MANAGEMENT OF ACUTE KIDNEY INJURY

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DEFINITION OF AKI

AKI
- Reflects the broad spectrum of acute diseases of the kidney

Stages
- Can be imperceptible clinically at early stages to severe and requiring renal replacement therapy

Human criteria
- Absolute increase in creatinine of > 0.3mg/dL
- Increase of creatinine by 50%
- Reduction in UOP

REVERSIBLE
- Near normal renal function and small changes in creatinine represent large changes in GFR
- Important to recognize EARLY
CAUSES OF AKI

- Intrinsic
  - Ischemic injury
- Nephrotoxicants
- Infectious diseases
- Pyelonephritis
- Ureteral obstruction
- Systemic Diseases
TYPES OF AKI

PreRenal

Intrinsic Renal
- Polyuric >2-3ml/kg/hr
- Oliguric <1ml/kg/hr
- Anuric <0.5ml/kg/hr

Postrenal
MANIFESTATIONS OF AKI

- Abnormal fluid balance
- Electrolyte disorders
- Metabolic acidosis
- Uremic intoxication
- Systemic complications
HYPERTENSION OF RENAL DISEASE

Blood pressure

- Product of cardiac output and SVR

Hypertension is multifactorial

- Altered Na excretion leads to volume expansion
- Altered RAAS/increased catecholamines leads to increased SVR
CLINICAL PRESENTATION

History
- Acute onset
- GI signs
- Variable urine output

Physical examination
- Dehydration
- Signs of uremia/hypertension
- Enlarged/painful kidneys
DIAGNOSTICS

- CBC/CHEM /blood gas/SDMA
- Urinalysis/UP C
- Urine culture
- Systolic blood pressure
- Imaging
- Infectious disease testing
- EG test Novel biomarkers
- CVP
- Renal biopsy
## IRIS AKI STAGING CRITERIA

<table>
<thead>
<tr>
<th>AKI Stage</th>
<th>Serum creatinine (mg/dL)</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>&lt;1.6</td>
<td>Evidence of renal injury nonazotemic increase in creatinine; &gt;0.3mg/dL in 48hrs</td>
</tr>
<tr>
<td>Stage II</td>
<td>1.7-2.5</td>
<td>Mild AKI—evidence of AKI and mild static or progressive azotemia</td>
</tr>
<tr>
<td>Stage III</td>
<td>2.6-5.0</td>
<td>Moderate to severe AKI: documented AKI and increasing severities of azotemia and functional renal failure</td>
</tr>
<tr>
<td>Stage IV</td>
<td>5.1-10.0</td>
<td></td>
</tr>
<tr>
<td>Stage V</td>
<td>&gt;10.0</td>
<td></td>
</tr>
</tbody>
</table>

Sub stages would include (NO) for nonoliguric and (O) for oliguric and on the basis of the need for RRT.
TREATMENT

Antidote

• 4-methylpyrazole or ethanol for EG
  • Very short window of opportunity to intervene (5-8 hrs dogs, 3 cats)

Fluid therapy

• Replace dehydration deficit, ongoing losses, maintenance
• Correct acid/base and electrolyte abnormalities
• Avoid fluid overload—associated with poor prognosis
• Enteral water
  • NE or E tube
• Consider maintenance fluids after rehydration with replacement fluids
  • 0.45% NaCl + 2.5% dextrose
**ADDITIONAL TREATMENT**

### Antacids:
- Famotidine 0.5mg/kg IV BID
- Pantoprazole 0.7-1mg/kg IV SID-BID
- Carafate ¼-1g PO TID-QID

### Antiemetics:
- Cerenia 1mg/kg SQ
- Anzemet 0.6mg/kg IV or Ondansetron 0.1-0.5mg/kg IV BID
- Metoclopramide 0.5-2mg/kg/d CRI

### KCL supplementation
- If not oliguric/anuric—maintenance rates
- Can become profoundly hypokalemic and require supplementation at high rates
- If <3.0mEq/L give 0.5mEq/kg/hr (diluted 1:1 with saline) over 4 hours then recheck and supplement accordingly—use syringe pump

### Antibiotics
- Unasyn 22mg/kg IV TID
- Doxycycline 5mg/kg IV BID
- Fluoroquinolone
- Ideally based on UCS
**ADDITIONAL TREATMENT**

### Antihypertensives
- Indicated if BP > 160-180mmHg
- ACEi?
  - Can be deleterious in the acute setting
- Calcium channel blocker
  - Amlodipine 0.2-0.75mg/kg/d (can give rectally)
  - Hydralazine 2.5mg/cat PO, 0.5-3mg/kg PO Dog (1hr onset)

