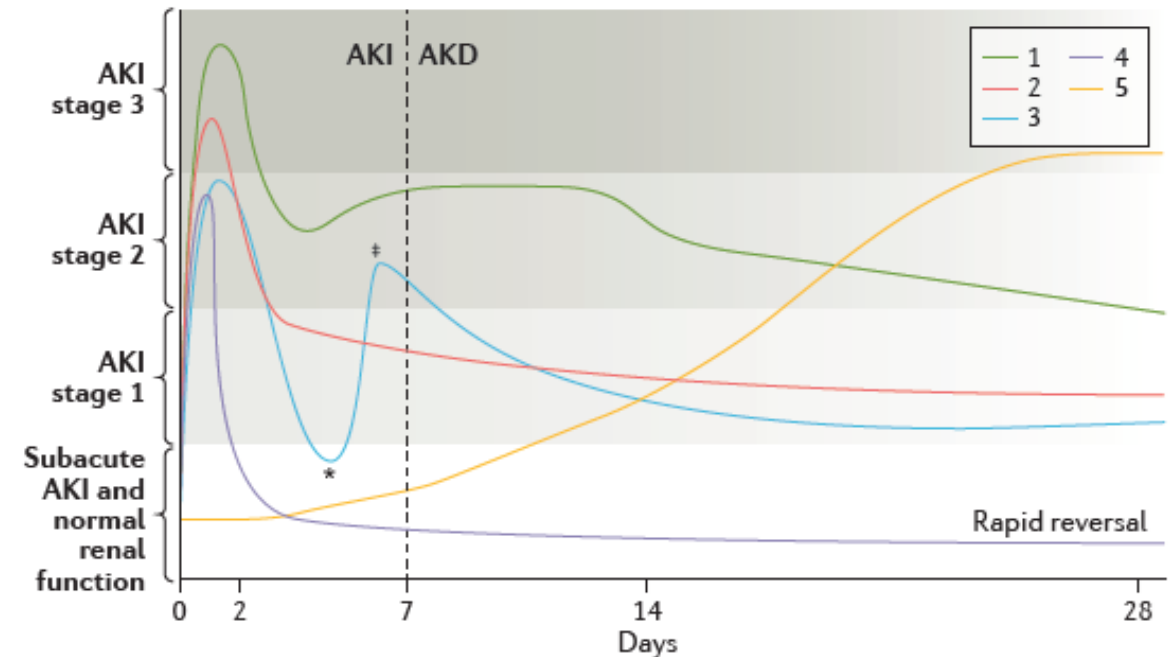
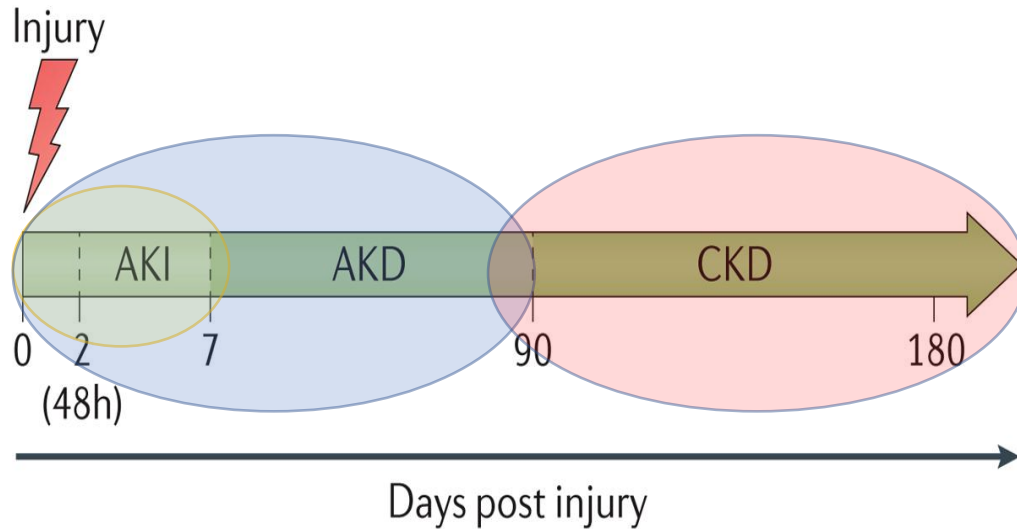
Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Newsome <i>et al.</i> (14)	15.0	3.26 (2.87–3.70)
Ishani <i>et al.</i> (20)	14.8	12.99 (10.57–15.96)
Wald <i>et al.</i> (17)	14.9	3.22 (2.70–3.85)
Hsu <i>et al.</i> (10)	13.5	1.47 (0.95–2.28)
James <i>et al.</i> (15,23)	12.5	4.15 (2.32–7.41)
Lafrance <i>et al.</i> (18)	15.0	2.33 (2.08–2.61)
Choi <i>et al.</i> (12)	14.4	1.37 (1.02–1.84)
Total (95% CI)	100.0	3.10 (1.91–5.03)

Heterogeneity: $\tau^2 = 0.40$; $\chi^2 = 252.85$, d.f. = 6 ($P < 0.00001$);
 $I^2 = 98\%$. Test for overall effect: $Z = 4.58$ ($P < 0.00001$)



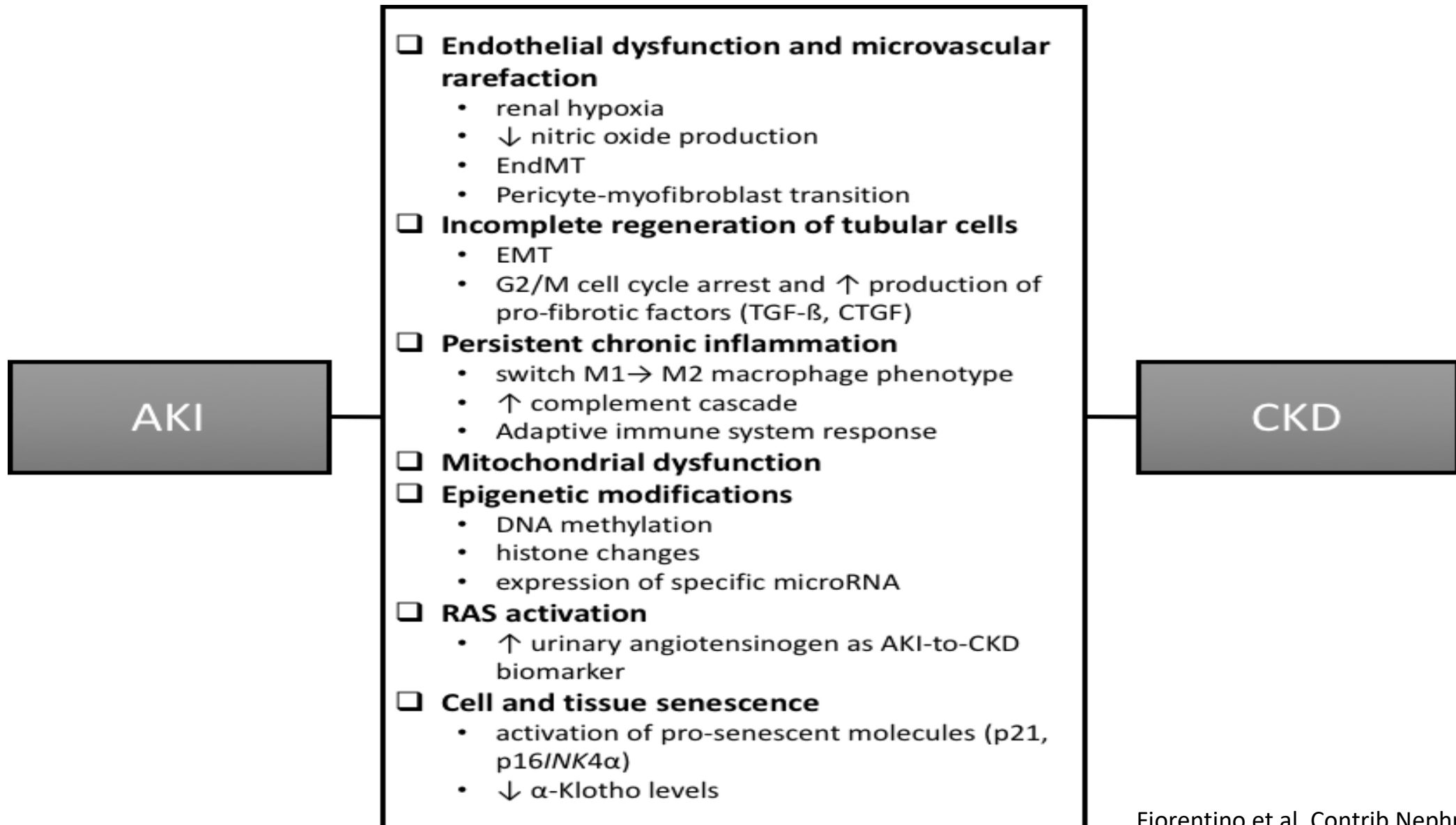
Il rischio di dialisi cronica e' aumentato di 4 volte

