Contrast-Induced/Associated Acute Kidney Injury

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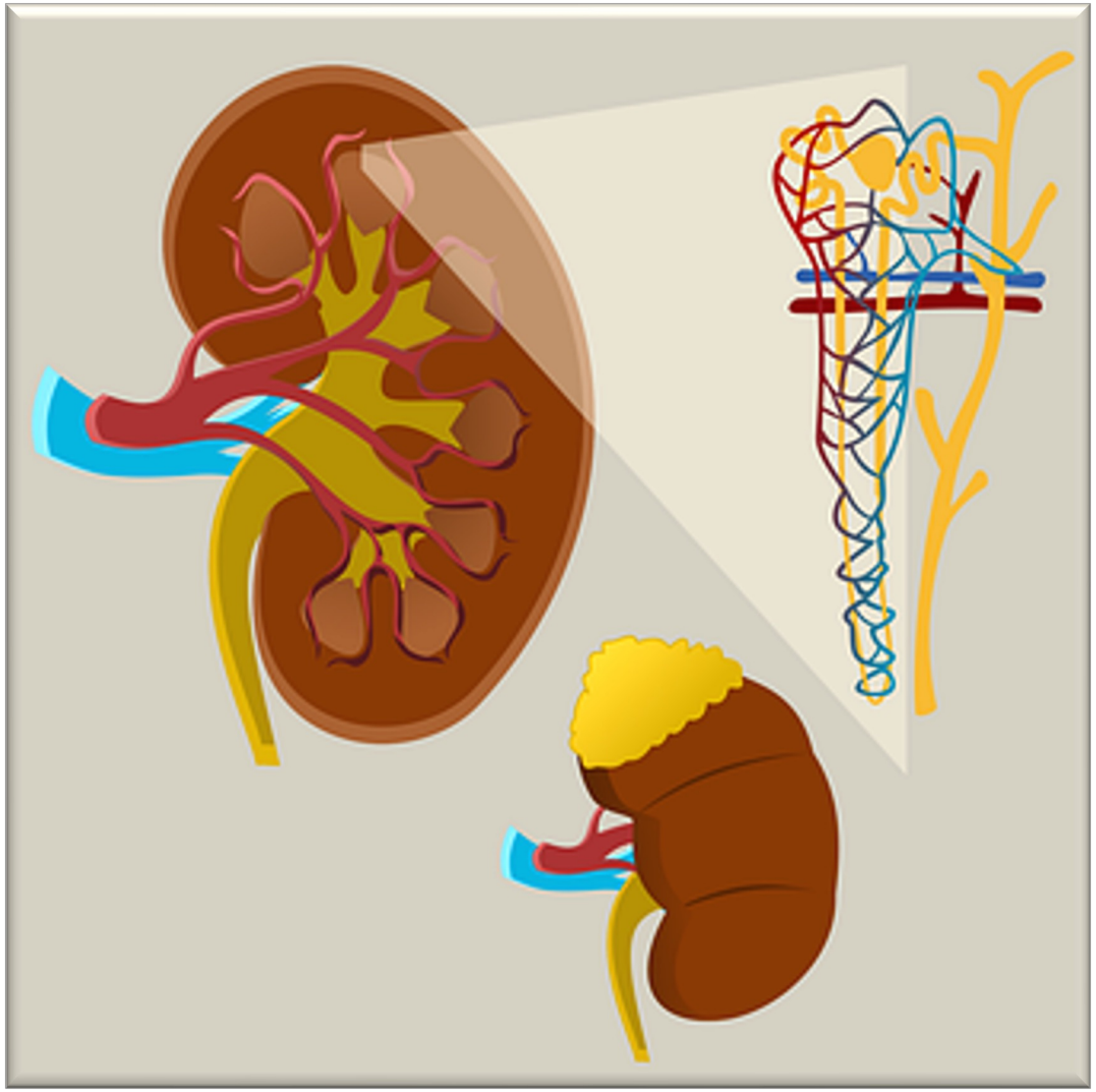
APP2APP lecturer



Lecture Objectives

Review acute kidney injury (AKI)

Discuss contrast-Associated AKI (CA-AKI)

Discuss management of contrast-associated AKI

Identify at-risk patient populations for CA-AKI

Discuss preventative measures used to decrease risk of CA-AKI

Kidney Terminology

Acute kidney injury (AKI)

- Pre-renal AKI (azotemia)
- Intrarenal AKI

  ATN – including CA-AKI/CIN/CI-AKI
- Post-renal AKI

Chronic kidney disease (CKD)

- Diabetes mellitus (DM)

End stage renal disease (ESRD)

Estimated glomerular filtration rate (eGFR)

eGFR is one of the **primary diagnostic methods for detecting and managing kidney diseases**

- It is used to make clinical decisions, medication dose adjustment, etc

The eGFR equation includes:

- Serum Creatinine and/or Serum Cystatin C
- Age
- Sex
- Race
- and/or body weight

However, race is a social, not a biological, construct.

