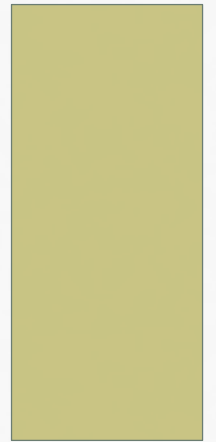


MANAGEMENT OF ACUTE KIDNEY INJURY

NICOLE GUMA, DVM, DACVECC, DACVIM (SAIM)



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 $> 0.3\text{mg/dL}$
- 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 $>2-3\text{ml/kg/hr}$
- Oliguric $<1\text{ml/kg/hr}$
- Anuric $<0.5\text{ml/kg/hr}$

Postrenal

MANIFESTATIONS OF AKI

Abnormal fluid balance

Electrolyte disorders

Metabolic acidosis

Uremic intoxication

Systemic complications

HYPERTENSION OF RENAL DISEASE

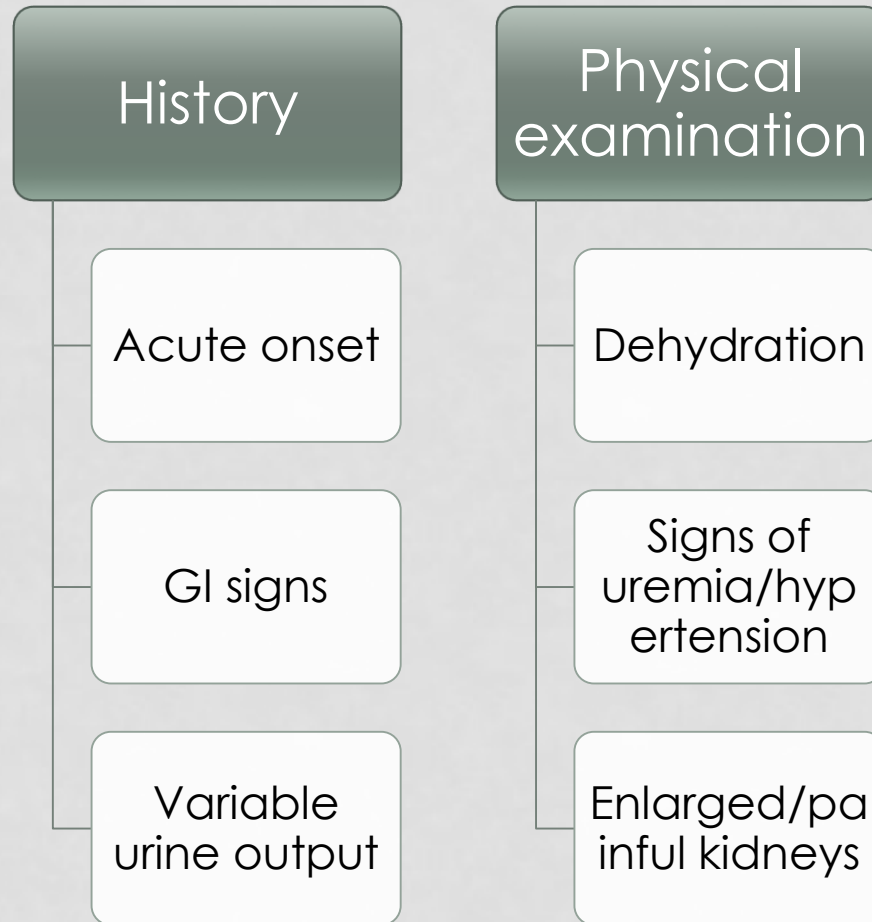
Blood pressure

- 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



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

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

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)

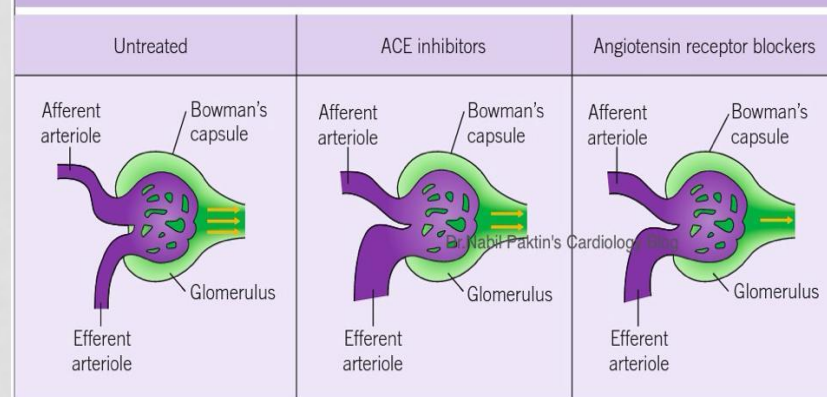
Phosphate binders

- 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)

INTRARENAL EFFECTS OF ACE INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS



DRUG DOSE ALTERATIONS

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

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



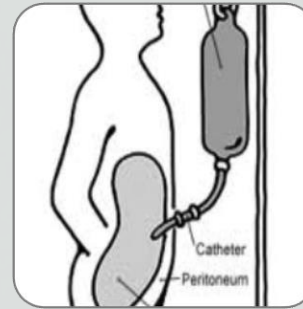
Lasix



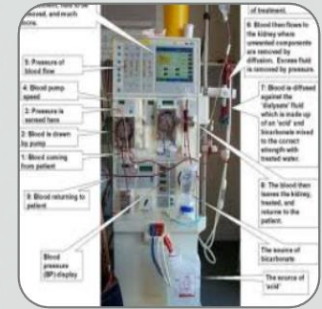
Diltiazem



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%)

LEPTOSPIROSIS

- 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, grippityphosa, icterohaemorrhagiae and pomona
 - Detects antibody 4 days post infection
 - Witness lepto greater detection of antibodies at day 7 than MAT
 - Sensitivity 93.5%, Specificity 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

LEPTOSPIROSIS

- 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 → 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)