ACUTE KIDNEY INJURY

GOLRIZ JAFARI, M.D.
ASSOCIATE CLINICAL PROFESSOR OF MEDICINE
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA
OLIVE VIEW – UCLA MEDICAL CENTER

1

DISCLOSURES

NONE

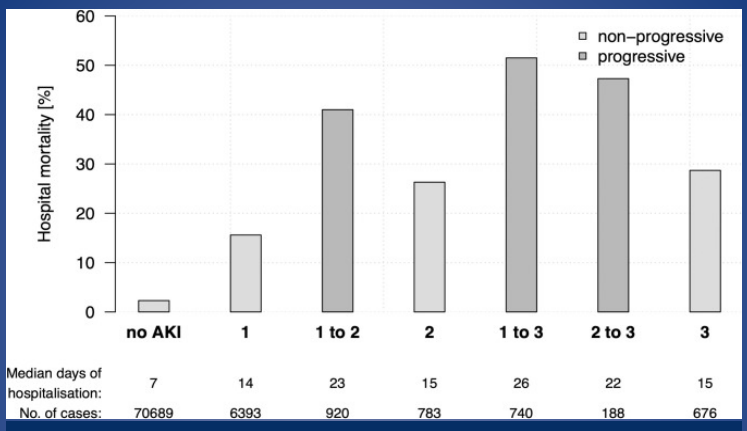
2

OBJECTIVES

- Epidemiology of Acute Kidney Injury (AKI)
- Definition and Diagnosis of AKI
- Evaluation of AKI
- Etiologies of AKI
- Management of AKI

3

EPIDEMIOLOGY

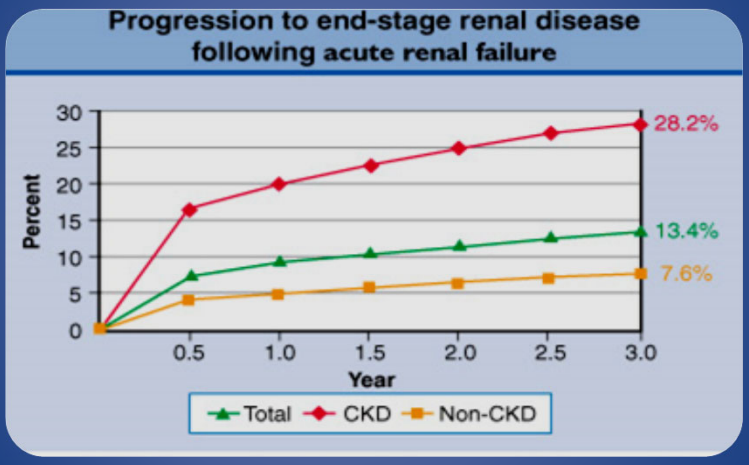


AKI incidence = 12.1%
Stage 1: 8%, Stage 2: 2%, Stage 3: 2.1%
AKI associate with higher mortality and LOS
19.1% of AKI cases showed progression of AKI
Over 50% lacked coding for AKI

Kister TS et al. (2021) Acute kidney injury and its progression in hospitalized patients. PLoS ONE 16(7)

