37. Renal Protection

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A 74-year-old woman with a history of severe, poorly controlled hypertension presents for urgent coronary artery revascularization. One week prior to admission she suffered an acute myocardial infarction complicated by acute pulmonary edema requiring tracheal intubation and mechanical ventilation. Her preoperative serum creatinine is 2.2 mg/dL. Cardiac surgery is uneventful except for a low urine output throughout cardiopulmonary bypass (CPB) which persists into the postoperative period. In the ICU her arterial blood gases and lung mechanics permit extubation the morning after surgery. However, oliguria persists despite treatment with furosemide, ethacrynic acid, and bumetanide. Rising pulmonary artery pressures and metabolic acidosis necessitates the institution of continuous veno-venous hemodialysis. Her subsequent postoperative course is complicated by persistent acute renal failure, intermittent pulmonary edema requiring reintubation, rapid atrial fibrillation, pneumonia, recurrent gastrointestinal bleeding, and ileus. One month after surgery she remains in the ICU, having undergone a Billroth II partial gastrectomy for a bleeding peptic ulcer and a tracheostomy to facilitate slow ventilatory weaning.

Acute renal failure is a devastating complication of surgery or trauma. As illustrated by the case above, it profoundly increases the duration of ICU and hospital stay, and is associated with an in-hospital mortality of 60-90%. Dialysis is able to control the immediate threats to life from hyperkalemia, metabolic acidosis, fluid overload and acute uremia, but patients may have protracted ICU courses because of weakness and debilitation, impaired wound healing, and multiorgan dysfunction, and may die from sepsis, bleeding, or cardiovascular complications. Although full recovery from acute renal failure is possible, continuing insults such as sepsis, bleeding, or hypotension (which may occur as a consequence of dialysis) represent secondary ischemic insults to the kidney that delay or halt its ultimate recovery. The following is an outline of topics related to the etiology and prevention of perioperative acute renal failure.

I. Etiology of Acute Renal Failure (ARF)
   A. Acute tubular necrosis (ATN)–90% of cases
      1. Ischemic–shock, sepsis, aortic cross-clamping
      2. Nephrotoxic
         a) Endogenous–hemolysis, bilirubin, myoglobin, urate
         b) Exogenous–aminoglycosides, cyclosporin A, amphotericin, NSAIDs, cisplatinum, radiocontrast dye
   B. Vascular injury
      1. Arterial–embolism, thrombosis, trauma
      2. Venous–thrombosis, elevated (intraabdominal) pressure
   C. Vasomotor nephropathy (prerenal)–sepsis, liver failure, CHF
   D. Abdominal compartment syndrome–intraperitoneal pressures ≥20 mmHg
   E. Acute on chronic renal insufficiency
   F. Systemic diseases–SLE, scleroderma, vasculitis, sickle cell crisis
   G. Interstitial nephritis–allergy to penicillin antibiotics
   H. Acute glomerulonephritis

II. Risk factors for perioperative ARF
   A. High risk procedures
      1. Cardiac surgery with cardiopulmonary bypass (CPB)
         a) Effects of CPB on renal function
         b) Effects of cardiac function
      2. Major vascular surgery
         a) Effects of suprarenal aortic cross-clamping
         b) Effects of infrarenal aortic cross-claiming
         c) Other complicating factors
      3. Intraabdominal sepsis
      4. Biliary surgery (obstructive jaundice)
      5. Genitourinary surgery (obstructive uropathy)

6. Trauma
    a) Increased intraabdominal pressure
    b) Rhabdomyolysis
    c) Direct renal/urinary tract injury
7. Complicated obstetrics
8. Radiologic procedures using radiocontrast dye

B. Patient risk factors and predisposing surgical complications:
1. Preexisting renal insufficiency (serum creatinine >2 mg/dL)
2. Advanced age
3. Diabetes, hypertension, abnormal lipids (diffuse atherosclerosis)
4. Hypovolemia (acute, chronic)
5. Sepsis
6. Hemolysis, rhabdomyolysis, jaundice
7. Coagulopathy, DIC, bleeding

III. Diagnosis of Renal Failure

A. Urine flow rate (but 75% of ARF is nonoliguric)

B. Urinalysis–oliguria
1. Features of urine osmolality, sodium, FE_{Na} (in prerenal syndrome)
2. Features of urine osmolality, sodium, FE_{Na} (in ARF)

