

Perioperative Care for the Patient with Renal or Hepatic Disease

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Patients with renal or hepatic disease present a challenge to anesthesiologists because these conditions imply abnormal handling of anesthetic agents, as well as multiorgan system dysfunction, general debility and specific problems associated with replacement therapy and transplantation. Moreover, in situations of hepatic or renal insufficiency, anesthesia and surgery may themselves precipitate acute failure (1–11).

Systemic Manifestations

Chronic Renal Failure

Fluid and Electrolyte Balance: Edema, Hyperkalemia.

- Metabolic acidosis, hyperkalemia and congestive heart failure are well controlled by dialysis. Anuric patients: only fluid loss is insensible, 500 mL/day. Polyuric chronic renal failure (CRF): urine output appears normal, but concentrating ability is absent and fluid loss quickly results in hypovolemia.
- Most patients have a moderate compensated anion gap acidosis but with a depleted buffer base (HCO_3^- 15–18 mEq/L). Shock, diarrhea, or hypercatabolism quickly result in profound metabolic acidosis.
- Acute hyperkalemia: catabolic stress, acidosis, potassium-sparing diuretics, red cell transfusion, or potassium replacement. A pH decrease of 0.1 can increase potassium by 0.5 mEq/L.
- Hypermagnesemia (muscle weakness, increased susceptibility to muscle relaxants), hypomagnesemia (arrhythmias), hyperphosphatemia (renal osteodystrophy) and hypophosphatemia (increased susceptibility to muscle relaxants, difficult ventilatory weaning, central nervous system dysfunction).

Cardiopulmonary Problems: Hypertension, Atherosclerosis.

- Pericarditis, hemorrhagic pericardial effusion: rare, usually well controlled by regular dialysis.
- Systemic hypertension is prevalent and left ventricular hypertrophy and even asymmetric hypertrophy are not uncommon. Associated hyperlipidemia predisposes to accelerated atherosclerosis.

- Anemia and arteriovenous shunts cause a hyperdynamic circulation with fixed low systemic vascular resistance, and impaired circulatory reserve with poor tolerance of myocardial ischemia or sepsis.
- The risk of postoperative pulmonary edema, atelectasis, and pneumonia is increased, and abdominal distention from peritoneal dialysis further compromises ventilation.

Hematologic Changes: Anemia, Platelet Dysfunction.

- Normochromic, normocytic anemia (Hct 25–28%): decreased erythropoietin, red cell survival and chronic blood loss (gastrointestinal [GI] tract, labs). Compensation requires increased cardiac output and 2,3-DPG (impaired by hypophosphatemia).
- Uremic coagulopathy (blood urea nitrogen >60–80 mg/dL): defective endothelial release of von Willebrand's factor and factor VIII [VWF-VIII]. Platelet function is abnormal, and the Ivy bleeding time prolonged >15 min (normal: 3–8 min).

Nutritional-Metabolic Problems: Malnutrition, Infection.

- Hyperglycemia, hypertriglyceridemia and protein malnutrition (kwashiorkor, hypoalbuminemic malnutrition) are common.
- Hypoalbuminemia: dietary protein restriction, albuminuria and/or losses via continuous peritoneal dialysis (10–40 g/day protein). Low colloid oncotic pressure promotes interstitial and pulmonary edema; functional residual capacity and ventilatory reserve are decreased.
- Resistance to infection is decreased, especially nosocomial and opportunistic infections at shunt or peritoneal catheter sites. Wound dehiscence, fistulas, and bedsores occur as a consequence of depleted lean body mass and the catabolic effects of uremia.

Gastrointestinal Problems: Uremic Enteropathy.

- Anorexia, hiccups, nausea and vomiting (hallmarks of acute uremia) and delayed gastric emptying increase the risk of regurgitation and aspiration.

- Mucosal inflammation, ulceration, and bleeding may occur in any portion of the GI tract. Peptic ulcer disease occurs in up to 25% of patients with CRF despite regular dialysis.
- High incidence of hepatitis B and C (anicteric, carrier state) in patients on chronic hemodialysis.