### Phosphate binders
- ALOH only if eating/with food 30-90mg/kg/d divided
- Renagel, lanthanum

### Nutrition
- Ideally enteral if can tolerate
- Place NE/NG or Etube if not voluntarily eating, avoid syringe/force feeding
- IV nutrition PRN (procalamine, TPN)

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**INTRARENAL EFFECTS OF ACE INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS**

<table>
<thead>
<tr>
<th>Untreated</th>
<th>ACE inhibitors</th>
<th>Angiotensin receptor blockers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afferent arteriole</td>
<td>Bowman's capsule</td>
<td></td>
</tr>
<tr>
<td>Glomerulus</td>
<td>Glomerulus</td>
<td>Glomerulus</td>
</tr>
<tr>
<td>Efferent arteriole</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## DRUG DOSE ALTERATIONS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Standard dose</th>
<th>Method to adjust</th>
<th>Iris stage 2 Creat 1.4-2.0</th>
<th>Iris stage 3 Creat 2.1-5.0</th>
<th>Iris stage 4 Creat &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>0.25mg/kg q 12hr</td>
<td>Dose/interval</td>
<td>0.19mg/kg q 12-24 hour</td>
<td>0.125mg/kg q 12-24hr</td>
<td>0.06mg/kg q 24hr</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>5-10mg/kg q 24hr</td>
<td>Dose/interval</td>
<td>1.25-5mg/kg q 24hr</td>
<td>1.25-5mg/kg q 24-48hr (not reco in cats)</td>
<td>0.8-3mg/kg q 24-48 hour (not reco in cats)</td>
</tr>
<tr>
<td>Reglan</td>
<td>1-2mg/kg/d CRI</td>
<td>Dose</td>
<td>1mg/kg/d CRI</td>
<td>0.5mg/kg/d CRI</td>
<td>0.25mg/kg/d CRI</td>
</tr>
<tr>
<td>Prazosin</td>
<td>1-4mg/dog q 12-24hr</td>
<td>Dose</td>
<td>None</td>
<td>1-2mg/dog q 12-24hr</td>
<td>0.75-1.5mg/dog q 12-24 hr</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>1-2mg/kg q 12hr</td>
<td>Dose/interval</td>
<td>0.5-1mg/kg q 24hr</td>
<td>0.25mg/kg q 24hr</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Tramadol</td>
<td>3-5mg/kg/q 8-12hr</td>
<td>Dose/interval</td>
<td>1-3mg/kg q 12hr</td>
<td>1-3mg/kg q 12hr</td>
<td>1-2mg/kg q 24hr</td>
</tr>
</tbody>
</table>
MONITORING

Vital signs
- Heart rate, pulses, RR, CRT
- Body temperature
- BP
- Body weight TID-QID!!

Urine output
- Often Ucath required
- Minimize CAI
- Monitor Ins/outs every 2-4 hours
- Can also weigh bedding (1gm = 1ml)

CVP Measurements
- Indirect measure of volume status
- Blood sampling
- Avoid if hemodialysis a possibility
MANAGING OLIGURIA

Assess volume/hydration status

- Physiologic
- Pathologic
  - Fluid challenge if not overhydrated, ins and outs monitoring
  - If anuric but euhydrated = insensible losses only (22ml/kg/d)
  - Avoid over hydration = poor prognosis

Medical management

- Conversion to polyuria does NOT always equal increased GFR
FOR OLIGURIA

- Mannitol
- Lasix
- Dextrose
- Diltiazem
- Dopamine?
- Fendolapam?
- Peritoneal dialysis
- Hemodialysis
FOR ANURIA

Lasix
Diltiazem
IV dextrose
Peritoneal dialysis
Hemodialysis
MANNITOL

Osmotic diuretic

Increases RBF, GFR, solute excretion

Increases osmotic tubular flow

Scavenges oxygen free radicals

Only if volume replete

- Not if overhydrated/anuric
- Hypotensive
- CHF

Dose:

- 0.25-1g/kg as a bolus over 20 minutes
- If effective UOP increases in 1 hour
- CRI can be considered at 1-2mg/kg/min—use filter, dilute 1:1 to 10% solution
- Avoid doses > 2-4gm/kg/d (can cause AKI)
LASIX

