

Renal Disease and Anesthesia

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Normal renal function is important for the excretion of anesthetics and medications, maintaining fluid and acid-base balance, and regulating hemoglobin levels in the perioperative period.

The kidneys play a vital role in

- ❑ Regulating the volume and composition of body fluids,**
- ❑ Eliminating toxins, and**
- ❑ Elaborating hormones, including renin, erythropoietin, and the active form of vitamin D**

Factors related to operative procedures and to **anesthetic management** frequently have a significant impact on kidney physiology and function and may lead to

- ❑ Perioperative fluid overload,**
- ❑ Hypovolemia, and acute kidney injury, which are major causes of:**
- ❑ perioperative morbidity, mortality, extended hospital length of stay, and increased costs.**

Anatomy

- ❑ Kidneys are located in the posterior abdominal wall, with the 11th and 12th ribs and diaphragm placed posteriorly.
- ❑ It is 10 cm in length, 5 cm in width, and 3 cm in thickness.

Renal Circulation

- ❑ Renal function is intimately related to renal blood flow (RBF).
- ❑ In fact, the kidneys are the only organs for which oxygen consumption is determined by blood flow; the reverse is true in other organs.
- ❑ The combined blood flow through both kidneys normally accounts for 20% to 25% of total cardiac output.
- ❑ Approximately 80% of RBF normally goes to cortical nephrons, and only 10% to 15% goes to juxtamedullary nephrons.

- ❑ **Autoregulation of RBF** normally occurs between mean arterial blood pressures of **80- and 180-mm Hg** and is **principally due to intrinsic myogenic responses of afferent glomerular arterioles to blood pressure changes.**
- ❑ Within these limits, **RBF and GFR are kept relatively constant by afferent arteriolar vasoconstriction or vasodilation.**
- ❑ Glomerular filtration generally **ceases when mean systemic arterial pressure is less than 40 to 50 mm Hg.**

Functions of the kidney

1. Regulation of ions in the blood: Sodium, Potassium, Calcium, Chloride, Phosphate.
2. Regulation of blood volume: adjust the volume of blood or eliminate water in the urine.
3. Regulation of blood pH: regulate by excreting a variable amount of Hydrogen ions in the urine, conserving bicarbonate HCO_3 ions.
4. Production of hormones:
 - Calcitriol: calcium hemostasis.
 - Erythropoietin: RBC production.
 - Renin: blood pressure control.
5. Excretion of Waste:
 - Urea and creatinine.
 - Ammonia and amino acid.
 - Drugs

Evaluating Kidney Function

- ❑ The underlying cause of impaired kidney function may be *glomerular dysfunction, tubular dysfunction, or urinary tract obstruction.*
- ❑ the traditional diagnosis of AKI, based upon serum creatinine and urine output, has been refined into an increase of serum creatinine of 0.3 mg/dL or more within 48 h or a 1.5-fold or greater increase in baseline within 7 days.
- ❑ Since AKI is a **systemic disorder**, it is important to recall that the kidney excretory function assessed *via serum creatinine and urine output ignores endocrine, metabolic, and immunological kidney functions.*

SERUM CREATININE

- ❑ Creatine is a product of muscle metabolism that is nonenzymatically converted to creatinine.
- ❑ Daily creatinine production in most people is relatively constant and related to muscle mass, **averaging 20 to 25 mg/kg in men and 15 to 20 mg/kg in women.**
- ❑ Creatinine is then filtered (and to a minor extent secreted) but not reabsorbed in the kidneys.
- ❑ The rate of creatinine production and its volume of distribution is frequently abnormal in the critically ill patient, and a single serum creatinine measurement often will not accurately reflect GFR in the physiological disequilibrium of AKI.
- ❑ **The normal serum creatinine concentration is 0.8 to 1.3 mg/dL in men and 0.6 to 1 mg/dL in women.**

Creatinine Clearance

- ❑ Creatinine clearance measurement is the most accurate method available for clinically assessing GFR.
- ❑ Although measurements are usually performed over 24 h, 2-h creatinine clearance determinations are reasonably accurate and more convenient to perform.
- ❑ Creatinine clearances less than 25 mL/min are indicative of overt kidney failure.

Blood Urea Nitrogen: Creatinine Ratio

- ❑ Low renal tubular flow rates enhance urea reabsorption but do not affect creatinine excretion.
- ❑ As a result, the ratio of serum BUN to serum creatinine increases to more than 10:1.
- ❑ Decreases in tubular flow can be caused by decreased kidney perfusion or obstruction of the urinary tract.
- ❑ BUN: creatinine ratios greater than 15:1 are therefore seen in volume depletion and in edematous disorders associated with decreased tubular flow (eg, congestive heart failure, cirrhosis, nephrotic syndrome) as well as in obstructive uropathies. Increases in protein catabolism can also increase this ratio.

