ATN Management and Hemodynamic Targets

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Acute Tubular Necrosis Management and Hemodynamic Optimization: Student Handout

Learning Objectives

By the end of this handout, you should be able to: - Understand ATN pathophysiology and why certain interventions fail - Apply evidence-based hemodynamic targets individualized to patient characteristics - Recognize the limitations of loop diuretics in established ATN - Explain the furosemide stress test and its clinical applications - Manage electrolyte abnormalities and complications in ATN - Determine when renal replacement therapy is indicated

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Acute Tubular Necrosis: Ischemic Injury Pattern

Definition: Acute tubular necrosis represents necrosis and loss of tubular epithelial cells, leading to: - Loss of tubular concentrating ability - Backleak of glomerular filtrate through damaged epithelium - Tubular obstruction from cellular debris - Marked elevation in fractional excretion of sodium (FENa >2%)

Incidence: Most common cause of intrinsic AKI in hospitalized patients (~45-50% of hospitalized AKI cases).

Triggers (Most Common): 1. **Prolonged hypotension** (septic shock, cardiogenic shock) 2. **Major surgical procedures** (especially cardiac surgery) 3. **Rhabdomyolysis** (myoglobin toxicity) 4. **Contrast exposure** (now called contrast-associated AKI) 5. **Nephrotoxic drug accumulation** (aminoglycosides, vancomycin, cisplatin)

Why Loop Diuretics DON'T Work in ATN: The Evidence

The Theoretical Rationale (Why It Should Work)

Proposed Mechanisms: 1. **Reduce metabolic demand** by blocking sodium-potassium-chloride cotransporter (NKCC) in thick ascending limb 2. **Enhance tubular flow** to prevent obstruction and backleak 3. **Improve renal blood flow** through vasodilatory effects

These mechanisms are physiologically sound… yet clinical evidence shows they don't translate to improved outcomes.

The Clinical Reality: Systematic Evidence Against Diuretics

Meta-Analysis Findings (20 Studies, 2,608 Patients): - Furosemide **NO IMPACT on mortality** (OR 1.015, 95% CI 0.825-1.339) - Furosemide **NO IMPACT on RRT requirement** (OR 0.947, 95% CI 0.521-1.721) - May convert oliguric to non-oliguric AKI (cosmetic change, no outcome benefit) - **More frequent electrolyte abnormalities** in diuretic-treated group

SPARK Trial (Randomized Controlled Trial, 216 Patients): - No difference in proportion with worsening AKI (43.2% vs 37.1%) - No difference in kidney recovery (29.7% vs 42.9%) - No difference in RRT requirements (27.0% vs 28.6%) - More adverse events in furosemide group

The Fundamental Problem: Dual Blood Pressure Effect

Critical Issue: Loop diuretics have **opposite effects** depending on volume status: - In **fluid-overloaded patients:** May reduce intravascular volume excessively, causing renal hypoperfusion - The same drug that might help in one scenario causes harm in another - Distinguishing appropriate from excessive diuresis is clinically difficult

Clinical Pearl: Converting oliguric AKI to non-oliguric AKI sounds beneficial but doesn't reduce mortality or dialysis need. The underlying injury remains unchanged; urine output is simply a cosmetic change.

Current Guidelines: What They Recommend

KDIGO Recommendation (Grade 1B Evidence): - **Do NOT use furosemide prophylactically** to prevent AKI - Use diuretics **ONLY for volume overload** after appropriate management of sepsis/cardiac dysfunction - Loop diuretics have **NO ROLE in treating established ATN**

Bottom Line: Fluid and electrolyte balance optimization is key; loop diuretics add toxicity without benefit in ATN.

Hemodynamic Management: Personalized Blood Pressure Targets

The Paradigm Shift: From Universal to Individualized Targets

Traditional Approach: MAP ≥65 mmHg for all critically ill patients.

