



## Oliguria: Perioperative management

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Acute Renal Failure (ARF) in the perioperative setting is a significant complication of anesthesia and surgery. More than half of **all** acute hemodialysis patients have ARF in the perioperative setting<sup>(1)</sup>. The mortality rate for perioperative ARF remains between 20-80% depending upon the patient's comorbidities<sup>(2)</sup> Perioperative ARF results from many etiologies. However, more than 90% of cases of perioperative ARF are due to relative hypovolemia and inadequate renal perfusion<sup>(3)</sup>.

Oliguric renal failure is **STRICTLY** defined as a urine output of 400 ml/day (urinary flow rate of 15 ml/hour)<sup>(4)</sup>. However, most anesthesia care providers would define perioperative oliguria as a urinary flow rate of 0.5 cc/kg/hour. In an average adult, this translates into a urinary flow rate of 30-40 cc/hour. Oliguria is a normal compensatory response to acute hypovolemia and thus, an important intraoperative sign of potentially inadequate renal perfusion. The etiology of acute oliguria must be investigated promptly in the perioperative setting. In cases of severe renal hypoperfusion, there is a narrow window of only **30 - 60 minutes** between the onset of oliguria (the protective compensatory mechanism of the renal conservation of sodium and water) and the initiation of ischemic Acute Tubular Necrosis (ATN)<sup>(5)</sup>. As a result, the anesthesia care provider must have the knowledge necessary to understand and promote renal viability in the perioperative setting.

### RISK FACTORS FOR POSTOPERATIVE RENAL FAILURE

Proper preoperative management of patients at high risk for perioperative ARF includes the following steps:

1. Identify patients at high risk for ARF
2. Evaluation of intravascular volume status
3. Optimization of Pre-existing medical conditions

4. Review of medications with discontinuation of any non-essential medications associated with renal insufficiency

PREEXISTING RENAL DISEASE is the most important preoperative risk factor for the development of perioperative ARF<sup>(6)</sup>. (Table I) reviews the multitude of risk factors for the development of postoperative ARF<sup>(5)</sup>.

It is vital to evaluate and optimize the patient's intravascular volume status in order to help prevent perioperative ARF in susceptible patients. Preoperative evaluation includes palpation of peripheral pulses, measurement of blood pressure and heart rate and the evaluation of orthostatic hypotension. Other qualitative measurements of volume status include skin color, turgor and assessment of mucus membranes. Of note, hypertensive patients have relative intravascular volume repletion and are at great risk for perioperative renal insufficiency despite strong peripheral pulses. Early consideration of central monitoring must be given in order to assess volume status more precisely in «at risk» patients.

Patients with pre-existing renal insufficiency, diabetes, hypertension, CAD and CHF for example are at increased risk for perioperative renal dysfunction. Early recognition and optimization of these conditions is of paramount importance in order to avoid or limit perioperative renal dysfunction. Hypertension is found in up to 85% of patients with renal insufficiency or renal failure. Hypertension is a major contributor to renal morbidity<sup>(7)</sup> Patients with untreated hypertension manifest hemodynamic lability more often than their normotensive counterparts<sup>(8)</sup> Thus, preoperative control of hypertension in elective procedures is of paramount importance.

Hypotension exerts the most severe stress on renal viability. Hypotension in combination with hypovolemia is extremely deleterious to renal viability. Again aggressive assessment of intravascular volume status, careful choice and titration of induction agents and early insertion of cen-