AKI and CKD are not separate entities: a continuum of disease

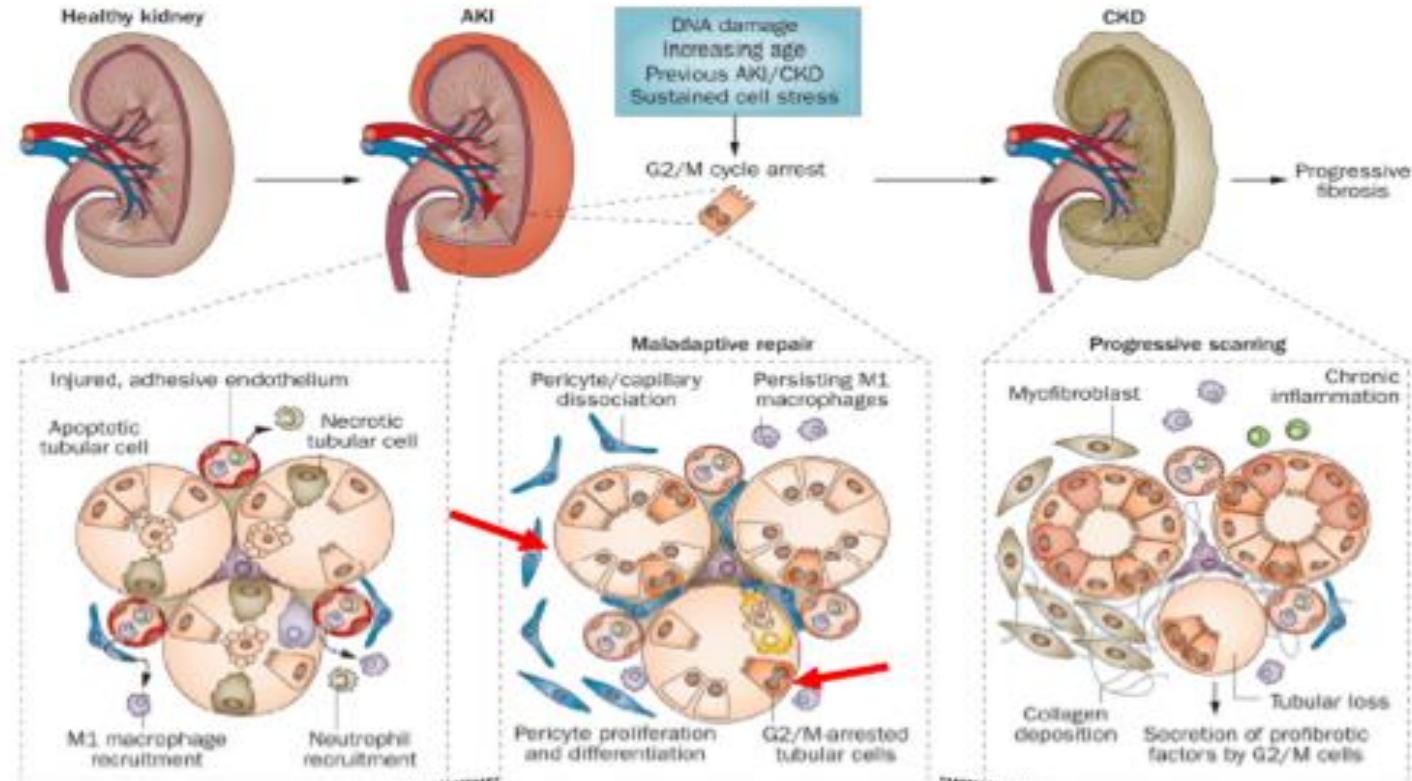


- AKI : an abrupt decrease in kidney function occurring **over 7 days or less**,
- CKD is defined by the persistence of kidney disease for a **period of >90 day**;
- AKD describes acute or subacute damage and/or loss of kidney function for a duration of **between 7 and 90 days** after exposure to an AKI initiating event;
- Recovery from AKI within 48h of the initiating event typically heralds rapid reversal of AKI.
- Patients who suffer AKD with pre-existing CKD are probably at high-risk of kidney disease progression