Effects of Anesthesia & Surgery on Kidney Function

1- Acute kidney injury

- ❑ Acute kidney injury (AKI) is a common and underappreciated perioperative problem, occurring in 1% to 5% of all hospitalized patients and in approximately 50% of all ICU patients.
- ❑ AKI is a systemic disorder that can include *fluid and electrolyte derangements, respiratory failure, major cardiovascular events, weakened immunocompetence leading to infection and sepsis, altered mental status, hepatic dysfunction, and gastrointestinal hemorrhage.*

- ❑ It is also **a major cause of chronic kidney disease** (CKD).
- ❑ Preoperative risk factors for perioperative AKI include *preexisting kidney disease, hypertension, diabetes mellitus, liver disease, sepsis, trauma, hypovolemia, multiple myeloma, and age greater than 55 years.*
- ❑ The risk of perioperative AKI is also increased by exposure to nephrotoxic agents such as *nonsteroidal anti-inflammatory drugs (NSAIDs), radiocontrast agents, and antibiotics.*
- ❑ The clinician must possess a thorough understanding of the risks of AKI, its differential diagnosis, and its evaluation strategy
- ❑ AKI is a major contributor to increased hospital length of stay, markedly increasing morbidity, mortality, and cost of care.
- ❑ Patients develop AKI and RF secondary to intrinsic kidney disease.

TABLE 1**Definition and staging of acute kidney injury according to the AKIN criteria**

Stage	Creatinine concentration	Urine output
1	1.5–1.9 × baseline or ≥ 0.3 mg/dL	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 × baseline	<0.5 mL/kg/h for >12 h
3	≥ 3.0 × baseline or ≥ 4 mg/dL or dialysis	<0.3 mL/kg/h for ≥ 24 h or anuria for ≥ 12 h

Risk factors for AKI in the perioperative setting include:

- Preexisting kidney impairment
 - Diabetes mellitus
 - Cardiovascular disease
 - Hypovolemia
 - The use of potentially nephrotoxic medications by older adult patients.
- **Reversible decreases in RBF, GFR, urinary flow, and sodium excretion occur during both neuraxial and general anesthesia.**
- **Such changes are usually less pronounced during neuraxial anesthesia.**
- **Most of these changes are indirect and are mediated by autonomic and hormonal responses to surgery and anesthesia.**
- **AKI is less likely to occur when an adequate intravascular volume and normal blood pressure are maintained.**
- **There is no evidence that currently utilized vapor anesthetic agents cause AKI in humans.**

Chronic Kidney Disease:

- ❑ CKD is defined as **either kidney damage or a GFR less than 60 mL/min for 3 months or more.**
- ❑ **Kidney damage** is defined as a **pathologic abnormality or markers of damage including abnormalities of the blood or on urine or imaging studies.**

Diagnosis of Chronic Renal Insufficiency

- **Oliguria does not set in** until late in the disease and is an unreliable marker of disease progression.
- **fluid overload and concomitant cardiac disease** and confirmed by laboratory testing.
- **Proteinuria & urinary sediment** are also helpful in diagnosis

Classification of Chronic Renal Disease:

- ❖ **Stage 1:** Kidney damage with normal or GFR (290 ml/min)
- ❖ **Stage 2:** Kidney damage with mild GFR (60-89 ml/min)
- ❖ **Stage 3;** Moderate GFR (30-59 ml/min)
- ❖ **Stage 4:** Severe GFR (15-29 ml/min)
- ❖ **Stage 5:** Kidney failure with GFR less than 15ml/min

Causes of renal failure

- 1) Diabetes Mellitus 25%**
- 2) Glomerulonephritis 14%**
- 3) Hypertension 8%**
- 4) Polycystic kidney disease 6%**
- 5) Pyelonephritis 6%**
- 6) Renal vascular disease 6%**
- 7) Others 17%**
- 8) Uncertain 15%**

Systemic effects of renal failure

Cardiovascular system:

- Left ventricular hypertrophy
- Atherosclerosis
- Hypertension

Respiratory system:

- Pulmonary edema

Metabolic acidosis

Coagulopathy

Autonomic neuropathy

Fluid and electrolyte:

- Volume overload
- Hyperkalemia

Altered Kidney Function & the Effects of Anesthetic Agents

INTRAVENOUS AGENTS

Propofol & Etomidate

- ❑ The pharmacokinetics of **both propofol and etomidate** are **minimally** affected by impaired kidney function.
- ❑ **Decreased protein binding** of etomidate in patients with **hypoalbuminemia** may enhance its pharmacological effects.