- Inhibits active Na/Cl reabsorption in distal nephron
  - Natriuresis/diuresis
  - Increases tubular flow rate
- Causes vasodilation
  - Increased renal blood flow
- Dose = 2-6mg/kg
- As a CRI = 0.25-1mg/kg/hr
  - CRI induces more reliable diuresis with lower dosing than intermittent boluses
  - Can result in hypovolemia
IV DEXTROSE

Hyperosmolar solution 20%

- Metabolized by the cells (unlike mannitol)
- Acts as an osmotic diuretic

Dose of 20%

- 2-10ml/min for 10-15 min then 1-5ml/min for total daily dose of 22-66ml/kg

Monitor for glucosuria
DILTIAZEM

MOA
- Causes pre-glomerular dilation
- Natriuresis independent of GFR

Studies
- Used in human kidney transplant patients/cyclosporine
- Used in 11 of 18 dogs with leptospirosis induced ARF with furosemide CRI
  - Rate of reduction of creatinine 1.76 times faster than for control—not ss

Dose
- 0.1-0.5mg/kg IV bolus
- Then 1-5ug/kg/min CRI until serum creatinine normal or stable
- Used conjunction with Lasix CRI, beneficial alone?
DOPAMINE

MOA
- Stimulates DA-1, DA-2, B, Alpha receptors
- Increases RBF and UOP in normal dogs, GFR unchanged
- DA-1 receptor found in cats

Humans
- No longer used in humans
- Negative effects identified

Dogs/cats
- Little to no documentation on efficacy in dogs/cats
- No longer in vogue/recommended
FENDOLOPAM

Selective DA-1 agonist
• Renoprotective in humans
• Vasodilates renal vessels

Retrospective study AKI dogs/cats
• Angell
• Administration of 0.8ug/kg/min dog and 0.5ug/kg/min cat well tolerated
• No improvement in survival to discharge, Length of hospital stay or creatinine
PERITONEAL/HEMODIALYSIS

Oliguria or anuria
Fluid overload
Hyperkalemia
Progressive azotemia
Dialyzable toxin
PEARLS OF MANAGING SPECIFIC AKI CASES
LEPTOSPIROSIS

• Spirochete
• Reservoir hosts—raccoon, voles, skunks, dogs, pigs, cattle, rats
• Leptospira interrogans (icterohaemorrhagiae, Canicola, Pomona, Bratislava, Autumnalis), Leptospira kirschneri (grippotyphosa)
• L Pomona results in more severe disease (50% survival compared to 80%)
• Common in warm/tropical areas
• Urban areas increasing in prevalence
• >20% may be chronic healthy carriers
LEPTOSPIROSIS

- Factors predisposing
  - Stagnant water, high rainfall
  - Rodent/wild-life exposure
  - Spring/fall
- Rare but is reported in cats
- Can remain viable in soil for weeks to months
- Inactivated by UV radiation/freezing
- Clinical signs same as for AKI BUT
  - Can see elevated liver enzymes, hyperbilirubinemia = big red flag
  - Thrombocytopenia seen in 58% of dogs
  - Azotemia noted in 80-90%
  - Can be coagulopathic (6-50%)
LEPTOSPIROSI S

• Testing
  • PCR—serum and urine
    • Detects antigen
    • Can be negative in urine until 7-14 days post infection, may be positive in blood
      • Can be negative with low levels of bacteremia/intermittent shedding
    • Has to be run prior to administration of antibiotics
    • Vaccination does not interfere with testing
  • Idexx Snap test
    • ELISA to detect LipL32 antibodies (IgG abi to outer membrane protein)
    • More likely to be positive at higher titers (83% agreement with MAT if titers >1:800, 64% if between 1:100-1:400)
    • Negative snap does not rule out lepto in acute phase (Just like MAT testing)
    • Vaccination can cause false positive, potentially up to a year post vaccination in 25%
LEPTOSPIROSIS

- Point of Care Zoetis test (Witness Lepto)
  - Tests anti-Leptospira IgM antibodies to canicola, grippotyphosa, icterohaemorrhagiae and pomona
  - Detects antibody 4 days post infection
  - Witness lepto greater detection of antibodies at day 7 than MAT
  - Sensitivity 93.5%, Sensitivity 98%
  - Can detect antibodies that have been generated due to vaccination within 6 months
    - Only 25% of dogs will be positive at 3 months post vaccination
  - Available April 20-27
  - Negative test does not rule out leptospirosis

- Microscopic agglutination test
  - Paired titers 2-3 weeks apart
  - 4 fold increase in titers consistent with active infection
  - Non-vaccinal serovar of >1:800
  - Antibiotics can blunt response
LEPTOSPIROSI