Modern Evidence: Optimal MAP targets vary significantly based on: - **Chronic hypertension status** (most important factor) - **Baseline blood pressure** (autoregulation curve shifts with chronic HTN) - **AKI etiology** - **Patient age** - **Comorbidities**

Major Trial Findings

SEPSISPAM Trial (776 septic shock patients):

Key Findings: - Overall: No mortality difference between MAP 65-70 vs 80-85 mmHg - **Crucial subgroup:** Chronic hypertensives (baseline SBP >140 mmHg pre-illness) - Higher MAP (80-85) reduced RRT need by ~30% (42.2% vs 31.7%) - Number needed to treat = ~9

Physiology Explanation: Chronic hypertension causes **rightward shift of renal autoregulation curve**. These kidneys require higher perfusion pressures to maintain blood flow.

The 65 Trial (2,600 elderly patients ≥65 years): - Permissive hypotension (MAP 60-65 vs usual care) showed **no harm** - Actually suggested potential mortality benefit - Challenged assumption that higher is always better

Etiology-Specific Hemodynamic Strategies

AKI Etiology	Recommended MAP Target	Rationale	Additional Considerations
Sepsis, no HTN	65-70 mmHg	Lower targets safe in this population	Avoid excessive vasopressor dose
Sepsis + chronic HTN	80-85 mmHg	Rightward autoregulation curve	SEPSISPAM findings
Cardiorenal syndrome	70-80 mmHg	Balance CO + perfusion pressure	Monitor CVP; MAP-CVP = mean perfusion pressure
Post-cardiac surgery	>80 mmHg	Highest sensitivity to hypotension	Each hour MAP <65 increases AKI risk ~20%
Hepatorenal syndrome	MAP +15 mmHg above baseline	Most aggressive target needed	Norepinephrine preferred; octreotide + albumin adjuncts
Rhabdomyolysis	Maintain euvolemia	Hydration more important than BP per se	Avoid hypotension; aggressive fluid resuscitation

Clinical Pearl: The optimal blood pressure target isn't universal—it's personalized based on baseline hypertension history and clinical context.

Systolic vs. Mean Arterial Pressure

Emerging Evidence: Systolic blood pressure may provide independent prognostic information beyond MAP.

Finding: SBP <90-100 mmHg independently associated with severe AKI in non-critically ill patients.

Clinical Application: Avoid SBP <90 mmHg even if MAP technically adequate.

The Furosemide Stress Test: Functional Assessment of Tubular Integrity

What It Is and Why It Matters

Principle: Furosemide is **actively secreted** by proximal tubular cells (not filtered). Diuretic response indicates tubular secretory capacity and structural integrity.

Clinical Significance: In early AKI, furosemide responsiveness predicts: - Severity of kidney injury - Risk of progression to Stage 3 AKI - Need for renal replacement therapy - Mortality risk

How to Perform the FST

Patient Selection: - Early AKI with evidence of tubular damage (muddy brown casts, FENa >1%, or RTEC casts) - Patient adequately resuscitated per clinical team - Stable hemodynamics

Standardized Protocol: 1. **Baseline assessment:** Measure urine output, document baseline vital signs 2. **Furosemide administration:** - **Diuretic-naive:** 1.0 mg/kg IV bolus - **Prior exposure within 7 days:** 1.5 mg/kg IV bolus 3. **Measurement period:** Collect all urine for 2-6 hours 4. **Primary interpretation: 2-hour urine output** (most clinically useful)

Clinical Interpretation

Cutoff Point: 200 mL at 2 hours

2-Hour Urine Output	Classification	Risk Level	Prognosis
>200 mL	FST-Responsive	Low risk	13.6% require RRT; better outcomes
100-200 mL	Intermediate	Moderate risk	Cautious interpretation needed
<100 mL	FST-Nonresponsive	High risk	75-98% require RRT; worse outcomes

Clinical Applications

Timing of RRT Initiation: - FST-responsive patients: May delay RRT initiation; monitor closely - FST-nonresponsive patients: Strong signal for earlier RRT consideration

Predicting CRRT Initiation: - FST-nonresponsive: **2.4× higher likelihood** of requiring CRRT - AUC for CRRT prediction: 0.966 (excellent discriminatory power)

Predicting Weaning from CRRT: - Response to furosemide after CRRT cessation predicts successful RRT discontinuation