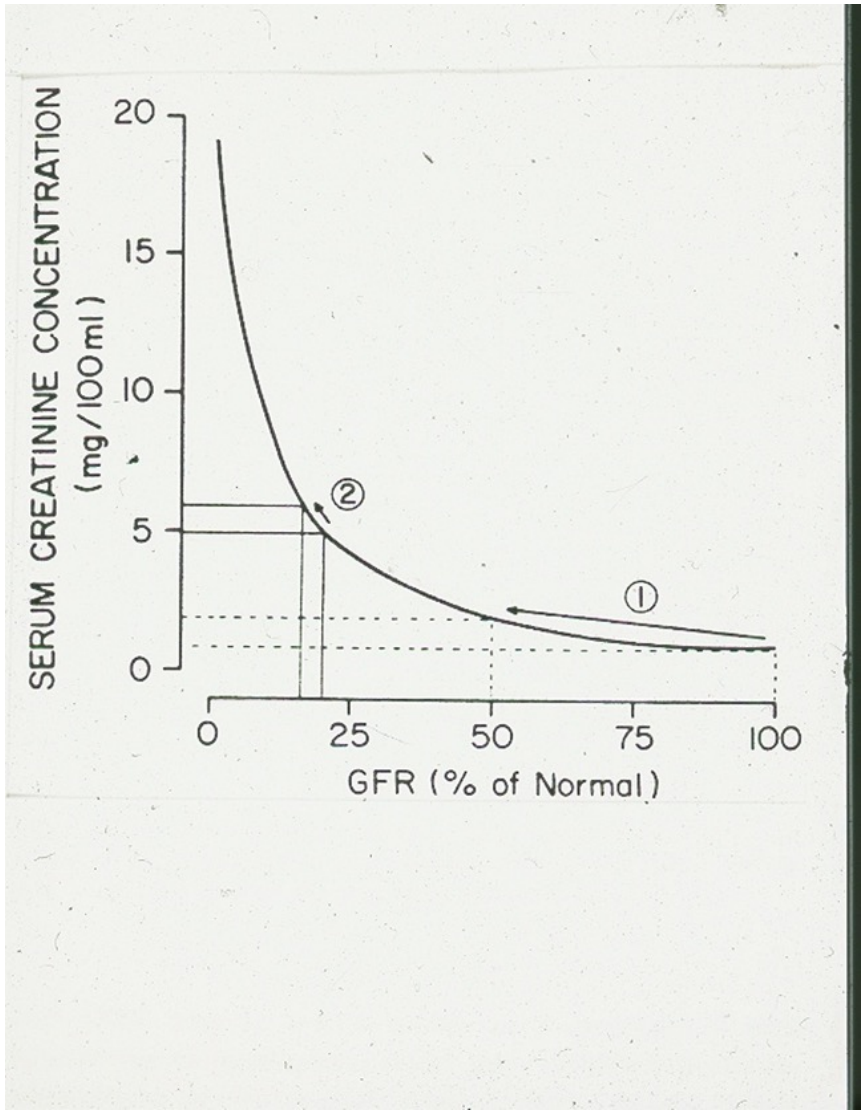
In adults, the most widely used equations are the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation

GFR (mL/min/1.73 m^2) = 141 × (Scr)-1.154 × (Age)-0.203 × (0.742 if female) × (1.212 if African American) (conventional units)

Serum Creatinine

The greatest loss of renal function occurs between a creatinine of 1-2mg/dL

- Creatinine 1 mg/dL is the baseline for a given patient with normal GFR
- Creatinine 2 mg/dL is 50% reduction in GFR
- Creatinine 4 mg/dL is 70 to 85% reduction in GFR
- Creatine 8 mg/dL is 90 to 95% reduction in GFR
- A change from 0.6 to 1.2 mg/dL reflects a 50% reduction in GFR though levels are still within normal range



Acute Kidney Injury (AKI)

Acute Kidney Injury (AKI) [1]