Neuropsychiatric Complications: Encephalopathy and Neuropathy.

- Central nervous system manifestations range from subtle personality changes to drowsiness, asterexis, myoclonus, and seizures. Major surgery, GI bleeding or infection may precipitate acute encephalopathy.
- Distal sensorimotor neuropathy is an important indication for dialysis.
- Autonomic neuropathy can predispose to delayed gastric emptying, silent myocardial ischemia, orthostatic hypotension, and impaired circulatory response to anesthesia.

Chronic Liver Disease

Fluid and Electrolyte Balance: Refractory Edema and Ascites.

- Hypoalbuminemia + portal hypertension = ascites + intravascular hypovolemia.
- Secondary hyperaldosteronism (salt and water retention, potassium loss) results in hypokalemic metabolic alkalosis, generalized edema (anasarca), and progressive ascites.
- Ascites causes decreased functional residual capacity, atelectasis, and hypoxemia. Venous return and renal blood flow are decreased. Spontaneous bacterial peritonitis occurs in approximately 10% of patients.
- Edema and ascites are resistant to loop diuretics, which exacerbate intravascular hypovolemia and hypokalemia and worsen hepatic perfusion. The aldosterone antagonist spironolactone is effective but its onset/offset is slow (2–3 d) and in acute renal insufficiency it can provoke acute hyperkalemia.

Gastrointestinal Problems: Portal Hypertension, Varices, and Jaundice

- All patients have potential for active viral hepatitis (A, C, D).
- Anorexia, hiccups, nausea and vomiting; delayed gastric emptying; increased risk of regurgitation and aspiration. Exacerbated by severe ascites (abdominal pressure).
- Major risk of hemorrhage from esophageal and/or gastric varices (portal hypertension).
- Increased risk of peptic ulcer disease—differentiate bleeding from varices.

Renal Problems: Hepatorenal Syndrome.

- Hepatorenal syndrome: obstructive jaundice (total bilirubin >8 mg/dL) or hepatic failure result in portal endotoxemia, intense renal vasoconstriction (vasomotor nephropathy).
- Prerenal syndrome: oliguria with low urine sodium (10 mEq/L), progressive azotemia.
- Blood urea nitrogen low even with GI bleeding or acute renal failure: failure of arginine cycle (converts urea to NH_3).

Cardiopulmonary Problems: Hyperdynamic Circulation, Hypoxemia.

- Hyperdynamic circulation with fixed low systemic vascular resistance. Arteriovenous (AV) shunts in skin (nevi, erythema), GI tract, lung: impaired circulatory reserve with hypovolemia, sepsis, or myocardial ischemia.
- Hepatopulmonary syndrome: hypoxemia (AV shunts), atelectasis, pulmonary hypertension.
- Increased risk of postoperative pulmonary edema, atelectasis, pneumonia.
- Alcoholic cardiomyopathy, arrhythmias (\pm thiamine deficiency).

Hematologic changes: Factor VII Deficiency, Thrombocytopenia.

- Factor VII deficiency—prolonged PT (impaired synthesis, vitamin K absorption).
- Thrombocytopenia: hypersplenism in portal hypertension, bleeding, disseminated intravascular coagulation.
- Factor V deficiency (acute marker after orthotopic liver transplantation)
- Dysfibrinogenemia (fibrinogen level may be normal).
- Macrocytic anemia (alcohol-induced bone marrow suppression).

Nutritional-Metabolic Problems: Hypoglycemia, Malnutrition, Infection.

- Hypoglycemia in acute hepatic failure or end-stage liver disease (failure to synthesize glycogen).
- Protein-malnutrition, catabolic effects of hepatic failure: depleted lean body mass, hypoalbuminemia, low colloid oncotic pressure.
- Nosocomial and opportunistic infections, wound dehiscence, fistulas and bedsores.

Neuropsychiatric Complications: Encephalopathy and Neuropathy.