Performance Compared to Biomarkers

Meta-Analysis Results: - Sensitivity: 81% (vs NGAL 63%, TIMP-2/IGFBP-7 75%) - Specificity: 88% (vs NGAL 73%, TIMP-2/IGFBP-7 85%) - **Superior to traditional biomarkers** for progression prediction

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Supportive Management in ATN

Fluid and Electrolyte Management

General Principles: 1. **Goal:** Euvolemia (not volume overload, not depletion) 2. **Strategy:** Careful daily fluid balance calculation 3. **Monitoring:** Daily weights, intake/output records, clinical assessment

Specific Electrolyte Considerations:

Hyperkalemia (Most Immediate Threat): - **Monitor:** Daily potassium; EKG for peaked T waves - **Treat if K+ >5.5-6.0 mEq/L or symptomatic:** - Calcium gluconate (cardiac stabilization) - Insulin + dextrose (shift intracellularly) - Albuterol (shift intracellularly) - Loop diuretics (if not anuric) + sodium polystyrene sulfonate (bind K in gut) - RRT if medical management insufficient

Hyponatremia: - Common in ATN (dilutional from oliguric state + free water administration) - Usually mild; rarely symptomatic - Correct slowly (risk of central pontine myelinolysis if corrected too rapidly)

Metabolic Acidosis: - Expected in ATN - Treat underlying AKI; correct as kidney function recovers - RRT if severe acidosis (pH <7.1-7.15) impacting hemodynamics

Medication Management

Dosing Adjustments: - All renally-cleared medications require dose reduction - Many ICU drugs need adjustment (aminoglycosides, vancomycin, etc.) - Use renal dosing guides and therapeutic drug monitoring

Avoiding Additional Nephrotoxins: - NSAIDs: **ABSOLUTE AVOID** in ATN - Aminoglycosides: Use only if essential; monitor levels - ACE/ARBs: May be continued if patient not oliguric; avoid in anuric phase - Contrast agents: **ABSOLUTELY AVOID** until kidney function recovered

Nutrition

Principles: - Provide adequate but not excessive protein (0.8-1.0 g/kg/day) - Avoid hypercatabolism - Monitor for electrolyte abnormalities (hyperphosphatemia, hyperkalemia) - Dialyze or filter if necessary to allow adequate nutrition

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Indicators for Renal Replacement Therapy Initiation

Absolute Indications (Refractory to Medical Management): 1. **Severe hyperkalemia** (K+ >6.0-6.5 mEq/L or EKG changes) unresponsive to medical therapy 2. **Pulmonary edema** or fluid overload unresponsive to diuretics 3. **Severe metabolic acidosis** (pH <7.1-7.15) compromising hemodynamics 4. **Uremic symptoms:** Pericarditis, encephalopathy, seizures 5. **Anuria** for >3-5 days with fluid overload/hyperkalemia

Relative Indications (Consider Based on Clinical Context): - Oliguria for >5-7 days - Rising BUN >100 mg/dL - Inability to provide adequate nutrition without fluid overload - Need for medications requiring frequent dosing (incompatible with oliguria)

Timing Controversy: Earlier RRT initiation (within 12-24 hours of AKI onset) shows no mortality benefit in most studies; standard approach is to delay until absolute indications develop.

Monitoring During ATN Recovery

Daily Assessments: - Vital signs (hypotension common early) - Urine output and character (darkening suggests worsening) - Fluid balance (cumulative) - Serum creatinine, BUN - Electrolytes, especially potassium - Acid-base status

Signs of Recovery: - Increasing urine output (typically non-oliguric first) - Decreasing serum creatinine trend - Improvement in electrolyte abnormalities - Resolving uremia

Expected Timeline: - Oligura phase: Usually 5-14 days (range 1-8 weeks) - Recovery phase: Progressive GFR improvement over weeks to months - Most patients achieve independence from RRT; some have residual CKD