Mechanisms of AKI to CKD transition

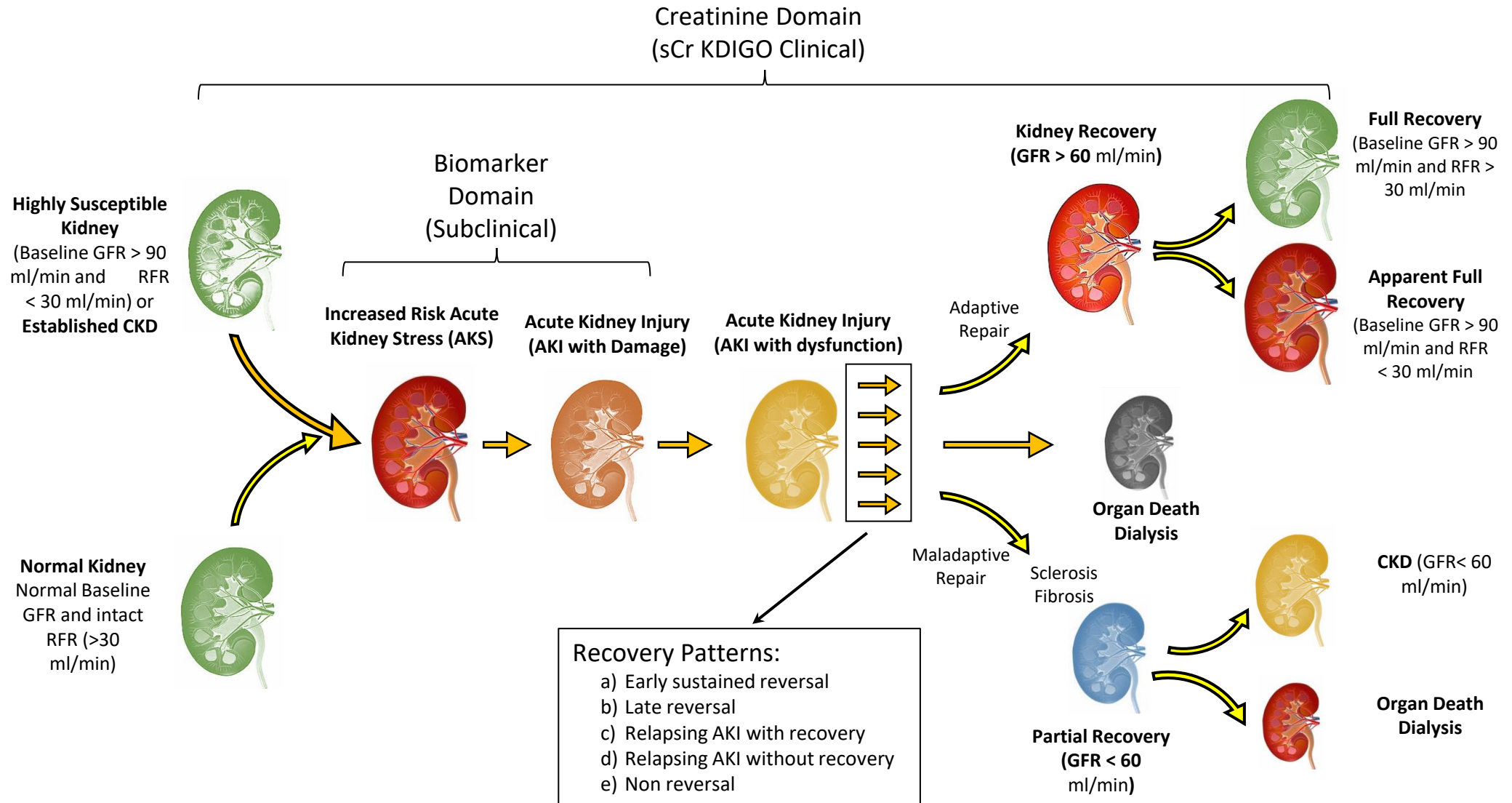


AKI is associated with maladaptive repair and incomplete resolution

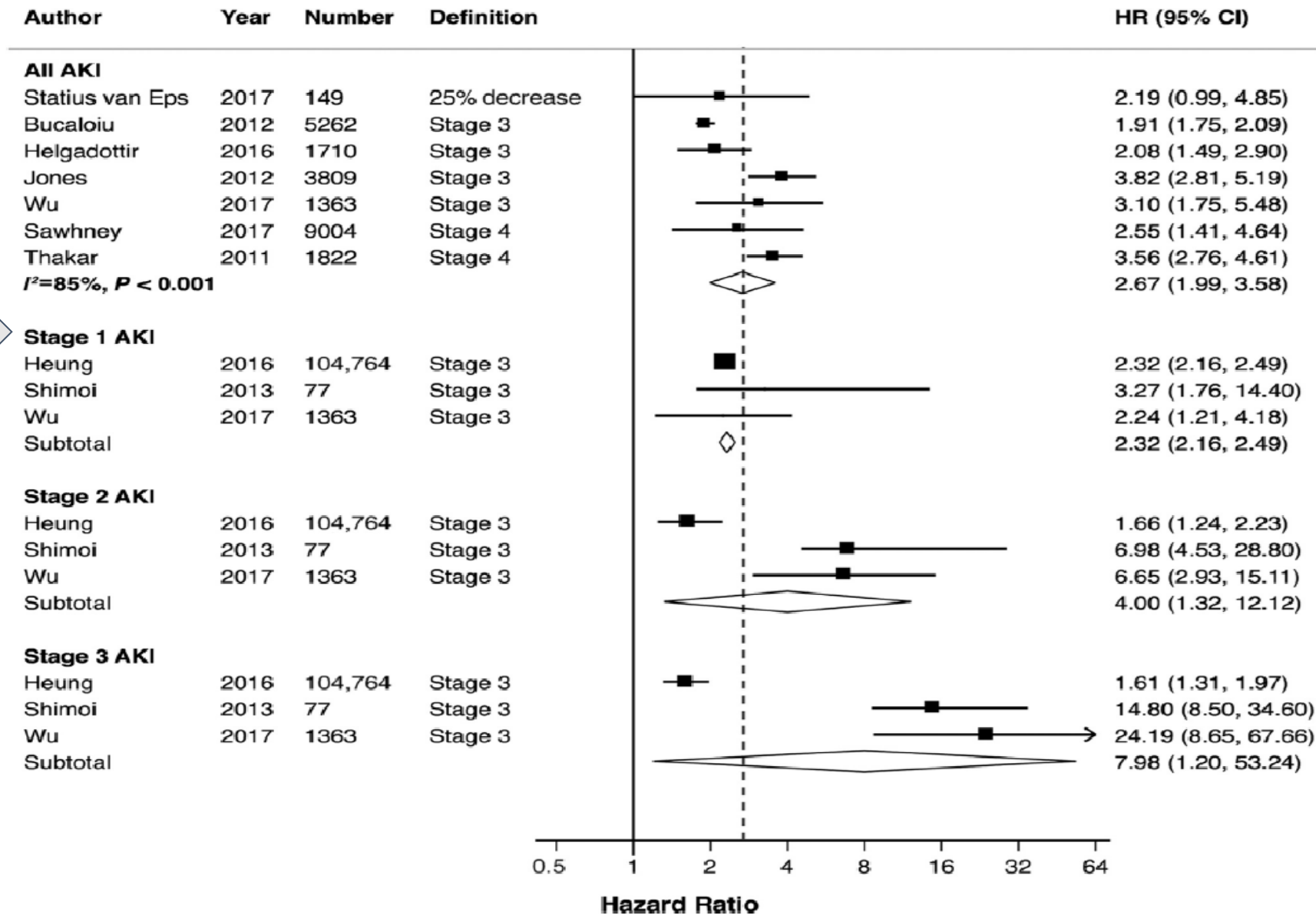


- Vascular rarefaction lead to 30-50% reduction in peritubular capillary density , the loss of vascularity lead to hypoxia and tubular atrophy.
- Injured renal tubular cells become arrested at G2/M and adopt a senescent profibrotic phenotype (releasing TGF β)
- Pericytes and endothelial cells-myofibroblasts trans-differentiation.

Acute Kidney Disease (3 months)



Risk of chronic kidney disease after acute kidney injury (AKI)