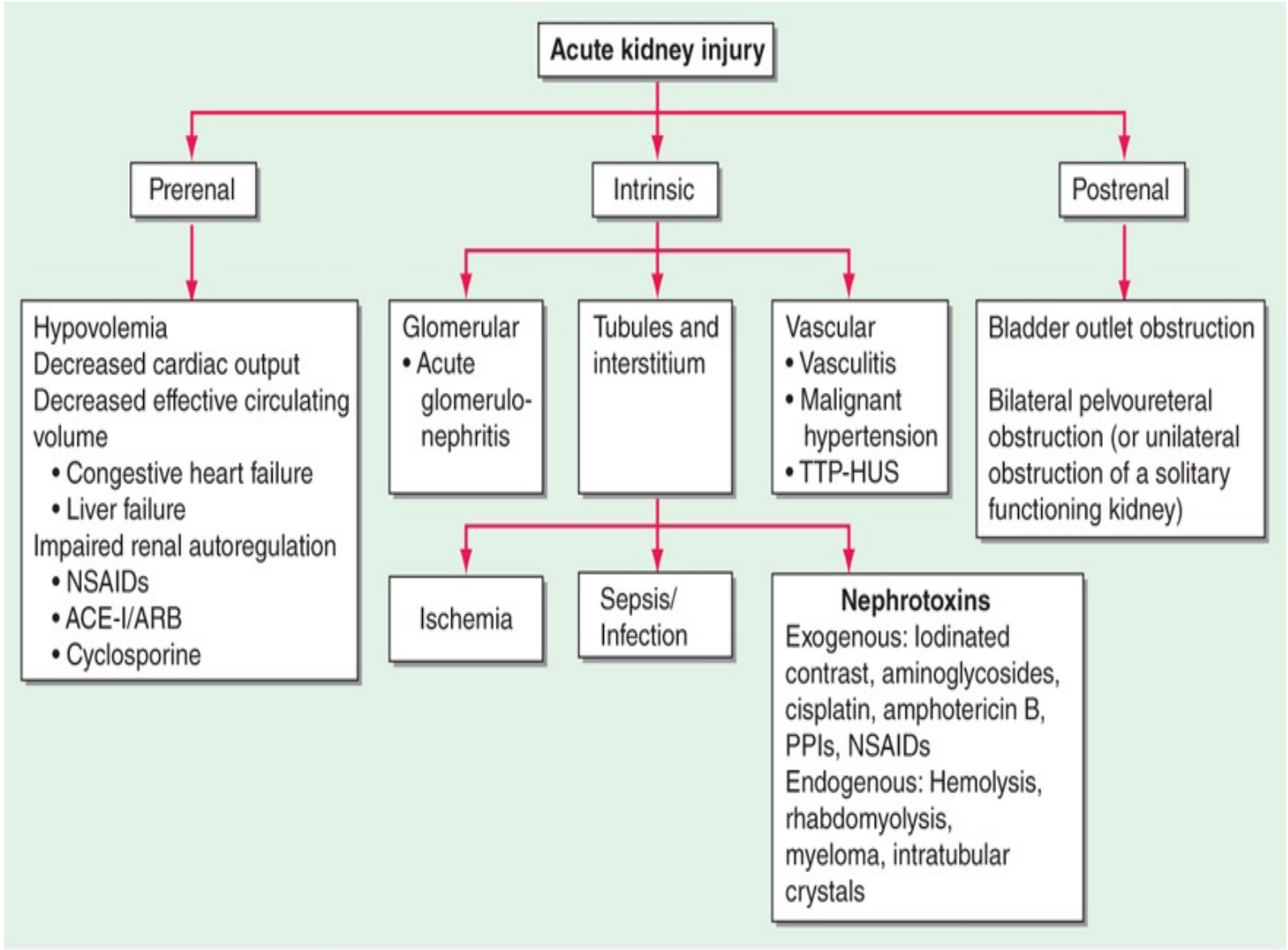
Impairment of kidney filtration and excretory function over days to weeks, resulting in the retention of nitrogenous and other waste products normally cleared by the kidneys

Criteria for the diagnosis of AKI is:

- a rise of creatinine from baseline of at least 0.3 mg/dL within 48 h OR at least 50% higher than baseline within 1 week
- or a reduction in urine output to less than 0.5 mL/kg per hour for longer than 6 h

There are 3 types of AKI

- Pre-renal
- Intrarenal
- Post-renal



Pre-renal: Hypoperfusion without renal parenchymal injury

Intrinsic: Renal parenchymal injury

Post-renal: Obstruction below the kidneys

Obstruction must be in bilateral ureters or at level of bladder and beyond to cause renal failure

Acute Tubular Necrosis[1]

Type of acute kidney injury (AKI) due to tubular damage.