**Table I.** Risk factors for postoperative acute renal failure.

Category	Disorder/Drug/Procedure/Comments
I. Pre-existing renal insufficiency	↓d GFR, ↓d renal reserve (likely more sensitive to all renal insults)
II. Systemic diseases associated with Chronic renal failure	Coronary artery disease, congestive heart failure Diabetes Hypertension: specially renovascular hypertension, also Pregnancy induced HTN Liver failure, jaundice Peripheral vascular disease Polycystic kidney disease Scleroderma Systemic lupus erythematosus Rheumatoid arthritis Wegener's granulomatosis Advanced Age Sepsis Shock
III. Nephrotoxic drug exposure	Acetaminophen (usually with hepatotoxicity) ACE II inhibitors (impairs renal autoregulation) Allopurinol Aminoglycosides (proximal tubule necrosis) Amphotericin B (glomerulonephritis and ATN) Asparaginase Cephalosporins (especially with aminoglycosides) Cimetidine, ranitidine (interstitial nephritis) Cisplatin (ATN) Cyclosporin A, tacrolimus Intravenous radiocontrast ( <b>oliguria</b> within 24 h) Methotrexate Metoclopramide (inhibits renal D <sub>2</sub> receptors) Nitrosoureas NSAIDs (especially phenacetin, indomethacin, Toradol) (generic is ketorolac tromethamine) (less with selective cyclooxygenase <sub>2</sub> [cox <sub>2</sub> ] inhibitors) Penicillins, sulfonamides (interstitial nephritis)
IV. Procedures associated with ARF	Biliary surgery Burns Cardiac surgery Genitourinary/obstetric surgery Transplant Trauma Vascular surgery (especially suprarenal cross-clamp)
V. Intraoperative hypovolemia Intraoperative hypotension	Prolonged hypotension or hypovolemia can cause ARF in normal patients, and exacerbates the renal effects of all the above conditions

↓d = decreased. ARF = acute renal failure; ATN = acute tubular necrosis; GFR = glomerular filtration rate; ACE = angiotensin-converting enzyme; D<sub>2</sub> = dopaminergic<sub>2</sub>; NSAIDs = nonsteroidal anti-inflammatory drugs.

tral venous access are all extremely helpful modalities in the prevention of perioperative renal dysfunction<sup>(5)</sup>.

A preoperative review of the patient's medication should be routinely undertaken. The goal is to identify and eliminate potential nephrotoxic agents. A list of common nephrotoxic drugs can be found in table I.

Contrast media should be given with great caution in patients at risk for perioperative renal dysfunction. Prehydration is mandatory whenever contrast media is required. In addition, high risk patients who require intravenous contrast administration should receive prophylactic oral administration of N-acetylcysteine (Mucomyst) prior to the administra-

tion of intravenous contrast. A recent study demonstrated a significant reduction in creatinine concentration (Cr) when prehydration was combined with N-acetylcysteine, 600 mg po bid the day prior and the day of intravenous contrast administration when compared with prehydration alone<sup>(9)</sup>. In addition, it is advisable to allow for several days of renal recovery following procedures or tests requiring intravenous contrast prior to elective surgery.

## ETIOLOGY OF OLIGURIA

The cause of oliguria can be defined as *postrenal, intrarenal or prerenal*. This classification provides a useful structure for the systematic approach to therapy.

Causes of *postrenal oliguria* include any form of urinary tract obstruction (renal pelvis, ureters, bladder, urethra or urinary catheter). Postrenal oliguria generally manifests as ANURIA. Sudden onset of anuria should trigger inspection, flushing and/or changing of the urinary catheter<sup>(4)</sup>. Renal ultrasound should be considered in cases where the cause of the postrenal obstruction is not due to a malfunctioning urinary catheter.

Perioperatively, oliguria is most often a physiologic response to hypovolemia and thus a *prerenal* response. Hypovolemia can be classified as either absolute or relative. Absolute causes of hypovolemia include acute hemorrhage, severe diarrhea, vomiting and fluid restriction. Relative causes of hypovolemia include CHF, sepsis or hepatic failure for example.

The physiologic response to dehydration, hypovolemia and hypotension is water and sodium retention and vasoconstriction through activation of osmoreceptors, volume receptors and baroreceptor reflexes. The sympathoadrenal and renin-angiotensin systems are activated and aldosterone and ADH are released. The net effect on renal tubules is the concentration of urine due to the avid reabsorption of sodium and water.

The characteristic findings in a *Prerenal state* are oliguria, high urine osmolality and low urine sodium. When normal renal hemodynamics are promptly restored, then urine flow returns to normal.

Vasomotor nephropathy is an exception to this rule. It is a state of resistant prerenal oliguria found in sepsis or hepatic failure. Circulating endotoxin induces intense renal vasoconstriction characterized by oliguria with a urine sodium of less than 10 mEq/l. Vasomotor nephropathy is resistant to fluid therapy and responds to treatment of the underlying condition<sup>(4)</sup>.