ACUTE KIDNEY INJURY

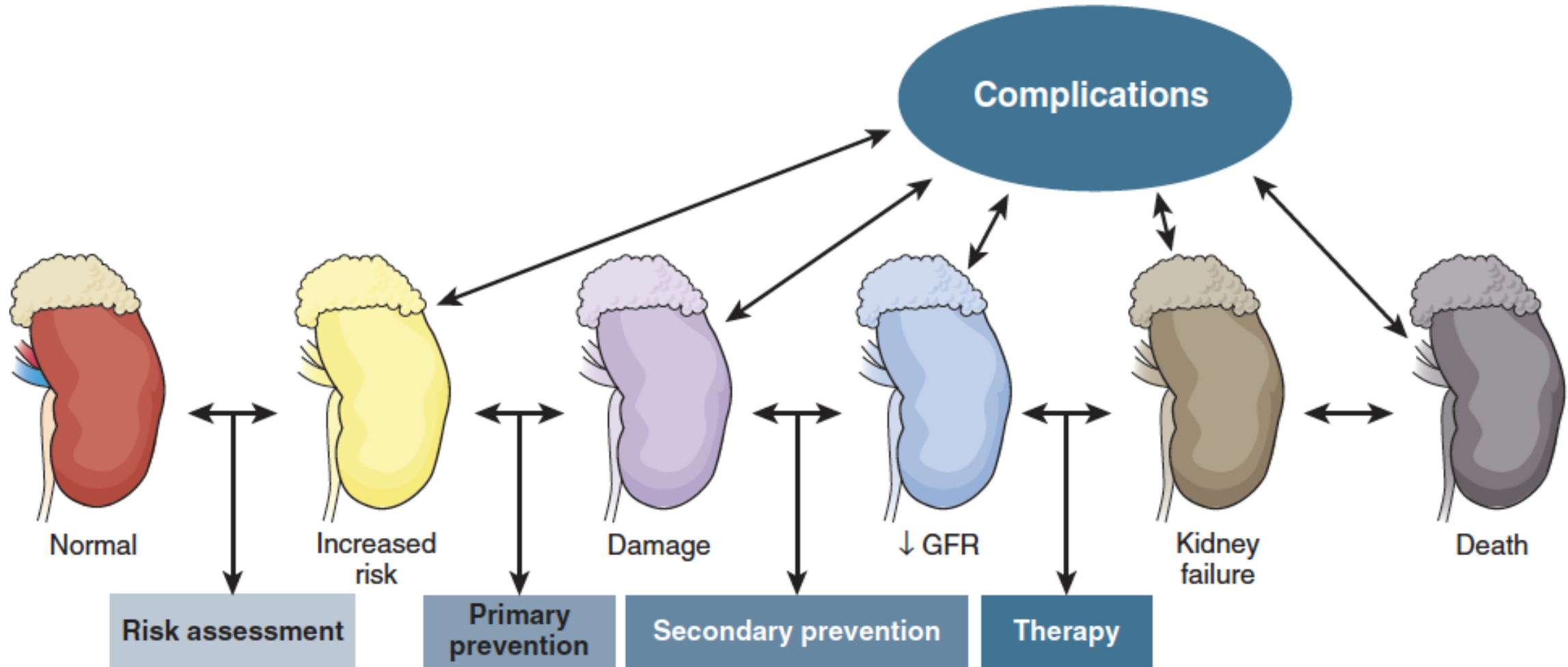


Fig. 70.1 Conceptual model for acute kidney injury (AKI). *GFR*, Glomerular filtration rate. (Modified from reference 48.)

***Risk assessment
and
Preventive measures***

Risk assessment

BOX 70.1 Major Risk Factors for Acute Kidney Injury

Patient Factors

- Older age (>75 years)
- Diabetes
- Liver failure
- Chronic kidney disease
- Atherosclerosis
- Renal artery stenosis
- Hypertension
- Hypotension
- Hypercalcemia
- Hyperuricemia
- Sepsis
- Perioperative cardiac dysfunction
- Rhabdomyolysis
- Tumor lysis syndrome

Medications and Agents

- Nonsteroidal antiinflammatory drugs
- Cyclooxygenase-2 inhibitors
- Cyclosporine or tacrolimus
- Angiotensin-converting enzyme inhibitors
- Angiotensin receptor blockers
- Iodinated radiocontrast agent
- Hydroxyethyl starch (HES)
- Aminoglycosides
- Amphotericin

Procedures

- Cardiopulmonary bypass procedures
- Surgery involving aortic clamp
- Increased intraabdominal pressure
- Large arterial catheter placement with risk for atheroembolization
- Liver transplantation
- Kidney transplantation

There are scarce data to evaluate the prevalence and potential impact of modifiable risk factors on AKI development and progression. The most common risk factor is chronic kidney disease (CKD), and thus adequate determination of baseline kidney function is fundamental.

Risk assessment

BOX 70.1 Major Risk Factors for Acute Kidney Injury

Patient Factors

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- Hydroxyethyl starch (HES)
- Aminoglycosides
- Amphotericin

Il medico di famiglia



There are scarce data to evaluate the prevalence and potential impact of modifiable risk factors on AKI development and progression. The most common risk factor is chronic kidney disease (CKD), and thus adequate determination of baseline kidney function is fundamental.

Table 1. Medications associated with pseudo-AKI and hemodynamically mediated AKI

Medications Associated with Pseudo-AKI	Mechanism of Increased Serum Creatinine	Medications Associated with Hemodynamically Mediated AKI	Mechanism of Reduced GFR
<ul style="list-style-type: none"> • Cimetidine • Trimethoprim • Dronedarone • Cobicistat and dolutegravir • Tyrosine kinase inhibitors (imatinib, bosutinib, sorafenib, sunitinib, crizotinib, gefitinib, and pazopanib) • Pyrimethamine • Dexamethasone 	<p>Decrease creatinine secretion through the proximal tubular cells into the urine</p> <p>Some formulations contain creatinine as an excipient</p>	<ul style="list-style-type: none"> • Angiotensin converting enzyme inhibitors and angiotensin receptor blockers • NSAIDs • SGLT2 inhibitors • Calcineurin inhibitors 	<p>Inhibit efferent arteriolar vasoconstriction and reduce GFR</p> <p>Inhibit production of vasodilatory prostaglandins with afferent arteriolar vasoconstriction (especially prominent in states of volume depletion, older age, hypercalcemia and effective arterial volume depletion such as cirrhosis, heart failure, nephrotic syndrome)</p> <p>Induce vasoconstriction of the afferent arteriole due to tubuloglomerular feedback</p> <p>Induce vasoconstriction of the afferent arteriole (due to an imbalance between vasoconstrictor agents such as endothelin, thromboxane, and activation of the renin-angiotensin system and decrease of vasodilator factors like prostaglandin E2, prostacyclin, and nitric oxide)</p>
<ul style="list-style-type: none"> • Cefoxitin • Flucytosine 	<p>Recognized as a creatinine chromagen by the alkaline picrate method of creatinine analysis</p> <p>Interferes with enzymatic assay for serum creatinine determination</p>		
<ul style="list-style-type: none"> • Corticosteroids 	<p>Catabolic state with release of creatine from muscle, which is converted to creatinine</p>		
<ul style="list-style-type: none"> • Calcitriol and alfacalcidol • Fenofibrate 	<p>Unclear</p> <p>Increase metabolic production of creatinine</p>		

NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 2. Medications associated with acute tubular injury and preventative strategies