C. BUN
1. Causes of elevated BUN without ARF
2. Causes of low BUN with ARF

D. Serum creatinine
1. Relationship to GFR
2. Causes of low serum creatinine with ARF

E. 2 hr creatinine clearance

F. Renal ultrasound

G. Renal scintiscan

IV. Prevention of ARF

A. Maintenance of renal blood flow (RBF)
1. Maintenance of preload (intravascular volume)
2. Maintenance of cardiac output
    a) Use of inotropic agents
    b) Use of afterload reduction–effects of vasodilators on renal function

B. Prevention of tubular obstruction (pigment nephropathy)
1. Use of volume loading
2. Mannitol, furosemide (controversial)

C. Maintenance of renal perfusion pressure
1. Situations with loss of renal autoregulation:
    a) Sepsis
    b) ARF
    c) CPB (?)
    d) Spinal/epidural anesthesia (?)
2. Interventions to normalize renal perfusion pressure
    a) Fluid administration
    b) Pressors-norepinephrine, vasopressin

D. Pharmacologic protection
1. Dopaminergic agonists–dopamine, fenoldopam
    a) Effects on renal blood flow (renal protection)
    b) Effects on sodium reabsorption (diuresis)
2. Mannitol
    a) Dosing and administration
    b) Actions and mechanisms
    c) Side-effects
3. Loop diuretics
    a) Dosing and administration

b) Actions and mechanisms
c) Side-effects
4. Calcium channel blockers
a) Role in hypertension
b) Role in protection against nephrotoxic insults
5. N-Acetylcysteine
a) Dosing and proposed mechanisms
b) Role in contrast-mediated nephrotoxicity
6. Sodium bicarbonate
a) Dosing and proposed mechanisms
b) Role in contrast-mediated nephrotoxicity

V. Treatment of oliguria
A. Examination of urine (see above) and collecting system
B. Restore intravascular volume and renal perfusion pressure
C. Diuretic therapy in the setting of hypervolemia considered if increased urine output would aid in patient management
1. Furosemide bolus
2. Furosemide infusion
3. Combination therapy (furosemide + others)
a) Dopamine, fenoldopam
b) Bumetanide, hydrodiuril, metolazone

This chapter is a revision of the original chapter authored by Rob Sladen, M.D.

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QUESTIONS:

37.1. A 28-year-old man is admitted to the ICU following emergency exploratory laparotomy for injuries sustained in a motor vehicle accident. At laparotomy he was found to have splenic and hepatic lacerations, which were repaired, and a large intraabdominal hematoma, which was evacuated. He also sustained a fractured left femur, which was immobilized by external fixation. Two hours after admission to the ICU his urine flow remains only 15 ML/hr. Which of the following urinary findings is most consistent with a diagnosis of a prerenal state?

A. Fractional excretion of sodium of 3.5%
B. Urine specific gravity of 1.010
C. Urine sodium of 12 mEq/L
D. Urine to plasma osmolar ration of 1.0
E. Urine to plasma creatinine ration of 15

37.2. The urine is tested for myoglobin and is found to be positive. Appropriate interventions include:

A. Send blood for creatinine phosphokinase (CPK) level
B. Add 50 mEq/L sodium bicarbonate to maintenance IV fluid
C. Increase maintenance IV fluid to 200 mL/hr
D. All of the above

37.3. Over the next 6 hours the patient's abdomen is noted to become progressively more distended. HR = 110/min, BP = 115/66, pulmonary artery pressure (PAP) = 34/18, pulmonary artery occlusion pressure (PAOP) = 16 mmHg, cardiac output = 6.8 L/min. Indirect measurement of intraabdominal pressure via the urinary catheter reveals it to be 24 mmHg. Urine flow has declined from 80 to 25 mL/hr. The most appropriate intervention to restore urine flow at this point is:

A. Furosemide 20 mg IV
B. Mannitol 6.25 g IV
C. Dopamine 3 mcg/kg/min infusion
D. Urgent return to the OR for exploratory laparotomy
E. All of the above

37.4. During infrarenal cross-clamping for aortic aneurysm resection in a 54-year-old, 78 kg man, the urine flow rate declines to 15 mL/hr. HR = 92 beats/min, BP = 145/90, PAP = 25/14, PAOP = 12 mmHg, cardiac output = 4.6 L/min. Dopamine is started at 3 mcg/kg/min and urine flow subsequently increases to 55 mL/hr. The most likely explanation for this response to dopamine is:

A. Increase in cardiac output
B. Increase in renal blood flow
C. Increase in glomerular flow rate
D. Decrease in tubular sodium reabsorption
E. Decrease in presynaptic norepinephrine release

38. Renal Replacement Therapy

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A 65-year-old female presents to the ER with nausea and vomiting and abdominal distention. A CT scan reveals a pelvic mass and a distended cecum. She is emergently taken to the OR for an exploratory laparotomy with en block removal of pelvic contents. However it is noted that her cecum is perforated. A diverting ileostomy is performed and the patient is taken to the ICU. In the ICU she remains hypotensive and a diagnosis of septic shock is made. A few hours after admission, it is noted that he urine output drops to less than 0.5cc/kg/hr and that her baseline creatinine has doubled.