Barbiturates

- ❑ Patients with kidney disease often exhibit **increased sensitivity to barbiturates during induction**, even though pharmacokinetic profiles appear to be unchanged.

- The mechanism appears to be an **increase in free circulating barbiturate secondary to decreased protein binding**.
- **Acidosis** may also favor a more rapid entry of these agents into the brain by increasing the nonionized fraction of the drug.

Ketamine, Benzodiazepines and Opioids

- ☐ **Ketamine** pharmacokinetics are **minimally** altered by kidney disease.
- ☐ **Some active hepatic metabolites** are dependent on renal excretion and can potentially accumulate in kidney failure.

- ❑ **Benzodiazepines** undergo hepatic metabolism and conjugation prior to elimination in urine.
- ❑ Because they are **highly protein bound**, **increased benzodiazepine sensitivity** may be seen in patients with **hypoalbuminemia**.
- ❑ **Diazepam and midazolam** should be administered **cautiously** in the presence of kidney impairment because of the potential for the accumulation of active metabolites.

Most opioids used in anesthetic practice (morphine, meperidine, fentanyl, sufentanil, and alfentanil) are **inactivated by the liver**; some of these metabolites are then excreted in urine.

❑ **Remifentanyl** pharmacokinetics are **unaffected by kidney function** due to rapid ester hydrolysis in blood.

❑ With the **exception of morphine and meperidine**, significant accumulation of active metabolites generally does not occur with these agents.

❑ **Accumulation of morphine** (morphine-6-glucuronide) and **meperidine** (normeperidine) metabolites may **prolong respiratory depression in patients with kidney failure**, and **increased levels of normeperidine may promote seizure activity**.

pharmacokinetics of **opioid agonist–antagonists** (butorphanol, nalbuphine, and buprenorphine) are **unaffected by kidney failure**.

INHALATION AGENTS

Volatile Agents

Nitrous Oxide

- ❑ Volatile anesthetic agents are *ideal for patients with kidney disease because they are not dependent on the kidneys* for elimination and they have minimal direct effects on kidney blood flow.
- ❑ Although patients with mild to moderate kidney impairment do not exhibit altered uptake or distribution, accelerated induction and emergence may be seen in severely anemic patients (hemoglobin <5 g/dL) with chronic kidney failure, possibly because of a decrease in the blood:gas partition coefficient.

- ❑ **Some clinicians avoid sevoflurane** (and avoid <2 L/min gas flows) for patients with kidney disease who undergo lengthy procedures
- ❑ **Some clinicians omit entirely or limit the use of nitrous oxide** (or air) to maintain an FiO_2 of 50% or greater in severely anemic patients with end-stage kidney disease in an attempt to increase arterial oxygen content.
- ❑ This may be justified in patients with **hemoglobin less than 7 g/dL**, in whom even a small increase in the dissolved oxygen content may represent a significant percentage of the arterial to venous oxygen difference.

MUSCLE RELAXANTS

Succinylcholine

- ☐ Succinylcholine can be safely used in patients with kidney failure in the absence of hyperkalemia at the time of induction.
- ☐ It **should be avoided** in patients with kidney failure when the serum potassium is known to be increased or is undetermined.
- ☐ Although **decreased plasma cholinesterase** levels have been reported in uremic patients following dialysis, significant prolongation of neuromuscular blockade with succinylcholine use is rarely seen in this circumstance.

Cisatracurium & Atracurium

- ❑ Both are degraded by plasma **ester hydrolysis and nonenzymatic Hofmann elimination**.
- ❑ These agents are often the **drugs of choice** for muscle relaxation in patients with kidney failure, especially in clinical situations where neuromuscular function monitoring is difficult or impossible.

Vecuronium & Rocuronium

- ❑ The elimination of vecuronium is primarily hepatic, but up to 20% of the drug is eliminated in urine.
- ❑ The effects of large doses of vecuronium (>0.1 mg/kg) are only modestly prolonged in patients with kidney disease.

❑ **Rocuronium** primarily undergoes hepatic elimination, but prolongation in patients with severe kidney disease has been reported.

❑ In general, with **appropriate neuromuscular monitoring, these two agents can be used with few problems** in patients with severe kidney disease.

Pancuronium

- ❑ is primarily dependent on **renal excretion (60–90%)**.
- ❑ Although is metabolized by the liver into less active intermediates, its elimination half-life is still primarily dependent on renal excretion (**60–80%**).
- ❑ Neuromuscular function should be **closely monitored if pancuronium is used in patients with abnormal kidney function**

Reversal Agents

- ❑ Renal excretion is the **principal route of elimination for edrophonium, neostigmine, and pyridostigmine**.
- ❑ The half-lives of these agents in patients with kidney impairment are therefore **prolonged at least as much as any of the above relaxants**

Anesthetic considerations

I. Pre-operative Assessment:

- Routine anesthetic assessment along with special attention to renal functions is made.
- Hypertension and ischemic heart disease are commonly seen in chronic renal failure.
- Proteinuria and hypoalbuminemia predispose to edema.
- Urinalysis is a cheap, readily available, and informative laboratory test.
- A complete blood count may reveal anemia, other causes of the anemia include excessive hematuria, and reduced production of erythropoietin by failing kidneys.
- Chest X-ray and ECG may be required.