When *prerenal oliguria* is severe or combined with other nephrotoxic injury, *intrarenal oliguria* and frank acute renal failure may ensue. Renal tubules become necrotic due to ischemic injury and lose their ability to conserve sodium and water. Physiologic, reversible prerenal states may dete-

riorate into frank Acute Tubular Necrosis (ATN) if the ischemic injury persists. Despite restoration of normal renal hemodynamics, urinary flow will remain low in the face of ATN. *Prerenal states* sensitize the kidney to other nephrotoxic insults. ATN is more easily induced by drugs such as NSAIDs, Aminoglycosides, Contrast media and Cyclosporin A in the dehydrated, prerenal patient.

Animal models of ischemic ATN are favorably impacted by the administration of renal protective agents (Saline, Mannitol, Vasodilators) prior to the experimental ischemic insult (norepinephrine infusion). In these cases, the animal becomes azotemic but urine flow rate remains adequate and renal recovery is rapid. Clinically, this is the syndrome of NonOliguric Renal Failure (NORF). (Table II) compares Prerenal and Intrarenal states<sup>(4)</sup>.

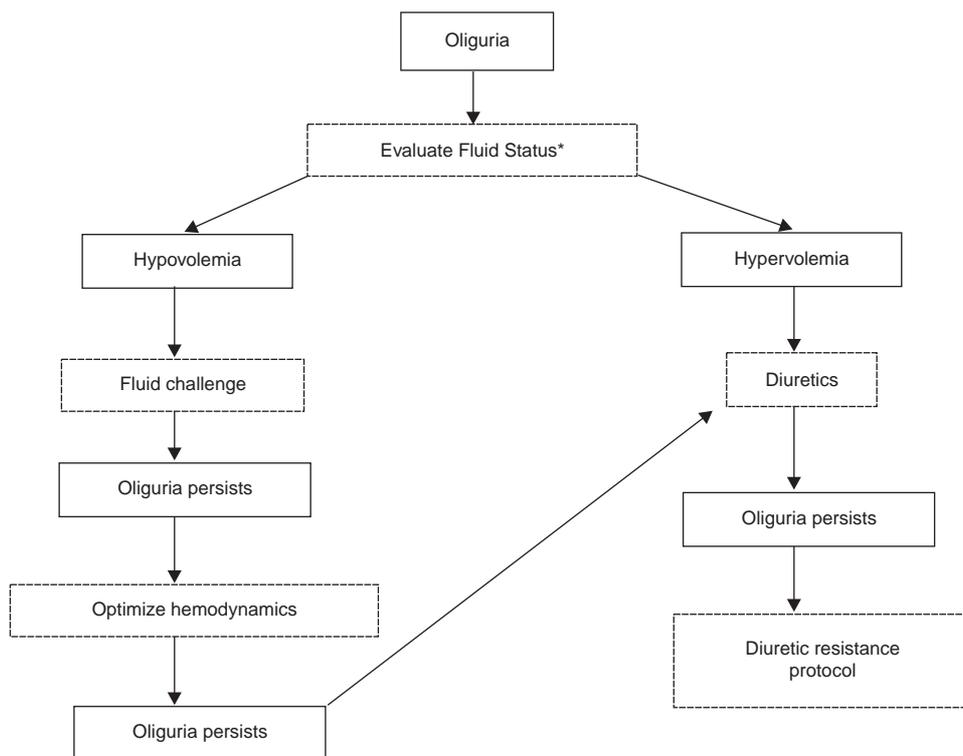
Fluid resuscitation is vital in order to prevent *Prerenal oliguria* from deteriorating into ATN. Aggressive fluid resuscitation can ameliorate the severity and duration of ATN as well. Shin et al. demonstrated that early diagnosis of renal dysfunction and aggressive hemodynamic intervention attenuates the renal insult of shock<sup>(10)</sup>. Shin's study found that the incidence of acute renal failure was the same in patients who did or did not receive early diagnosis and aggressive hemodynamic intervention. However, the aggressive treatment protocol increased the proportion of patients with NORF from 18 to 100%, halved time on dialysis, hyperkalemia and pulmonary edema. Overall mortality was reduced from 70 to 28%. In part, this physiologic finding is due to the release of atrial natriuretic peptide (ANP). Elevated atrial pressure mediates the release of ANP. ANP is a vital endogenous renal vasodilator that increases GFR and sodium excretion<sup>(11)</sup>.

Various algorithms approaching the management of oliguria have been developed. One published recently by Sladen is particularly practical (Figure 1)<sup>(4)</sup>.