Among critically ill patients, acute kidney injury (AKI) requiring dialysis is associated with mortality rates generally in excess of 50%.[1] Besides longer hospitalization, higher cost of therapy are associated with this entity.[2] Furthermore, some literature supports the aggressive use of renal replacement therapy in the critically ill that develops AKI. [3] One prospective study was performed to determine if daily dialysis results in better survival than every other day. One hundred sixty patients with acute renal failure were assigned to receive daily or conventional intermittent hemodialysis. Patients in the daily dialysis group had better uremia control, lower mortality (22 vs. 38%) and shorter time to renal recovery (9 vs. 16 days compared to the conventional group).

I. Indications for Renal Replacement Therapy

A. Fluid Overload
B. Hyperkalemia
C. Hyper/Hyponatremia
D. Metabolic Acidosis
E. Uremia (BUN > 100)
F. Progressive Azotemia without signs of uremia
G. Dialyzable toxin overdose
H. Oliguria/Anuria
I. Fluid Overload
J. Sepsis?

II. Classification

Dialysis is a generic name used commonly to refer to renal replacement therapy (RRT). There are multiple types of RRT. Intermittent hemodialysis (IHD), peritoneal dialysis (PD or CAPD) and continuous renal replacement therapy (CRRT) will be discussed. All of them have advantages and disadvantages. An excellent review of these modalities can be found on-line.[4] Before entering the discussion about the different types of RRT, there are some basic differences between hemodialysis (dialysis by diffusion) and ultrafiltration that are important to understand.

A. Diffusion dialysis

1. Solute diffuses from high to low concentration along an electrochemical gradient
2. Electrolyte solution runs countercurrent to opposite side of semi-permeable membrane filter
3. Larger molecules poorly removed/Better for smaller molecules
4. Solute removal proportional to dialysate rate

B. Ultrafiltration (UF)

1. Ultrafiltration works via Convection instead of Diffusion
2. Solute carried across membrane in response to a pressure gradient called a "solvent drag"
3. Mimics normal kidney function
4. Rate of UF proportional to hydrostatic pressure and blood flow
5. Very effective for fluid removal and middle molecules (i.e. cytokines in septic patients)

C. Semi-Permeable Membranes

In addition, there are two different types of semi-permeable membranes used for either dialysis or CRRT:

1. **The Cellulose-based**
    a) Thinner membrane/ Low permeability
    b) Activates Inflammatory Response Cascade including Complement
    c) Not typically used in critically ill

2. **The Synthetic**
    a) Thicker
    b) Higher Sieving Coefficient = Better for convective clearance
    c) Better for UF than diffusion dialysis
    d) If used on dialysis some UF will still occur
    e) Used in ICU patients

III. Intermittent Hemodialysis (IHD)

A. Most traditional approach
B. Requires central vein access or arteriovenous fistula
C. A specialized pump provides the driving force
D. Eliminates–solutes very effectively and fluid
E. Hemodynamic instability related to impaired sympathetic response, volume and solute shifts, and buffers, therefore not suitable for many ICU patients as it may worsen ischemic injury to kidneys or other organs
F. Therefore daily IHD typically used for ICU patients that can tolerate fluid shifts.
G. Requires specialized personnel and machinery

IV. Peritoneal dialysis

A. Represents an alternative to IHD because of patient preference in the outpatient setting, and because of less hemodynamic fluctuations in the ICU setting when continuous RRT is not available
B. Cost effective and simple
C. No need for heparin or venous access
D. Requires peritoneal access (surgical or percutaneous)
E. An osmotic gradient acts as driving force
F. Eliminates–fluids and, to a lesser extent, solutes resulting in poor solute and uremic control
G. May compromise diaphragmatic excursion
H. Increased potential for infection