Summary of pre-operative assessment:

- **Patients should be optimized in the preoperative period,**
 - **hypertension should be managed with anti-hypertensives,**
 - **antibiotic coverage for urinary infections.**
 - **Routine transfusion is not recommended in chronic kidney disease and may predispose to CHF.**
 - **Electrolytes should be corrected appropriately and dialysis may be needed in severe renal failure.**
 - **Pre-medications may be necessary and antacids prophylaxis may be considered**

Intra-operative:

- ❑ **For open or laparoscopic renal surgery,**
 - general anesthesia with positive pressure ventilation using muscle relaxation is recommended.
 - Rapid sequence intubation is preferred in patients with chronic renal failure.
 - Induction of anesthesia may be achieved with intravenous and inhalational agents.
 - Maintenance of anesthesia is achieved with inhalational agents.

- The induction agent of choice in renal disease is **Propofol** as it is metabolized by the liver and its excretion is not renal dependent.
- **Atracurium** is the preferred muscle relaxant as it is metabolized by Hoffman degradation.
- **A large-bore intravenous line** is required as there may be a sudden risk of bleeding.
- A limb with an **arteriovenous fistula must not be used** for intravenous infusions

Monitoring:

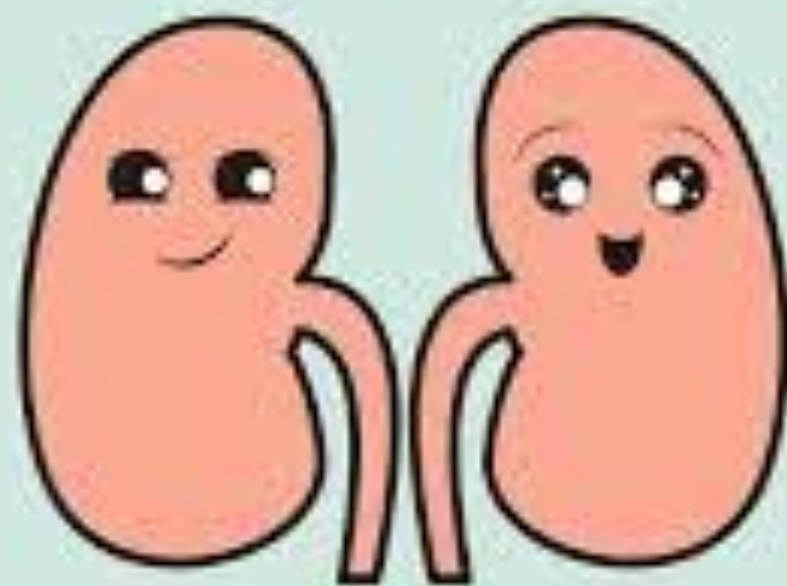
- ☐ Routine standard monitoring is a must.
- ☐ Patients with end stage disease may require **central venous pressure monitored fluid administration.**
- ☐ **Temperature monitoring** is required as renal surgery may take many hours.
- ☐ Warm intravenous fluids and a warming blanket may be used.

IV. Fluid therapy:

- ❑ Patients may be dehydrated as they are given bowel preparation and may be on dialysis, particularly in old age individuals.
- ❑ Appropriate fluid resuscitation to avoid sudden hypotension at induction with crystalloid fluid aiming for **urine output should be 0.5-1 ml/kg/h** is required in patients with signs and symptoms of dehydration.

Post-operative pain relief:

- ☐ There can be **significant pain**, especially in an open approach to kidneys.
- ☐ **Multimodal analgesia** is required for early mobilization and to reduce the incidence of postoperative pulmonary complications.
- ☐ **Epidural analgesia** should be used unless contraindicated.
- ☐ Regional analgesia is **contraindicated in presence of coagulopathy, thrombocytopenia, anticoagulation, or recent hemodialysis**.
- ☐ **Fentanyl and other short-acting opioids** are useful as they are largely metabolized in the liver.
- ☐ **Nonsteroidal anti-inflammatory drugs are contraindicated** because of their nephrotoxic potential.
- ☐ **Paracetamol** is a safe drug and is a **good adjuvant analgesic**.



THANK YOU

for your continuous support!

