CONTRAST-ASSOCIATED ACUTE KIDNEY INJURY (CA-AKI) / CIN

Prepared by **Dr. Sidhartha Mullapudi**, DrNB (Cardiology), MD (General Medicine)
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I DEFINITION AND NOMENCLATURE SHIFT

- **Nomenclature Update:** Contemporary guidelines (ACC/ESC/KDIGO) have shifted terminology from Contrast-Induced Nephropathy (CIN) to **Contrast-Associated Acute Kidney Injury (CA-AKI)**, recognizing that contrast media is often a contributing factor alongside hemodynamic instability, atheroembolism, and nephrotoxic drugs rather than the sole cause in hospitalized cardiac patients.
- **Diagnostic Definition (KDIGO):** An **absolute increase in serum creatinine by 0.3 mg/dL or greater** (within 48 hours), or a **relative increase of 25 percent or greater** (or 1.5-fold per KDIGO) from baseline, occurring within **48 to 72 hours** after intravascular administration of iodinated contrast media.
- **Clinical Implications:** Development of CA-AKI increases short- and long-term all-cause mortality, accelerates progression to **End-Stage Renal Disease (ESRD)**, prolongs hospital length of stay, and increases 1-year **Major Adverse Cardiovascular Events (MACE)**.

II CORE DUAL-HIT PATHOPHYSIOLOGY

- **Medullary Ischemia (The Hemodynamic Hit):** Iodinated contrast media induces a transient initial vasodilation followed by **intense, prolonged intrarenal vasoconstriction** (mediated by **endothelin and adenosine** release combined with nitric oxide and prostaglandin depletion); the **renal outer medulla**, which physiologically operates at low oxygen tension, suffers acute ischemic tubular injury.
- **Direct Tubular Cytotoxicity (The Cellular Hit):** Filtered contrast molecules become concentrated within the renal tubules, increasing tubular fluid viscosity, generating **Reactive Oxygen Species (ROS)**, and exerting direct **osmotic cytotoxicity** that triggers tubular epithelial cell apoptosis and cast obstruction.

III PRE-PROCEDURAL RISK STRATIFICATION (THE MEHRAN SCORE)

- **The Mehran Risk Score (Pre-Procedural Risk Tool):** Quantifies baseline CA-AKI risk using eight clinical and procedural variables: **Hypotension**, **Intra-Aortic Balloon Pump (IABP) use**, **Congestive Heart Failure**, **Age greater than 75 years**, **Anemia**, **Diabetes Mellitus**, **Contrast Media Volume**, and **baseline eGFR / Serum Creatinine**.
- **Vulnerability Thresholds:** A baseline **eGFR less than 60 mL/min/1.73 m2** identifies the at-risk cohort, while an **eGFR less than 30 mL/min/1.73 m2** denotes extreme risk.

IV PREVENTIVE STRATEGIES (THE NEPHROPROTECTION ALGORITHM)

A Intravascular Volume Expansion (The Gold Standard — Class I)

- **Standard Hydration Protocol:** Administer intravenous **isotonic saline (0.9% NaCl) at 1.0 to 1.5 mL/kg/hour** starting **12 hours before** and continuing for **24 hours after** the procedure.
- **Physiological Rationale:** Expands intravascular volume, suppresses vasopressin and RAAS activation, dilutes intratubular contrast concentration, and accelerates tubular transit.

B Contrast Volume Minimization and Intravascular Imaging

- **The Contrast-to-eGFR Ratio:** Keep total **Contrast Volume (in mL) to eGFR ratio strictly less than 3.0** (and **less than 2.0** in severe CKD).
- **Contrast Selection:** Use **Low-Osmolar Contrast Media (LOCM)** or **Iso-Osmolar Contrast Media (IOCM — Iodixanol)**; high-osmolar contrast media are contraindicated.
- **Imaging-Guided PCI:** Utilize **IVUS or OCT** for vessel sizing and stent optimization to minimize or eliminate angiographic contrast injections.

C Pharmacological Optimization

- **High-Dose Statin Pre-Loading (Class IIa):** Pre-procedural loading with high-intensity **Rosuvastatin or Atorvastatin** reduces CA-AKI incidence via pleiotropic antioxidant, anti-inflammatory, and endothelial-protective effects.
- **Withholding Nephrotoxins and the Metformin Rule:** Discontinue **NSAIDs** and aminoglycosides 24 to 48 hours prior to contrast exposure. **Metformin** is withheld at the time of the procedure and for **48 hours post-procedure** (restarting once renal function is confirmed stable) strictly to prevent **metformin-associated lactic acidosis** should CA-AKI occur, as Metformin itself is not nephrotoxic.

D Ineffective Interventions (Class III — No Benefit or Harm)

- **Oral or Intravenous N-Acetylcysteine (NAC):** Provides zero renoprotective benefit.
- **Intravenous Sodium Bicarbonate:** Not superior to isotonic normal saline.
- **Prophylactic Hemodialysis:** Does not prevent CA-AKI (Class III); prophylactic hemofiltration may be considered only in selected severe CKD before complex PCI (Class IIb).

Landmark Trial	Intervention Evaluated	Key Clinical Outcome & Practice Impact
PRESERVE Trial	2x2 Factorial: **IV Sodium Bicarbonate vs. IV 0.9% Saline** & **Oral NAC vs. Placebo**	**No benefit** of Sodium Bicarbonate over Normal Saline, and **zero benefit** of N-Acetylcysteine; confirmed **Isotonic Saline** as the gold standard
POSEIDON Trial	**LVEDP-Guided Isotonic Saline Hydration** vs. Standard Fixed Hydration	Tailoring IV fluid rate to cath-lab **LVEDP** significantly reduced CA-AKI without precipitating pulmonary edema
REMEDIAL III Trial	**Urine-Flow-Rate-Guided Hydration (RenalGuard)** vs. LVEDP-Guided Hydration	Furosemide-induced high urine output (>300 mL/h) matched with automated IV saline replacement further reduced CA-AKI in very-high-risk patients

V MANAGEMENT OF ESTABLISHED CA-AKI

- **Supportive Hemodynamic and Metabolic Care:** Strict intake/output charting, daily serum creatinine and electrolyte monitoring, maintenance of euvolemia, and correction of **hyperkalemia** and **metabolic acidosis**.
- **Indications for Urgent Renal Replacement Therapy (Hemodialysis — "AEIOU"):** Reserved strictly for refractory **Acidosis**, **Electrolyte derangement (hyperkalemia)**, **Intoxication**, **Volume Overload (diuretic-refractory pulmonary edema)**, or **Uremic complications (pericarditis or encephalopathy)**.

KEY REFERENCES

- **Weisbord SD, Gallagher M, Jneid H, et al. (PRESERVE Trial Investigators):** Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine, *New England Journal of Medicine*.
- **Brar SS, Aharonian V, Mansukhani P, et al. (POSEIDON Investigators):** Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial, *The Lancet*.
- **Mehran R, Dangas GD, Weisbord SD:** Contrast-Associated Acute Kidney Injury, *New England Journal of Medicine*.