Medication Class	Individual Medications	Preventative Strategies ^a
Antibiotics	Aminoglycosides (gentamicin, neomycin, amikacin)	<ul style="list-style-type: none"> • Once daily dosing • Adjust dose for underlying eGFR • Use tobramycin over gentamicin if possible
	Vancomycin (+/- piperacillin-tazobactam)	<ul style="list-style-type: none"> • Adjust dose for underlying eGFR • Therapeutic drug monitoring (maintain trough concentrations <15 ng/ml) • Avoid combination with piperacillin-tazobactam
	Colistin/polymyxins	<ul style="list-style-type: none"> • Use alternative agents • Adjust dose for underlying eGFR • Avoid prolonged use
Antifungals	Amphotericin B products	<ul style="list-style-type: none"> • Use alternative agents • Use lipid or liposomal forms • iv isotonic crystalloid hydration
Antiviral agents	Cidofovir, tenofovir, adefovir	<ul style="list-style-type: none"> • Adjust dose for underlying eGFR • Screen for tubular toxicity to identify early injury
Analgesics	Foscarnet NSAIDs including COX-2 inhibitors Acetaminophen overdose	<ul style="list-style-type: none"> • Use alternative agents • Avoid use in high-risk patients • Avoid excessive dosing especially in liver disease
Chemotherapeutic agents	Cisplatin (less common with other platin analogs)	<ul style="list-style-type: none"> • Adjust dose for underlying eGFR • iv isotonic crystalloid-induced diuresis • Use of lower-dose regimens • Use of cisplatin analogs • Consider sodium thiosulfate in high-risk patients
	Ifosfamide	<ul style="list-style-type: none"> • Adjust dose for underlying eGFR • Limit dose • Mesna and N-acetylcysteine of unproven efficacy
	Pemetrexed	<ul style="list-style-type: none"> • Adjust dose for underlying eGFR • Avoid in patients with eGFR<45 ml/min per 1.73 m²
Radiocontrast agents	Iodinated radiocontrast agents	<ul style="list-style-type: none"> • iv isotonic crystalloid hydration • Low or iso-osmolar contrast agents
Calcineurin inhibitors	Cyclosporine, tacrolimus	<ul style="list-style-type: none"> • Reduce dose and follow drug levels • Consider alternative agents such as mTOR inhibitors
Bisphosphonates	Pamidronate	<ul style="list-style-type: none"> • Lengthen infusion times to >2 h • Use lower doses • Use alternative agents such as denosumab
	Zoledronic acid	<ul style="list-style-type: none"> • Use lower doses especially if eGFR<60 ml/min per 1.73 m² • Contraindicated in AKI and eGFR<30 ml/min per 1.73 m² • Use alternative agents such as denosumab

iv, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs; COX, cyclo-oxygenase; mTOR, mammalian target of rapamycin.
^aVolume expansion to correct hypovolemia and enhance tubular flow is recommended as prevention for many of the drugs noted in this table.

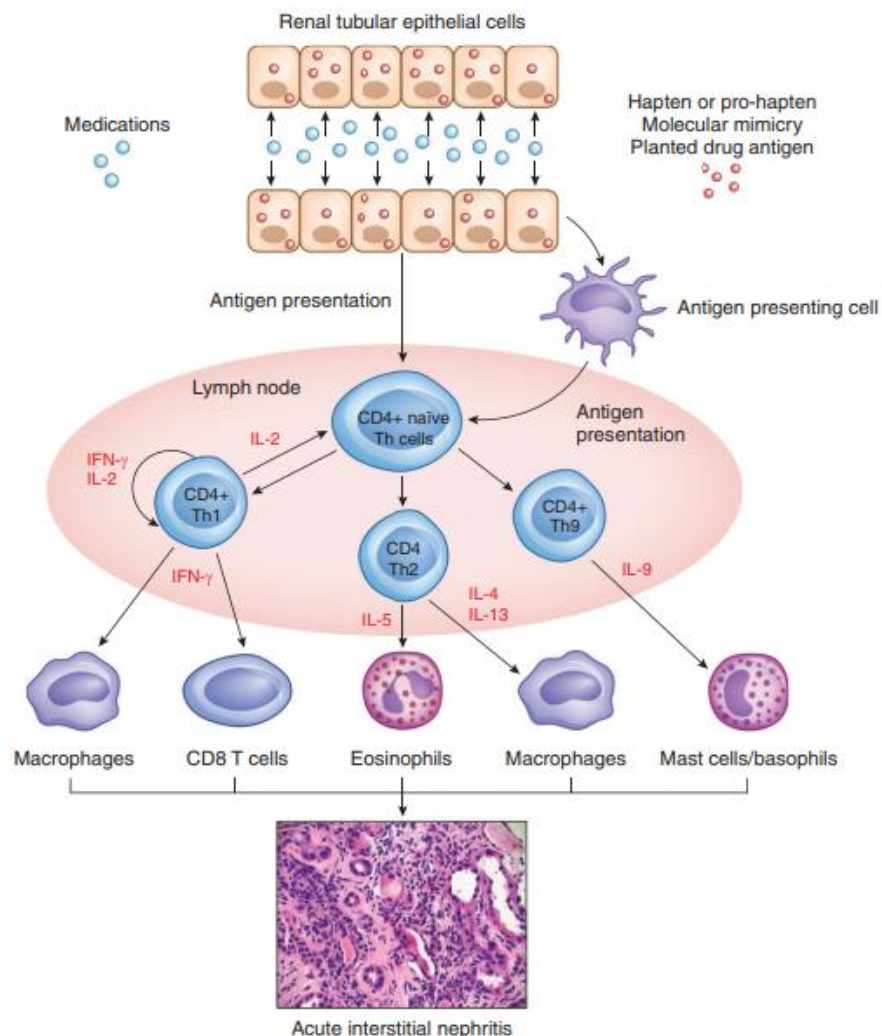


Figure 2. | Pathogenesis of drug-induced acute interstitial nephritis. Medications or their metabolites can incite an immune response through various processes. They can bind to TBM and act as haptens or prohaptens, Drugs can mimic an antigen that is normally present on TBM or interstitium, thereby inducing an immune response directed at this antigen. Drugs can also bind TBM or deposit within the interstitium, acting as a planted antigen. Dendritic and tubular cells present antigen to CD4⁺ naive Th cells, stimulating the formation of various subsets of Th cells. These cells then produce various cytokines such as ILs and IFNs, which attract a number of cells (macrophages, eosinophils, CD8 T cells, and mast cells/basophils) to the tubulointerstitium. These cells can participate in the development of acute interstitial nephritis. TBM, tubular base-membrane; Th, T-helper. This figure was generously provided by Dr. Dennis Moledina, with permission.