- Hepatic encephalopathy: Grade 1: confabulation, constructional apraxia; Grade 2: drowsiness, asterexis, confusion; Grade 3: stupor; Grade 4: coma.
- Fulminant hepatic failure: coma with acute cerebral edema.

- Precipitating factors: hypovolemia (excessive diuresis), alkalosis, GI bleeding, surgery, infection.
- Alcohol-induced encephalopathy (thiamine deficiency): Wernicke's encephalopathy (oculomotor palsy, cerebellar ataxia), Korsakoff's psychosis (amnesia, confabulation).

Pharmacologic Effects of Renal and Hepatic Failure

Most IV anesthetic agents are lipid-soluble and non-ionized and undergo hepatic biotransformation to active or inactive water-soluble metabolites, which are then excreted in the bile or the urine. Lipid insoluble, highly ionized drugs (mostly muscle relaxants) are directly excreted by the kidney. Renal and hepatic disease alter anesthetic and parenteral drug clearance by several mechanisms: decreased blood flow (drug delivery), increased unbound free fraction of highly protein-bound drugs (hypoalbuminemia or acidosis), and decreased enzymes and transport processes that irretrievably remove the drug from the blood.

The duration of action of many drugs administered by bolus or short-lived infusion is dependent on redistribution, not elimination. Their loading doses may not require to be decreased unless unbound free fraction is increased or there is known to be a greater pharmacodynamic effect. However, maintenance doses can accumulate and should be reduced accordingly.

Both liver and renal disease alter drug pharmacodynamics even if pharmacokinetics are not changed. Patients are often debilitated, with depleted lean body mass. Respiratory depression is much more likely with opioid or volatile anesthetic agents: consider reducing all drug dosages by 25%–50%.

Drugs Independent of Liver and Renal Function for Elimination

Enzymatic or spontaneous breakdown in the blood. Accumulation is unlikely, but altered pharmacodynamic responses should be anticipated. (e.g., succinylcholine, remifentanyl, atracurium and cisatracurium, esmolol.)

Drugs with Increased Unbound Fraction in Hypoalbuminemia

Increased free or active fraction. Doses should be decreased 20%–50%, depending on the degree of hypoalbuminemia. (e.g., thiopental, methohexital, diazepam.)

Drugs Predominantly Dependent on Hepatic Biotransformation

Avoid or decrease dosage in hepatic failure. (e.g., all benzodiazepines, all opioids, nondepolarizing muscle relaxants, except atracurium, cisatracurium.

Drugs Predominantly Dependent on Renal Elimination

Avoid or decrease maintenance dose in CRF (loading doses remain unaltered). (e.g., gallamine, me-tubine, digoxin, penicillins, cephalosporins, aminoglycosides, vancomycin, cyclosporin A.)

Drugs Partially Dependent on Renal Elimination

Decrease maintenance doses by 30%–50% or titrate carefully to effect. (e.g., anticholinergic, cholinergic agents, pancuronium, pipecuronium, vecuronium, rocuronium, doxacurium, milrinone, amrinone, phenobarbital, aprotinin, aminocaproic acid, tranexamic acid.)

Drugs with Active Metabolites that are Renally Eliminated

Drugs that may exert a prolonged effect in CRF despite rapid hepatic biotransformation of the parent compound. They should be avoided, or have their maintenance doses decreased by 30%–50% or titrated carefully to effect.

(e.g., morphine [m-3-glucuronide, m-6-glucuronide, normorphine], meperidine [normeperidine], diazepam [oxazepam], midazolam [1-hydroxy midazolam], pancuronium [3-hydroxypancuronium], vecuronium [desacetylvecuronium], sevoflurane, enflurane [fluoride], sodium nitroprusside [thiocyanate].

Perioperative Management

Chronic Renal Failure

Preoperative Evaluation and Preparation.