Accounts for ~ **90% of intrinsic AKI**

ATN is a pathological diagnosis based on characteristic histologic findings

- Proximal tubule most susceptible to injury
- Sloughing of brush border membrane into the lumen
- Obstruction of tubular lumen

May result from persistent “pre-renal” AKI

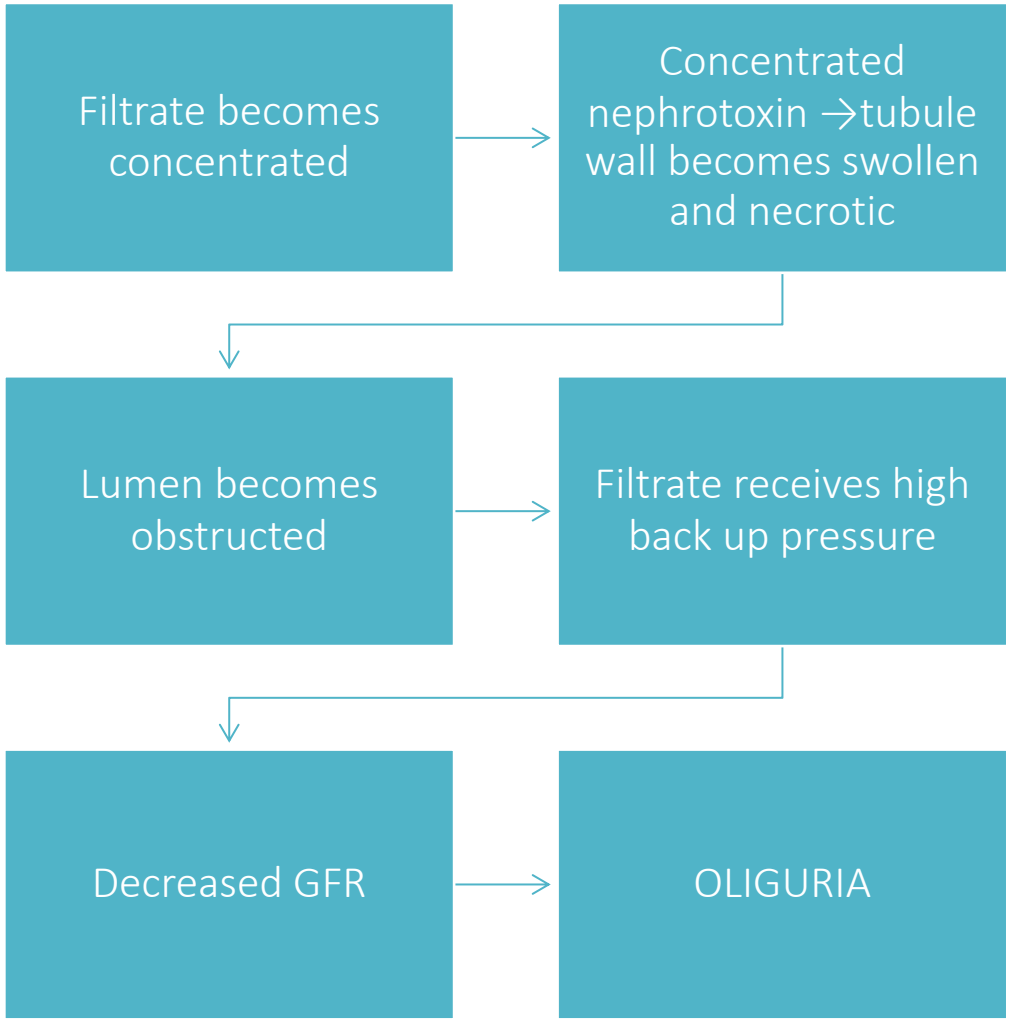
Often reversible

Acute Tubular Necrosis

Two major causes are:

- ❑ Ischemia (from prolonged pre-renal AKI)
- ❑ Nephrotoxin exposure (divided into 2 categories)
  - ***Exogenous***- *Aminoglycosides, Amphotericin B, Vancomycin,* ***Radiographic contrast media*** *(more in presence of CKD, DM, dehydration) more common*
  - ***Endogenous***- *Myoglobinuria (rhabdo), Hemoglobin (hemolysis), Hyperuricemia (tumor lysis), Bence-Jones protein*