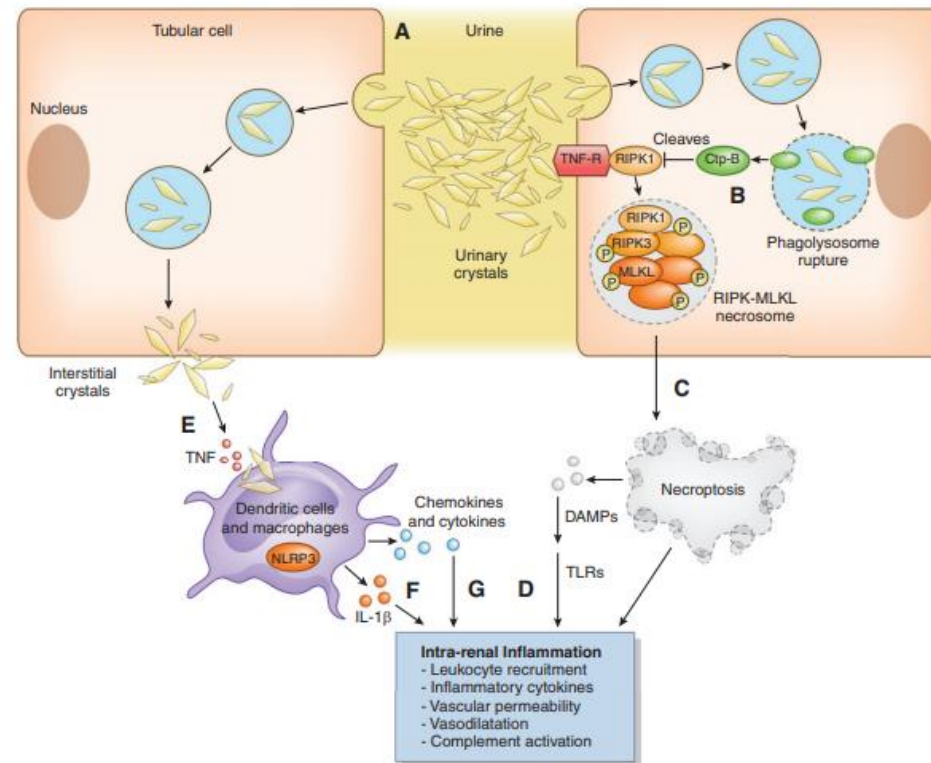


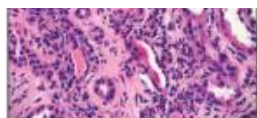
Figure 3. | Pathogenesis of drug-induced crystalline-related AKI. Drug crystals precipitating in the tubular lumen cause tubular obstruction (A) and induce tubular cell necroptosis by activating a number of pathways. Crystal uptake into lysosomes and phagolysosomes is associated with release of ctp-B when the lysosomes are destabilized (B). ctp-B cleaves and degrades the negative regulator of necroptosis RIPK1, which triggers the formation of the RIPK3-MLKL necrosome complex, which causes tubular cell necroptosis (C). Necroptosis stimulates DAMPs, which induce TLR-dependent inflammation and cell necrosis (D). Dendritic cells phagocytose crystals present in the renal interstitium (E) and activate NLRP3 inflammasome and IL-1 β secretion by dendritic cells (F), which leads to IL-1 receptor-dependent inflammation in the kidney. Other cytokine and chemokine production produces further tubular injury and inflammation (G). Overall, these pathways promote an autoamplification loop of crystal-induced intrarenal inflammation. ctp, cathepsin-B; DAMPs, damage-associated molecular patterns; MLKL, mixed lineage kinase domain-like protein; NLRP3, NACHT-, LRR-, and PYD-domains-containing protein-3; RIPK1, receptor-interacting protein kinase-3; TLR, toll-like receptor.

Renal tubular epithelial cells



Medication Class	Individual Medications
Antibiotics	β-Lactam drugs (penicillin and derivatives, cephalosporins) Sulfa-based antimicrobials (trimethoprim-sulfamethoxazole, sulfadiazine) Fluoroquinolones Macrolides Rifampin
Antacid GI drugs	Proton pump inhibitors (class effect for all agents) Histamine-2 blockers
Analgesics	NSAIDs including COX-2 inhibitors (class effect for all agents)
Immunotherapies	PD-1 inhibitors (nivolumab, pembrolizumab, cemiplimab) PD-L1 inhibitors (atezolizumab, durvalumab, avelumab) CTLA-4 inhibitors (ipilimumab, tremelimumab)
Antiangiogenesis drugs	Bevacizumab, tyrosine kinase inhibitors (sorafenib, sunitanib)
Diuretics	Loop diuretics (furosemide, bumetanide) Thiazide diuretics (hydrochlorothiazide)
Antiviral agents	Acyclovir Abacavir Indinavir Atazanavir Foscarnet
Anticonvulsants	Phenobarbital Carbamazepine Phenytoin
Other agents	Ifosfamide Pemetrexed Lithium Allopurinol Mesalamine and other 5-aminosalicylates

GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; COX-2, cyclooxygenase-2; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; CTLA-4, cytotoxic T lymphocyte associated protein-4.



Acute interstitial nephritis

Figure 2. | Pathogenesis of drug-induced acute interstitial nephritis. Medications or their metabolites can incite an immune response through various processes. They can bind to TBM and act as haptens or prohaptens. Drugs can mimic an antigen that is normally present on TBM or interstitium, thereby inducing an immune response directed at this antigen. Drugs can also bind TBM or deposit within the interstitium, acting as a planted antigen. Dendritic and tubular cells present antigen to CD4⁺ naive Th cells, stimulating the formation of various subsets of Th cells. These cells then produce various cytokines such as ILs and IFNs, which attract a number of cells (macrophages, eosinophils, CD8 T cells, and mast cells/basophils) to the tubulointerstitium. These cells can participate in the development of acute interstitial nephritis. TBM, tubular basement membrane; Th, T-helper. This figure was generously provided by Dr. Dennis Moledina, with permission.

Culprit Medication	Clinical Renal Syndromes	Histologic Findings	Preventive and Therapeutic Strategies ^a
Methotrexate	Crystalluria, AKI, and CKD	Crystals form annular structures consisting of small needle-shaped crystals that stain yellow, golden, or brown on H&E stain, weak rim staining on PAS, black staining on JS, and positively birefringent on polarization	IVFs before/during drug, alkalinize urine, adjust drug dose for kidney function; folic acid; glucarbitase (<60 h after methotrexate); high-flux HD in certain circumstances
Sulfadiazine, sulfamethoxazole	Crystalluria, AKI, CKD, and nephrolithiasis	Interstitial fibrosis with mild mononuclear inflammation observed in absence of sulfa crystals within tubules or interstitium	Alkalinize urine, adjust dose for kidney function, assure euvoolemia before drug exposure
Indinavir, atazanavir, darunavir	Crystalluria, AKI, CKD, and nephrolithiasis	Translucent, needle-shaped indinavir, atazanavir, or darunavir crystals within tubules with an associated monocytic infiltrate and giant-cell reaction	No role for urine acidification, assure euvoolemia during drug therapy; switch to different medication
Acyclovir	Crystalluria, AKI, and CKD	Needle-shaped crystals within tubules +/- peritubular inflammation and positively birefringent on polarization	Avoid rapid iv bolus, adjust drug dose for kidney function, assure euvoolemia during drug therapy
Ciprofloxacin, levofloxacin	Crystalluria and AKI	Needle-shaped crystals within tubules and strongly birefringent with polarization	Assure euvoolemia during drug therapy and avoid alkaline urine (if possible)
iv ascorbic acid, orlistat (by causing enteric hyperoxaluria), ethylene glycol	Crystalluria, AKI, and CKD	Crystals are translucent to pale blue fan-like or sunburst shapes within tubules and interstitium with interstitial inflammation and positively birefringent on polarization	Ascorbic acid and orlistat: assure euvoolemia during drug therapy, avoid other nephrotoxins; fomepizole and HD for ethylene glycol
Sodium phosphate purgative (oral rather than enema)	AKI and CKD	Granular bluish-purple crystal deposits with positive von Kossa staining and negative birefringence on polarization	Assure euvoolemia before exposure, avoid concomitant NSAIDs, diuretics, and RAS blockers
Triamterene	Crystalluria, AKI, CKD, and nephrolithiasis	Crystals stain yellow/brown on H&E and PAS, silver-positive on JS, and strongly birefringent on polarization	Alkalinize urine, assure euvoolemia during drug therapy
Amoxicillin	Crystalluria and AKI	No histologic evidence of intrarenal deposits of amoxicillin crystals on biopsy	Assure euvoolemia, adjust drug dose for kidney function
Foscarnet	AKI, hematuria, proteinuria, and CKD	Plates and geometric shapes in dilated capillary loops and tubular lumens associated and positively birefringent on polarization	Assure euvoolemia during drug therapy and adjust drug dose for kidney function

H&E, hematoxylin and eosin; PAS, periodic acid-Schiff; JS, Jones methenamine silver; IVF, intravenous fluid; iv, intravenous; HD, hemodialysis; NSAIDs, nonsteroidal anti-inflammatory drugs; RAS, renin-angiotensin system.
^aTreatment includes drug discontinuation, intravenous fluids for hypovolemia, and supportive care including dialysis.