- In evaluating the patient, note the etiology of CRF (i.e., \pm systemic disease), urine output, type of dialysis, and most recent treatment. Look for physical signs of systemic complications (anemia, left ventricular hypertrophy, congestive heart failure, neuropathy, sepsis, malnutrition) and examine shunt sites and/or CAPD catheter site for infection.
- Relevant lab studies include Hct, complete blood count, electrolytes (total CO₂ if arterial blood gases impracticable), blood urea nitrogen, creatinine, Ivy bleeding time, electrocardiogram, and chest radiograph.
- Human recombinant erythropoietin: normal Hct; —risk of hypertension, thrombosis.

Preoperative Preparation.

- Hemodialysis: schedule day before surgery to avoid acute fluid and electrolyte shifts.
- Continuous ambulatory peritoneal dialysis: continue until time of surgery (assess abdominal girth).

- Preoperative blood transfusion is indicated only to treat acute blood loss or for patients with cardiopulmonary disease undergoing major surgery with Hct <28%.
- Transfuse during dialysis to avoid fluid overload and hyperkalemia.
- Platelet dysfunction (bleeding time >15 min despite platelet count >100 k/mm³), should be corrected before major surgery with deamino-8-d-arginine vasopressin (0.3 µg/kg over 20 min), which stimulates endothelial release of VWF-VIII, or with cryoprecipitate (10 U), which contains VWF-VIII.
- Labile or symptomatic hypertension must be controlled before elective surgery. Patients on long-term clonidine or guanabenz should receive a clonidine transdermal patch to prevent rebound hypertension.

Operative Preparation.

- Minimize sedative or opioid premedication, provide aspiration prophylaxis (anticholinergic, H₂-blocker, metoclopramide, sodium bicarbonate).
- Use universal and aseptic precautions throughout.
- Avoid BP cuffs or arterial catheters on arm with arteriovenous fistula or shunt, and avoid urinary catheter in anuric or oliguric patients.
- Invasive hemodynamic monitoring is indicated if large fluid shifts are anticipated, or with sepsis or cardiopulmonary insufficiency.
- Avoid pressure or stretch on fistula sites, bony prominences, joints. Patients with sensory neuropathy may not complain of positional discomfort. Renal osteodystrophy = fragile bones and joints.
- Use active warming devices (e.g., forced-air convection blanket) to prevent hypothermia.
- Consider intraoperative hemodialysis (CPB).

Anesthesia.

- Regional anesthesia is not contraindicated if coagulopathy is corrected, but there is increased risk of hypotension (autonomic neuropathy) and infection. When sympathetic block wears off after surgery, sudden increase in systemic vascular resistance could precipitate pulmonary edema.
- For general anesthesia, use aspiration precautions (e.g., head up, rapid sequence, cricoid pressure).
- Preoxygenate and give adequate fluid load (250-1000 mL) before induction.
- Succinylcholine is not contraindicated in CRF if serum potassium is <5.0 mEq/L and the patient has been dialyzed within the last 24 h. Avoid pancuronium and pipercuronium.
- After tracheal intubation, increase minute ventilation to compensate for chronic metabolic acidosis.

- Keep maintenance fluids to a minimum but fully replace fluid losses.
- Nephrotoxicity is a theoretic possibility with enflurane (fluoride) or sevoflurane (Compound A).
- Anticipate labile BP: hypotension (deep anesthesia, fluid losses, positional changes) or hypertension (inadequate anesthesia). Beta-blockers or calcium blockers are helpful.
- Anticipate hyperkalemia (β-blockers), arrhythmias, and potential for digoxin toxicity.

Postoperative Care.

- Anesthetic emergence may be delayed, and complicated by vomiting, aspiration, hypertension, persistent neuromuscular blockade, respiratory depression, or pulmonary edema.
- CO₂ retention in chronic metabolic acidosis: acute acidosis, hyperkalemia.
- If in doubt, a short period of postoperative mechanical ventilation allows controlled emergence, avoids reversal agents, and facilitates evaluation of neurologic and ventilatory function before extubation.
- Restrict maintenance fluid, replace sequestration or overt losses. Anticipate and treat hyperkalemia.
- For severe uremia, use hemodialysis. Hemodynamically unstable: consider peritoneal dialysis.
- CVVH/D: Large volume removal with hemodynamic stability, requires heparinization.