Practice Questions

Question 1: A 62-year-old with chronic hypertension (baseline BP 150/90) develops septic shock. Current MAP is 68 mmHg on norepinephrine. Creatinine is rising (1.2 to 2.1). According to SEPSISPAM trial findings, which MAP target would most benefit his kidneys? A) Maintain current MAP 65-70 mmHg (standard target) B) Increase MAP to 80-85 mmHg (higher target for hypertensives) C) Reduce MAP further to 60-65 mmHg (permissive hypotension) D) MAP irrelevant; focus on urine output instead

Answer: B) Increase MAP to 80-85 mmHg (higher target for hypertensives). The SEPSISPAM trial demonstrated that chronically hypertensive patients benefit from higher MAP targets (80-85 mmHg) compared to non-hypertensives. This patient's baseline HTN (150/90) indicates a rightward-shifted autoregulation curve; his kidneys require higher perfusion pressures. The trial showed ~30% reduction in RRT need with this approach in hypertensives.

Question 2: A 58-year-old post-CABG (day 2) has developing AKI (Cr 2.1, muddy brown casts on UA). A furosemide stress test is performed: 1.0 mg/kg IV bolus given; urine output over 2 hours is 85 mL. Which statement is most accurate? A) Patient is FST-responsive; low risk of progression B) Patient is FST-nonresponsive; high risk for progression and RRT need C) FST unreliable post-op; repeat later D) Result indicates dehydration; increase hydration

Answer: B) Patient is FST-nonresponsive; high risk for progression and RRT need. With 85 mL urine output at 2 hours (below 200 mL threshold), this patient is FST-nonresponsive. This indicates severe tubular dysfunction and predicts ~75-98% will need RRT. The clinical team should prepare for RRT initiation and heighten hemodynamic/electrolyte monitoring. This functional assessment provides crucial prognostic information.

Question 3: A 71-year-old with post-surgical ATN is anuric on day 5. Potassium is 5.8 mEq/L (flat T waves on EKG, no peaked changes yet). Current fluid status: euvolemic. Which approach best represents evidence-based practice? A) Start furosemide 40 mg IV to increase urine output and manage hyperkalemia B) Continue supportive care; RRT indications not yet met (no absolute indication) C) Initiate RRT; anuric >5 days is indication regardless of K+ D) Give insulin + glucose IV; reassess RRT need in 24 hours

Answer: B) Continue supportive care; RRT indications not yet met (no absolute indication). While this patient has been anuric for 5 days, he is euvolemic (no fluid overload) and his hyperkalemia is mild (K+ 5.8, no EKG changes). Furosemide (choice A) has no role in ATN and may worsen hemodynamics. RRT is indicated for absolute indications (uncontrolled hyperkalemia, fluid overload, severe acidosis). Insulin + glucose (choice D) is reasonable temporizing measure. The evidence base supports delaying RRT until absolute indications develop. This patient should be monitored closely but medical management continued.

Key Takeaways

1. **Loop diuretics in ATN:** NO mortality benefit, NO RRT reduction, more complications
2. **Hemodynamic targets:** NOT universal; adjust based on chronic hypertension (80-85 mmHg if hypertensive)
3. **Furosemide stress test:** Powerful prognostic tool; <200 mL at 2 hours = high RRT risk
4. **Core management:** Fluid/electrolyte balance, avoid additional nephrotoxins, prepare for RRT
5. **RRT indications:** Wait for absolute indications (refractory hyperkalemia, pulmonary edema, acidosis)
6. **Expected course:** Most ATN patients recover; timeline weeks to months; some residual CKD

See Also

Related Student Handouts

- AKI Workup and Diagnostic Approach
- AKI Biomarkers and Early Detection
- Drug-Induced AKI
- Dialysis Fundamentals

Clinical Content (01-Clinical-Medicine/Nephrology)

- AKI Hub - Full Clinical Reference
- Essential Renal Laboratory Tests

Atomic Notes (ZK)

- CRRT Principles
- RRT Modality Selection

Butler-COM Resources

- Butler COM - Nephrology Deep Dive

Related Resources

- Loop Diuretics in ATN: Comprehensive Review
- Hemodynamics Detailed
- AKI Workup and Diagnosis

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