Table 3. Common risk factors for drug-induced acute tubular injury

Modifiable Risks	Nonmodifiable Risks
<p>Volume depletion and/or hypotension Exposure to concomitant nephrotoxins High-level exposure to nephrotoxins (high-dose and long-duration therapy) Excessive medication dose for underlying GFR</p>	<p>Advanced age especially with concomitant CKD (eGFR < 45 ml/min per 1.73 m²) Comorbid conditions such as liver disease, diabetes mellitus, heart failure, major surgery (especially cardiovascular) High-risk settings such as intensive care unit, burn unit, cardiovascular care unit Shock states such as sepsis Solid organ transplantation Stem cell transplantation Genetic vulnerability</p>

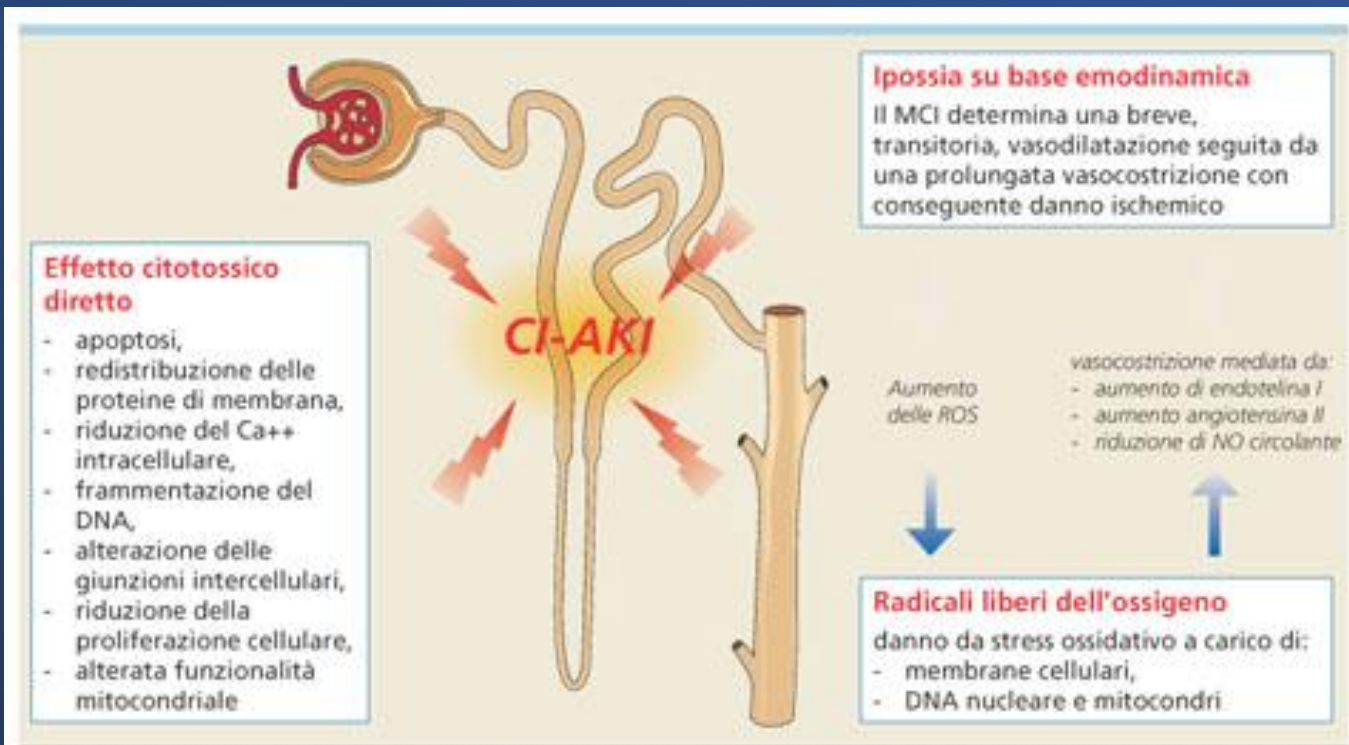
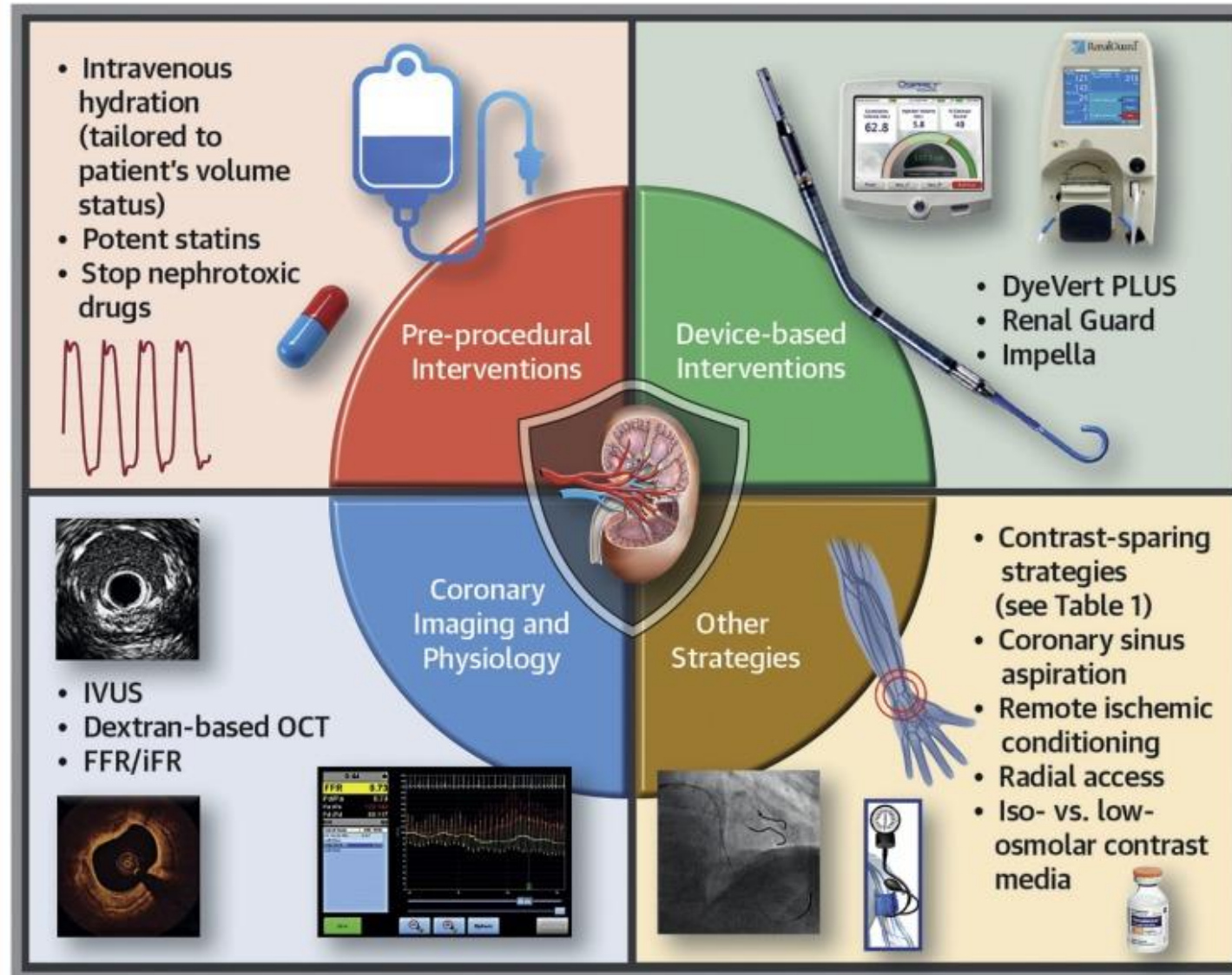


Figura 1. Fisiopatologia del danno renale acuto da mezzo di contrasto (CI-AKI).
 NO, ossido nitrico; MCI, mezzo di contrasto iodato; ROS, specie reattive dell'ossigeno.