Nephrotoxins



Acute Tubular Necrosis[1]

Laboratory findings

↑ K, ↑ PO4 are common

BUN:creatinine ratio <20:1

UA- urine sediment is brown (due to tubular damage)

Microscopy – pigmented granular casts “muddy brown casts”, renal tubular epithelial cells, and epithelial cell casts

UrNa is typically elevated

FENa >1 % (with oliguria)

Acute Tubular Necrosis[1]

Treatment

Aimed at hastening recovery and preventing or treating complications

Nephrotoxic drugs should be stopped

Preventive measures to **avoid fluid overload and hyperkalemia**

- Monitor volume status closely

Doses of all medications that are eliminated by the kidney should be adjusted.

Serial labs to monitor for electrolyte/acid-base disturbances

Acute Tubular Necrosis[1]

Course & Prognosis

Course divided into 3 phases (injury, maintenance, and recovery)

Maintenance

Either oliguric (UO < 500mL/d) or non-oliguric

Non-oliguric has better outcome

On average, this stage duration is between 1-3 weeks but may be several months

Cellular repair and removal of debris occur during this time

Recovery

Signaled by diuresis

GFR begins to increase

BUN and serum creatinine decrease

Contrast-Associated AKI (CA-AKI)

Contrast-Associated AKI (CA-AKI)[2]

This term has been adopted because it is often not possible to exclude other causes of AKI

- Includes both CI-AKI as well as coincidental AKI

CA-AKI is a generally reversible form of AKI, although its development may be associated with adverse outcomes

Recovery is relatively quicker (a few days versus weeks) than compared with other types of ATN

CA-AKI versus CI-AKI[2]

Intravascular iodinated contrast media have been considered nephrotoxic based in large part upon animal experiments and uncontrolled human studies

However, because many of these older reports lacked comparable control groups that did not receive contrast material, their applicability to our understanding of CI-AKI is unclear.

Large controlled studies have since suggested that many cases of AKI following contrast administration may in fact be related to coincident nephrotoxic exposures (eg, hypovolemia, cardiac dysfunction, infection) present at the time that contrast material was administered

Contrast-Induced Acute Kidney Injury (CI-AKI)[2]

Historically, AKI that developed 1-2 days (peaking at days 3-5) after the administration of iodinated contrast material was called contrast-induced nephropathy (CIN).

CI-AKI or CIN should be reserved for AKI that can be causally linked to contrast material administration.

If other potential etiologies have not been excluded or if other potential etiologies are identified, then AKI occurring shortly after contrast exposure should be referred to as CA-AKI or post-contrast AKI

Contrast-Induced Acute Kidney Injury (CI-AKI)[2]

In most cases, the kidney function starts to improve within 3-7 days, and the patient returns to, or close to, baseline estimated GFR (eGFR)

CKD patients have the highest risk of having persistent kidney injury

Risk for dialysis is low, though may be higher in patients with severe, underlying chronic kidney disease (CKD)

CI-AKI Clinical Features[2]

- ❑ **Early, mild increase in serum creatinine**
- ❑ **Non-oliguria**
- ❑ **Urinary sediment consistent with acute tubular necrosis (ATN)**
- ❑ **Other: decreased GFR, hyperkalemia, acidosis, and hyperphosphatemia**

Management[2]

Supportive measures including

- ❑ elimination and avoidance of other potential kidney insults,
- ❑ hemodynamic and electrolyte assessment and management,
- ❑ appropriate dose adjustment of medications for the reduction in glomerular filtration rate (GFR),
- ❑ among those with severely decreased kidney function, monitoring for uremic signs and symptoms.

Risk factors for CA-AKI[3]

PATIENT-RELATED

CKD, especially diabetic nephropathy

Volume depletion

Reduced renal perfusion from HF

Hemodynamic instability

PROCEDURE-RELATED

Much higher risk with arterial versus venous administration of contrast

Specific type of procedure (interventional versus diagnostic angiography)

Dose and type of contrast

Very small amounts of contrast (<10 mL) have been safely used in patients with advanced kidney disease for examination of arteriovenous fistulas.

However, diabetic patients with a serum creatinine concentration >5 mg/dL (440 micromol/L) may be at risk from as little as 20 to 30 mL of contrast.