• Urinary catheter essential
  • Prevents contamination of hospital and zoonotic risk
  • Allows quantification of urine output closely
    • Oliguria
    • Profound polyuria

• Treatment
  • Standard therapy as for AKI
  • Unasyn @ 22mg/kg IV TID, Doxycycline 5mg/kg IV q 12hr
  • Doxycycline 5mg/kg PO BID x 2 weeks needed to resolve carrier phase
    • Usually given after 2 weeks of amoxicillin or Clavamox
  • No longer leptospiremic after 24 hours of IV antibiotics
LEPTOSPIROSIS

- Oliguria managed medically or with dialysis
- Often profound polyuria follows
- Prognosis
  - 85% survival but can require considerable supportive care
  - If polyuric can discharge on SQF if unable to afford continued care
    - Careful monitoring of hydration status still recommended
  - Chronic renal disease possible outcome with recovery
- Zoonotic disease
  - Barrier isolation—wear gloves, gown, goggles
  - Discuss risk with owners
  - Clean with bleach (10%), iodine based disinfectant, accelerated hydrogen peroxide, quaternary ammonium solutions
- Vaccination post infection?
  - Wait until recovered x 2 months
  - Vaccinate house mates
  - Environmental control
PYELONEPHRITIS

• Routes of infection
  • Ascends from the lower urinary tract
    • Breakdown in barrier for prevention of ascending infection
  • Hematogenous

• Predisposing factors
  • Urinary specific
  • Systemic illness
PYLEONEPHRITIS

- **Organisms**
  - Ecoli most common
  - Staphylococcus, Streptococcus, Enterococcus
  - Klebsiella, Pseudomonas, Enterobacter, Proteus, fungi
- **Diagnosis:**
  - Asymptomatic to critically ill/septic
  - May have renomegaly/fever—absence does not rule out
  - Blood work may be normal or show leukocytosis/AKI
  - UA (via cystocentesis or pyelocentesis)—pyuria, bacteriuria, positive culture
  - Antibiotic responsive
- **Ultrasound**
  - Kidneys may be small/chronic or enlarged
  - Echogenic material in collecting system
  - Dilation of renal pelvis/proximal ureter
    - Can also be seen with CKD, diuresis, urinary/ureteral obstruction
COMPARING ULTRASOUND IMAGES OF CKD, PYELO, URETERAL OBSTRUCTIONS

• Feline study
• Renal pelvic dilation seen in all groups
• If > 13mm attributed to UO
  • Greatest transverse pelvic diameter
    • CKD 1.7 +/- 2.6mm, Pyelo 3.2 +/- 3.1mm, UO 10.5 +/- 5.5mm
• Over lap between them all
  • 30% of normal cats had renal pelvic dilation
  • 66% of CKD cats had pelvic dilation
  • 84.6% of pyelonephritis cats had renal PD
  • 100% of ureteral obstruction cats
• Ureteral dilation
  • No normal cats
  • 6% of CKD cats
  • 46.2% of pyelonephritis cats
  • 81.8% of ureteral obstruction cats
• Get normal baseline for CKD cats so can monitor going forward
PYELONEPHRITIS

- Imaging recommended to document renal/ureteral pelvic dilation, concurrent diseases (stones, CKD etc)
  - May be useful to monitor this going forward to document treatment duration
- Culture negative pyelonephritis rare
  - Pyelocentesis necessary
  - Risks—hemorrhage, urine leakage
    - Only if clinically warranted
PYELONEPHRITIS

- Treatment/monitoring
  - Supportive as previously outlined
  - Initial empiric therapy broad spectrum
    - Unasyn/enrofloxacin
      - Careful dosing of enrofloxacin in cats if azotemic
  - De-escalate antibiotics based on culture/sensitivity
  - Perform UA 1 week into therapy and ideally repeat ultrasound after 3-4 weeks of therapy.
  - Continue antibiotics for 2 weeks beyond resolution of renal pelvic dilation if applicable
  - Usually 4-6 weeks needed
  - Repeat culture 3-5 days after discontinuation of antibiotics then at 1 month, 3 months, and 6 months
URETERAL OBSTRUCTIONS

• Technically post-renal cause for azotemia
  • Can cause kidney injury with chronicity
• Causes:
  • Stones
  • Dried blood clots, strictures (25% of cats), tumors (<5% dogs/cats)
  • Obstructive pyonephrosis
• Cats
  • >90% Calcium oxalate
  • Usually sterile
  • Do not dissolve
• Dogs
  • 50% of the time struvite 50% calcium oxalate
  • 50% of the time associated with pyelonephritis
URETERAL OBSTRUCTIONS