CENTRAL ILLUSTRATION: Measures to Decrease the Risk of CI-AKI Before and During PCI








CENTRAL ILLUSTRATION: Measures to Decrease the Risk of CI-AKI Before and During PCI

RISK

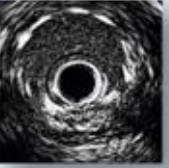
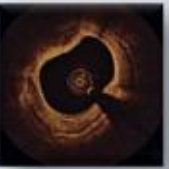


BENEFIT

- Intravenous hydration (tailored to patient's volume status)
- Potent statins
- Stop nephrotoxic drugs

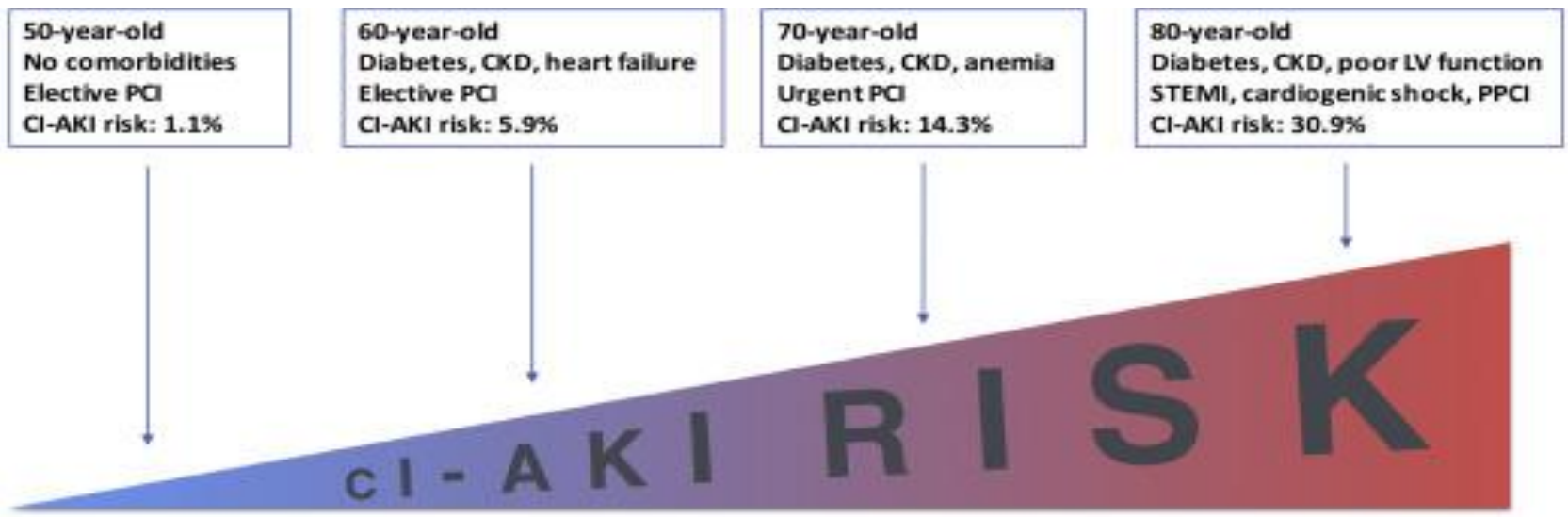






DyeVert PLUS
Renal Guard
Tempella

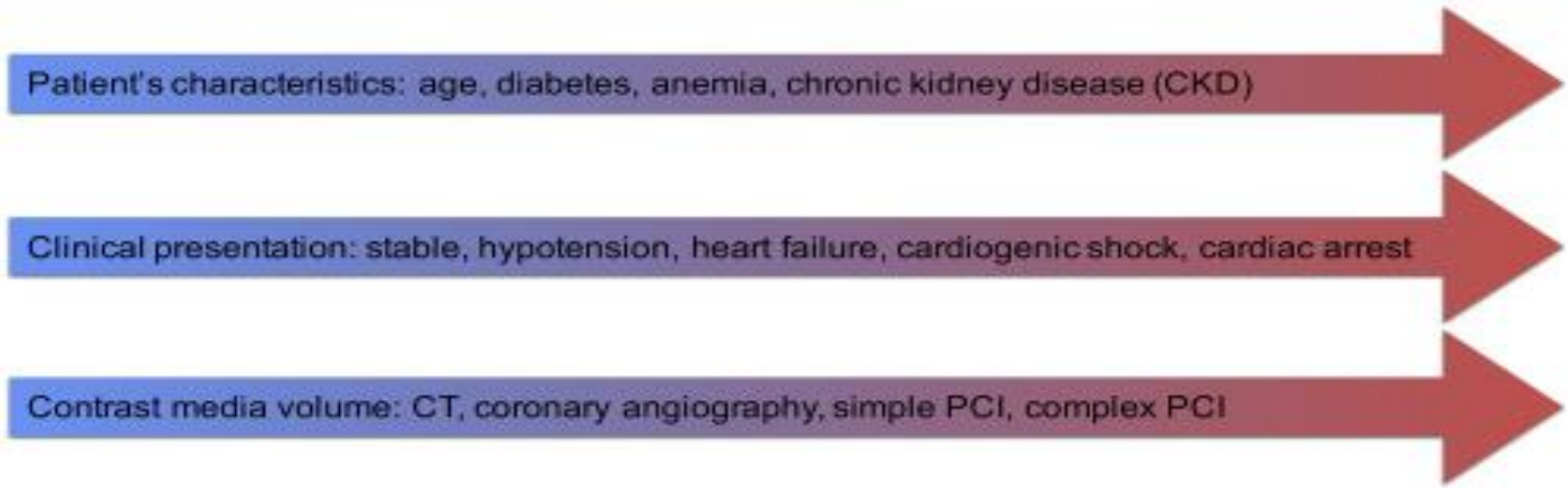
- Contrast-sparing strategies (see Table 1)
- Coronary sinus aspiration
- Remote ischemic conditioning
- Radial access
- Iso- vs. low-osmolar contrast media

- IVUS
- Dextran-based contrast
- FFR/iFR



Low risk



High risk

PREVENTIVE MEASURES

Optimizing Volume and Hemodynamic Status (actually no guidelines):

Isotonic fluids and vasopressors can be administered depending on the clinical scenario.

Prevention of Contrast-Induced Acute Kidney Injury:

- BEFORE CONTRAST: NaCl 0.9% 500 cc + NaHCO₃ 8.4% 100 cc + ½ fl n-acetylcysteine
- AFTER CONTRAST: NaCl 0.9% 500 cc

Prevention of Drug-Induced and Nephrotoxin-Induced Acute Kidney Injury:

- Knowledge of mechanisms of renal injury
- patient-related risk factors: older age (60 years or older), CKD, diabetes, heart failure, volume depletion, and sepsis
- drug-related risk factors

Correctly estimating the GFR before initiation of therapy, adjusting the dosage, monitoring renal function and drug dosage during therapy, and the administration of intravenous saline before exposure if possible. Alternative non-nephrotoxic drugs should BE used, and nephrotoxic drug combinations should be avoided whenever feasible.