V. Continuous Renal Replacement therapy (CRRT)

A. More suitable for the hemodynamically unstable patients
B. Less drastic fluid shifts and precise volume control, which is immediately adaptable to changing circumstances.
C. Very effective control of uremia, hypophosphatemia and hyperkalemia.
D. Rapid control of metabolic acidosis
E. Improved nutritional support (full protein diet).
F. May have an effect as an adjuvant therapy in sepsis.
G. Probable advantage in terms of renal recovery.
H. Diffusion or Convection or both
I. Effective at regulating very specific fluid losses/gains throughout a specific period of time (i.e. -1.5 L/day)
J. Requires venous access and anticoagulation
K. Available 24 hours a day with minimal training.
L. Hypothermia.and severe depletion of electrolytes – particularly K+ and PO4, where care is not taken.
M. Three major subtypes
    1. Continuous veno-venous hemofiltration (CVVH)
    2. Continuous veno-venous hemodialysis (CVVHD)
    3. Continuous veno-venous hemodiafiltration (CVVHDF)
    4. Continuous arteriovenous hemofiltration (CAVH)
    5. Continuous arteriovenous hemodiafiltration (CAVHD)

VI. **CVVH**

A. Convection Dialysis
B. UF rate high
C. Replacement electrolyte solution is required to maintain hemodynamic stability
D. This mode is also very effective for clearing mid sized molecules, such as inflammatory cytokines.
E. It is hypothesized that removal of such mediators may play a role in improving outcome in sepsis.
F. A very simple version of this is slow continuous ultrafiltration, (SCUF) which is used for volume control in fluid overloaded patients.
G. SCUF does not require the use of replacement fluid, and fluid removal is 300ml to 500ml per hour.

VII. **CVVHD**

A. Continuous diffusive dialysis,
B. The dialysate is driven in a direction countercurrent to the blood.
C. This provides reasonably effective solute clearance, although mostly small molecules are removed.

VIII. **CVVHDF**

A. Better solute clearance than CVVH
B. Most popular in ICU
C. Combines Convection and Diffusion
D. Medium and Small solutes removed
E. Dialysate and Replacement fluid used

IX. **CAVH**

A. Access–artery and vein
B. Driving force – arterial blood pressure
C. Eliminates – fluid and solutes
D. Prevents hemodynamic instability
E. Requires arterial access and heparinization
F. Filtration rates may decrease to less than 20 mL/minute

X. **CAVHD**

A. Access–artery and vein
B. Driving force – arterial pressure
C. Eliminates–fluid and solutes to a greater degree than CAVH
D. Prevents hemodynamic instability
E. Disadvantages–requires arterial access and heparinization

XI. **IHD vs CRRT**

Mortality in the patients that develop AKI remains high. The literature suggests an aggressive approach may be beneficial to these patients in terms of the use of RRT. In recent years use of CRRT has become more frequent in the critically ill. One of the reasons for this observation includes the fact that CRRT ensures adequate creatinine clearance while preserving hemodynamic stability. This fact may prevent secondary ischemic injury to the kidneys or other organs that could occur during hypotension related to hemodialysis. In addition CRRT is superior to intermittent hemodialysis for volume control. Although still controversial, CRRT with UF might clear or filter the plasma of pro-inflammatory cytokines modulating the immune response during SIRS or sepsis. There are not strong data that support that this property alters outcomes in humans. Furthermore, there is no strong evidence that CRRT is superior that HD. A recent study found worse outcomes with CRRT when compared with IHD but the sample was small and the authors recommended larger, prospective, randomized clinical trials to compare these modalities in severe AKI. [2] In addition, meta-analysis comparing the two modalities did not found a difference.[5] It seems for the actual evidence that what is important is to aggressively initiate RRT in patient that develop AKI.

This chapter is a revision of the original chapter authored by C. William Hanson, III, M.D.

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QUESTIONS:

38.1. Acute kidney injury in the critically ill:
- A. It is a relatively infrequent entity
- B. It is better treated with every other day diffusion dialysis
- C. It is associated with a mortality between 40-65%
- D. It has no impact in ICU or Hospital stays

38.2. The following are true in regards to CRRT EXCEPT:
- A. May be of benefit in the septic patient
- B. A better control of the hemodynamics and fluid shift is possible
- C. It may lead to hypothermia
- D. It is better than intermittent hemodialysis in the critically ill

38.3. The following are true in regards to peritoneal dialysis EXCEPT:
- A. Has lower costs
- B. It is very effective in solute removal
- C. Has been largely replaced by CRRT in the ICU setting
- D. Does not require anticoagulation

38.4. Of the options for CRRT in the ICU the one that is more popular is
- A. CVVH
- B. CVVHD
- C. CVAHDF
- D. CVVHDF

38.5. In relation to the membranes use during dialysis, the following are incorrect EXCEPT:
- A. There is no difference among the membranes used
- B. The natural cellulose based membrane is more favorable for the critically ill
- C. The synthetic membrane is thicker
- D. The synthetic membrane is better for ultrafiltration purposes