1. Assume Perioperative Oliguria is Prerenal until proven otherwise.
  - a. Perioperative Oliguria is MOST COMMONLY due to intravascular hypovolemia

**Table II.** Evaluation of oliguria.

Urinary Indices	Prerenal states	Intrarenal states (ATN)
U:P Osmolality	> 1.4: 1	1: 1
U:P Creatinine	> 50: 1	< 20: 1
Urine Na (mEq/L)	< 20	> 80
FENa (%)	< 1	> 3
Ccr (mL/Min)	15-20	< 10



**Figure 1.** Algorithmic approach to oliguria<sup>(4)</sup>.

- i. Prerenal pattern on urine analysis supports this assumption.
- ii. If CLINICAL ASSESSMENT does not suggest fluid overload then serial fluid boluses should be administered as guided by vital signs and urine output.
- iii. Diuretic therapy should be deferred unless:
  - There are UNEQUIVOCAL signs of fluid overload:
  - Oliguria persists despite fluid challenges, assessment of hemodynamic status (eg: central monitoring), and restoration of stable hemodynamics or there is evidence of pigment nephropathy.
2. Evaluate and treat intravascular volume:
  - a. Appropriate hemodynamic and urinary monitoring is essential.
    - i. To properly identify and treat intravascular hypovolemia and oliguria.
    - ii. CVP and Arterial pressure monitoring is indicated when large fluid shifts are anticipated.
    - iii. Pulmonary artery catheterization should be considered in patients with pre-existing renal dysfunction, sepsis, severe pulmonary disease or CHF.
3. Maximize Renal Blood flow:
  - a. Optimize Cardiac Function.
    - i. Normalize heart rate and rhythm.
    - ii. Adequate Preload.

- iii. Judicious use of Inotropic Support.
- iv. Judicious use of Afterload Reduction (vasodilators or inodilators).
4. Maintain Renal Perfusion Pressure:
  - a. Critically important to states where renal autoregulation is blunted or absent
    - i. HTN, Sepsis, ARF
5. Diuretic Therapy:
  - a. Therapeutic:
    - i. Diuretic therapy should be reserved for oliguria that persists despite optimization of intravascular volume, hemodynamic status and renal perfusion pressure. If diuretic agents are administered while the etiology of oliguria is intravascular hypovolemia or hypotension, then these conditions are exacerbated and the risk of renal injury is increased<sup>(4)</sup>.

#### DIURETIC AGENTS: PHARMACOLOGY

Diuretic agents benefit renal function as follows: (Table III)

1. Renal Cortical Vasodilation = Dopaminergic agents, loop diuretics
2. Prevention of Tubular Obstruction = osmotic and loop diuretics
3. Suppression of vasoconstriction = Dopaminergic agents, ANP

**Table III.** Diuretic agents.

Class	Example	Site of action	Mechanism	FENa	K
Loop diuretics	Lasix, bumex, ethacrynic acid	mTAL	Inhibits Na-K-2Cl	20-25%	+
Thiazides	Hctz, metolozone	Early distal tubule	Inhibit NaCl uptake	5-8%	+
K-sparing	Triamterene, Amiloride, Spironolactone	Late distal tubule, collecting ducts	Inhibit Na uptake (T,A) Aldosterone antagonist (S)	< 5%	-
Carbonic anhydrase inhibitor	Acetylzolamide	Proximal tubule	Bicarbonate loss	< 5%	
Osmotic diuretics	Mannitol	Entire tubule	Osmotic pressure prevention of H <sub>2</sub> O absorption	< 5%	

#### 4. Decreased Tubular O<sub>2</sub> consumption = Dopaminergic agents, loop diuretics

##### Specific Agents:

**Mannitol:** Is an inert sugar that serves to expand the intravascular volume and induce an osmotic diuresis. Renal protection occurs via:

1. Increased preload
2. Increased CO
3. Release of ANP
4. Release of intrarenal prostaglandins
5. Prevention of tubular obstruction
6. Scavenging of free radicals
7. Prevention of postischemic cell swelling

The greatest effect of mannitol is demonstrated if it is administered at the time of renal insult. Mannitol is often given 15 minutes prior to aortic cross clamping at doses of 6.25 – 12.5 gm iv and repeated as needed every 4-6 hours. Alternatively an infusion of 10% mannitol can be given at a rate of 50 ml/hour. Mannitol given rapidly can precipitate pulmonary edema and hyperosmolar syndrome (Sosm > 320 mOs/kg) if more than 1.5 grams of mannitol is given within a 24 hour period<sup>(4)</sup>. Neither Mannitol nor Dopamine prevent the decline in GFR and tubular injury following suprarenal cross clamping<sup>(12)</sup>.