Prevention or risk reduction CA-AKI

Identify all at risk patients, especially those at high-risk for developing CA-AKI[3]

- patients with eGFR < 60 and DM, HF, Liver failure, or Multiple Myeloma
- patients with eGFR < 60 and significant proteinuria (albuminuria > 300 mg/day)
- patients with eGFR < 45 even in absence of comorbidities/proteinuria

High-risk

- patients with eGFR < 45 and DM and proteinuria or other comorbidities
- all patients with eGFR < 30

Prevention or risk reduction CA-AKI

Avoid volume depletion and avoid NSAIDs[3]

Volume depletion and NSAIDs can increase renal vasoconstriction, which increases the risk for CA-AKI

Avoid volume depletion and withhold NSAIDs for 24-48 hours prior to procedure

Prevention or risk reduction CA-AKI

Selection of contrast dose and type[3]

Use lowest effective dose of contrast possible and avoid repetitive contrast studies closely timed (within 48-72 hours)

Use iso-osmal agent iodixanol, or nonionic low-osmolal agents, such as iopamidol or ioversol, rather than iohexol

Contrast Used[3]

Among newer agents, the iso-osmolal agent iodixanol has been purported to have a lower risk of AKI than low-osmolal agents, particularly iohexol, among high-risk patients

The decreased risk of newer agents is likely related to the decreased osmolality and the absence of charge that characterizes newer agents.

A meta-analysis that included 25 randomized trials comparing iodixanol with a diverse group of low-osmolal agents (n = 5053, approximately 72% with known renal impairment or diabetes) reported a modest reduction in risk of AKI with iodixanol. However, the small reduction in risk is unlikely to be clinically meaningful, although it was marginally statistically significant. There was no difference between groups in the risk for renal replacement therapy (RRT), cardiovascular outcomes, or death.[2]

Contrast Used[3]

It is possible that iohexol carries an increased risk of AKI compared with non-iohexol low osmolal agents.

In a trial that compared iodixanol and iohexol in 129 high-risk patients with diabetes and CKD (mean serum creatinine 1.5 mg/dL) who underwent angiography, iodixanol was associated with a lower incidence of AKI (3 versus 26% with iohexol). However, three trials that compared iodixanol with two other nonionic low-osmolal contrast agents (ioversol and iopamidol) found no difference between groups in the incidence of AKI. In addition, a meta-analysis of 16 randomized trials also suggested that iodixanol was associated with a reduction in risk among patients with CKD who received contrast when compared with iohexol but not when compared with other nonionic low-osmolal contrast agents.[2]

Prevention or risk reduction CA-AKI[3]

-Patients with near-normal kidney function are at low risk for CA-AKI, therefore, few interventions required besides avoidance and/or correction of volume depletion

-In all at-risk patients undergoing intra-arterial contrast administration, consider isotonic IV fluid administration prior to and several hours after contrast administration unless contraindicated due to volume expansion

- This is the standard of care despite insufficient data showing benefit
- Further studies needed to assess prophylactic fluid administration

Prevention or risk reduction CA-AKI[3]

Bicarbonate provides no additional benefit to saline, needs to be compounded, and is more expensive.

Acetylcysteine not recommended

Mannitol and other diuretics given prophylactically not recommended, however, diuretics may be used to treat volume overload if present

Prophylactic hemofiltration or hemodialysis after contrast exposure to prevent CA-AKI in CKD patients is not recommended

POSEIDON Trial[3]

Evaluated a new fluid protocol to prevent CI-AKI

Protocol guided by left ventricular end-diastolic pressure (LVEDP) compared with standard IV fluid administration among patients with eGFR < 60 and other risk factors

All patients received IV isotonic saline 3 mL/kg 1hr prior to cardiac cath

LVEDP group received 5mL/kg/hr if < 13mmHg, 3mL/kg/hr if 13-18mmHg, and 1.5mL/kg/hr if > 18mmHg

Control group received 1.5 mL/kg/hr

Results: LVEDP group had less occurrence of CA-AKI than control group (6.7 vs 16.3). Three patients in each group had IV fluid discontinued due to dyspnea

CA-AKI Adverse Outcomes[4]

Associated with

- Longer hospital stay
- Cardiovascular events
- Worsening renal function
- Increased mortality

Clinical Application

1. Patient with end stage kidney disease to undergo AV fistula creation.
2. Patient with normal kidney function to undergoing CT scan with contrast.
3. Patient with eGFR < 60 and diabetes mellitus undergoing angioplasty.

References

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