Chronic Liver Disease

Preoperative Evaluation.

Note the Child-Pugh Classification of Preoperative Risk in Liver Disease (Table 1).

Preoperative Preparation.

- Acute viral hepatitis, Child's C: postpone elective surgery (high morbidity and mortality).
- Ascites: discontinue spironolactone 3-4 days preoperatively, cautiously drain tense ascites.
- Correct prolonged PT with parenteral Vitamin K and/or fresh-frozen plasma. Refractory PT = severe liver damage.
- Treat and remove precipitating factors of encephalopathy: protein restriction, lactulose, neomycin.
- Acute GI bleeding: 1) fluid resuscitation, transfusion, correction of coagulopathy; 2) establish diagnosis (varices versus peptic ulcer); 3) options for continued bleeding include endoscopic sclerotherapy, Sengstaken-Blakemore tube (± tracheal intubation), vasopressin infusion, emergency decompression.
- TIPPS (transjugular intrahepatic portosystemic shunt): relieves ascites, improves renal function. Risk of endotoxemia, pulmonary edema, encephalopathy.

Table 1. Child-Pugh Classification of Preoperative Risk in Liver Disease

	A (minimal risk)	B (moderate risk)	C (severe risk)
Serum bilirubin (mg/dL)	<2	2–3	>3
Serum albumin (g/dL)	>3.5	3–3.5	<3
PT (sec > control)	1–4	4–6	>6
CNS (coma grade)	Normal	Confused (1–2)	Coma (3–4)
Ascites	None	Easily controlled	Poorly controlled
Nutrition	Excellent	Good	Poor

PT = prothrombin time; CNS = central nervous system.

Operative Preparation.

- Omit oral premedication except for aspiration prophylaxis. If necessary, give small doses of IV sedation in induction room or operating room under direct observation.
- Use universal precautions and asepsis throughout. All staff should have hepatitis B vaccine.
- Indications for invasive monitoring as for CRF, but it should be remembered that these patients are at very high risk of perioperative acute renal failure (hepatorenal syndrome) and intravascular volume status is difficult to assess because of ascites and anasarca.
- Considerations for positioning and avoidance of hypothermia are as for CRF. Tense ascites adds an additional degree of difficulty.

Anesthesia.

- If BP and cardiac output are maintained, regional anesthesia preserves hepatic blood flow. However, coagulopathy and ascites limit its application.
- Drug handling is extremely variable. Alcoholics may require large loading doses, but have delayed elimination and emergence. Decrease doses of all sedative agents in severe liver disease.
- Preoxygenate and fluid load before anesthetic induction. Use aspiration precautions as for CRF.
- Succinylcholine OK, but duration could be prolonged with severe liver dysfunction. Metabolism of atracurium and cisatracurium is independent of liver function.
- All volatile anesthetic agents and hypercarbia decrease hepatic blood flow. All opioids may accumulate. Propofol remains relatively short acting in cirrhosis.
- Anticipate hypoxemia (ascites, shunting), bleeding (coagulopathy), oliguria (vasomotor nephropathy).
- Renal protection (?): dopamine, furosemide infusion, fenoldopam.
- Avoid excessive volume loading (CVP >10 mm Hg); can induce acute hepatic congestion. Fluid restrictive approach during hepatic resection may decrease venous oozing.

Postoperative Care.

- Anesthetic emergence may be delayed and complicated by vomiting and aspiration, hypotension, respiratory depression, and acute respiratory failure.
- Extubate trachea when patient is fully awake to reduce risk of aspiration.
- If in doubt, a short period of postoperative mechanical ventilation allows controlled emergence, avoids reversal agents, and facilitates evaluation of neurologic and ventilatory function before extubation.
- Potential postoperative problems include bleeding, oliguria, encephalopathy, acute respiratory failure, sepsis, wound dehiscence, and acute hepatic failure.

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