Mannitol is no more effective than volume loading to prevent a decrease in GFR<sup>(13)</sup> Mannitol confers renal protection during «pigment induced nephropathy» by «washing out» renal tubules. Mannitol administration for renal protection must be accompanied by volume loading in order to avoid dehydration and thus, exacerbate renal injury.

**Loop Diuretics:** Inhibit sodium reabsorption in the mTAL (Medullary Thick Ascending Loop of Henle). Loop diuretics can induce a diuresis even with marked renal impairment. Lasix attenuates renal injury if administered PRIOR to the ischemic or nephrotoxic insult. Some degree of renal protection is conferred when lasix is administered within 18 hours of renal injury<sup>(4)</sup>. The administration of IV High Dose Lasix (2-10 mg/kg) to convert oliguric ARF to NORF is based upon a single clinical study that notably excluded patients with shock or perioperative renal failure<sup>(14)</sup>.

Loop diuretics can induce:

1. Hypotension due to systemic venodilation (high dose)
2. Excessive diuresis resulting in hypovolemia (exacerbating renal injury)
3. Sodium and potassium wasting
4. Metabolic alkalosis
5. Ototoxicity (Limit individual doses to 250 mg/day especially with other ototoxic agents eg: aminoglycosides)

**Dopaminergic Agonists:** There are DA1 and DA2 receptor subtypes. DA1 receptor stimulation results in:

1. Inhibition of active sodium transport in the proximal tubule
2. Natriuresis
3. Diuresis

Stimulation of presynaptic DA2 receptors:

1. Inhibits the release of NE
2. Promotes peripheral vasodilation
3. Attenuates the beneficial effects of DA1 receptor stimulation on renal blood flow

Dopamine is a nonselective DA1 and DA2 agonist. This explains its variable effect on renal blood flow. Fenoldopam is a new DA1 selective agonist which is a potent renal vasodilator.

Dopamine at «renal dose» (eg: 1-3 ug/kg/min) promotes both diuresis and renal blood flow in normal patients<sup>(15)</sup>. Dopamine DOES NOT avert or ameliorate the course of perioperative ARF<sup>(16)</sup>. Diuretics and Dopamine should be avoided for the promotion of diuresis in prerenal (eg: hypovolemic) patients. Dopamine is not recommended for routine use for the prophylaxis or treatment of ARF.

Fenoldopam is the first selective DA1 receptor agonist. When given intravenously, its effects have a rapid onset and offset. Its elimination half-life is 10 minutes. At constant infusion rates of 0.03-0.3 ug/kg/min, it induces a dose dependent increase in renal blood flow. Low dose fenoldopam (0.01-0.03 ug/kg/min) is touted as a new renal protective agent and diuretic. Low doses of fenoldopam seldom causes hypotension. Other advantages over dopamine include increased dopaminergic potency, lack of B1 effect (eg tachycardia), safe infusion via peripheral catheter. Its potential renal protective effects are being studied during CPB, Renal Transplantation and the administration of contrast agents<sup>(4)</sup>.

Atrial Natriuretic Peptide (ANP): ANP is a potent endogenous renal protective hormone and diuretic. ANP is synthesized by cardiac atrial myocytes during conditions of atrial stretch or increased pressure. ANP acts on the renal glomeruli to increase glomerular hydrostatic pressure by dilating afferent arterioles, constricting efferent arterioles and increasing GFR<sup>(17)</sup>. A recent study of Anaritide (a synthetic form of ANP) was given prospectively to 504 critically ill patients with ATN<sup>(18)</sup>. Patients with ATN and oliguria improved significantly. In 120 oliguric patients, dialysis free survival was 27% in the anaritide treated patients compared to only 8% in the placebo group. The benefit of anaritide in oliguria without ATN is being studied.

A priority for anesthesia care providers is to limit perioperative renal impairment. This process begins with the identification of patients at increased risk for perioperative renal dysfunction, understanding basic renal physiology, the influence of perioperative events and drugs on the pathophysiology of renal function. At the present time, maintenance of adequate intravascular volume, mean arterial pressure as well as cardiac output are the most important renal protective measures under the purview of the perioperative anesthesiologist.

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