- Complete ureteral obstruction
  - Increase pressure in renal pelvis $\rightarrow$ reduced renal blood flow by 60% in 24 hours and 80% within 2 weeks
    - Partial obstructions may preserve renal function for a bit longer and recovery may be better than complete obstruction
    - Majority of cases are partial based on pyelography
    - GFR may normalize after several weeks post relief of obstruction if partial

- Renomegaly not sensitive to make a diagnosis of obstruction
- Imaging necessary to make diagnosis
DIAGNOSIS URETERAL OBSTRUCTION

- Preferably a combination of radiographs and ultrasound
  - Rads document stone size, number location and presence of concurrent nephroliths
  - Ultrasound—identifies hydronephrosis, hydroureter and location
  - If no stone or tumor is found, stricture
  - In a recent study 60% of cats with ureteral stricture had peri-ureteral hyperechoic tissue at the site on AUS
  - Sensitivity for rads in cats 81%, dogs 88%, and for AUS 77% in cats and 100% in dogs
  - In combination the sensitivity of both is 90% in cats
URETERAL OBSTRUCTIONS

• Systemic illness common
• Dogs often dysuric, uncommon in cats
• Most dogs have concurrent pyelonephritis and cystitis
  • 77%
• Less common to have concurrent UTI in cats (33%)
• Dogs commonly have neutrophilia and 44% have thrombocytopenia (< 40 K sometimes)
  • Sepsis, ITP
URETERAL OBSTRUCTION

• Medical management
  • Should be initiated immediately following diagnosis
  • Always attempted for 24-48 hours unless:
    • Already overhydrated, oliguric, anuric
    • Hyperkalemic
• IV fluid therapy
  • Monitor body weight, electrolytes, hydration status, ideally central venous pressures closely
  • Fluid overload common
  • Protocol used by Dr. Berent
  • Maintenance fluids at 50-60ml/kg/d with 0.45% NaCl + 2.5% dextrose + replacement fluid to correct dehydration deficit and promote diuresis (45-75ml/kg/d)
MEDICAL MANAGEMENT URETERAL OBSTRUCTION

- Mannitol
  - IV bolus at 0.25-0.5g/kg over 20-30 minutes then
  - 1mg/kg/min for 24 hours
  - Use a filter, do not use if overhydrated, cardiac compromise
  - If after 24 hours no improvement, discontinue CRI

- Alpha 2 adrenergic antagonist
  - Spasmolytic
  - Tamsulosin (alpha 1a/1d adrenergic antagonist) used to expel distal ureteral stones <5mm in people
  - Study in dogs comparing alpha adrenergic antagonists (tamsulosin, prazosin, experimental B-2/B-3 adrenergic agonists, calcium channel blocker and a phosphodiesterase inhibitor
    - Experimental b-adrenergic agonist best, tamsulosin next best
    - Prazosin had little effect and worsened ureteral spasming at high doses
URETERAL OBSTRUCTIONS

- **Amitriptyline**
  - Urinary smooth muscle relaxer mediated by opening of voltage gated potassium channels
  - Evaluated in cats with urethral obstructions
  - Extrapolated to ureteral obstructions
  - 1mg/kg PO/day, not documented to be efficacious

- **Glucagon**
  - Out of favor
  - Relaxes ureteral smooth muscle
  - Abstract showed improved urine output in oliguric cats but no short or long term benefit in ureteral obstruction
  - Side effects

- **Majority of the time medical management fails**
  - 10% success rate
INTERVENTIONAL/SURGICAL MANAGEMENT OF URETERAL OBSTRUCTIONS

• Ureteral stents—canine
• SUBs—feline
• See Dr. Garnett’s lecture
• Prognosis:
  • Dependent on chronicity of obstruction, cause, response to medical management, need for surgical intervention, timing of intervention
  • Recovery can take weeks to months
PROGNOSIS FOR AKI

Species Mortality

- Dogs—53-60%
- Cats—50%

Based on cause:

- Leptospirosis 85% survival
- 50% of cats with nephrotoxicity survive
- 75% of cats with ischemic induced AKI survived
- 40-60% of patients treated with RRT for AKI survive

Negative prognostic indicators

- Dog—Creat >10mg/dL, hypocalcemia, anemia, decreased UOP, hyperphosphatemia, comorbid disorders
- Cat—hyperkalemia, hypoalbuminemia, decreased bicarb, level of azotemia not associated with px

Long term prognosis of those that survive

- 50% of patients treated medically have CKD, 50% have complete renal recovery (d/c)