4

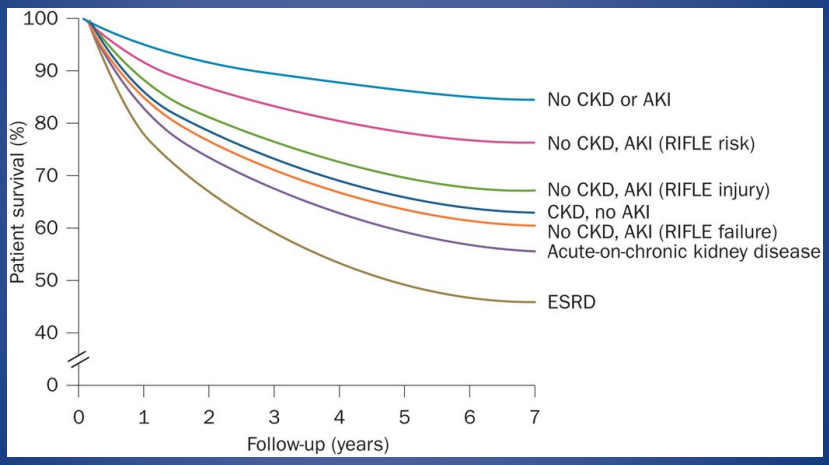
LONG TERM IMPACT OF AKI



Comprehensive Clin Nephrol Fig 64.4 (Courtesy of P. Eggers, presented at the 2004 ASN Congress)

5

LONG-TERM SURVIVAL STRATIFIED BY CKD AND AKI



*Wu, V. C. et al. Kidney Int. **80**, 1222–1230 (2011)*

6

AKI: DIAGNOSIS

7

CASE PRESENTATION

- 65-year-old male admitted with 3 weeks of increasing shortness of breath, for consideration of MVR and CABG
- History of DM type 2 x 20 years, HTN, and CAD (first MI 15 years ago)
- CKD stage 3bA3
- Known HFrEF with EF 35-30%
- 3 weeks prior to admission he developed increasing shortness of breath and was unable to walk any distance or climbs stairs. He presents to ED with SOB.
- Medications: Carvedilolol 25 mg BID, Losartan 50 mg daily, Asa 325 daily, Bumetanide 1 mg daily, Linagliptin 5 mg daily, Insulin - NPH 20qPM, Lipitor 40 mg daily

8

CASE PRESENTATION - EXAM

- Afebrile, BP 120/60, HR reg @60
- Alert and oriented x3 in no significant distress
- JVP to 15 cm
- Heart: RRR, + apical S3, III/VI holosystolic murmur at the apex
- Pulm: Decreased breath sounds at the bases with adjacent rales, speaking in full sentences, no tachypnea, no accessory muscle use
- Abdomen soft, nt, nondistended , + liver edge
- LE: femoral pulses 2+, trace edema at the ankles

9

CASE PRESENTATION: DATA

141 | 115 | 40

----------< 230 Ca: 8.6 P: 4.0 Mg: 1.6 0

4.8 | 21 | 2.5

Baseline Cr 1.6 mg/dl 1 month ago

WBC: 5.6 / Hb: 10.6 / Hct: 31.2 / Plt: 125

BNP: 850 pg/ml

Troponin: 1.06

EKG: NSR @ 84, left bundle branch block, new from '08 but unchanged from previous

Echo from < 1 month ago: LV dilated distal anteroseptal wall and apex akinetic, inferior wall contracts normally, and all other wall hypokinetic, EF 35 -40%, left atrium dilated 4.9 cm,3+ MR (TEE suggested 4+ MR)

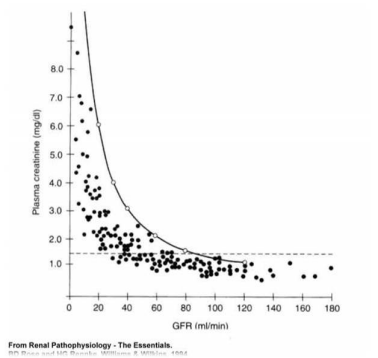
10

DEFINITION OF AKI

RIFLE Acute Dialysis Quality Initiative		AKIN Acute Kidney Injury Network	
Risk	↓GFR >25%	Stage 1	Same as Risk
	↑SCr 1.5 x baseline		Scr 1.5-1.9x Baseline
	↓UO <0.5 ml/kg/hr x 6 hours		Acute ↑Scr ≥0.3 mg/dl
Injury	↓GFR >50%	Stage 2	Same as Injury
	↑SCr 2 x baseline		Scr 2.0-2.9 x Baseline
	↓UO <0.5 ml/kg/hr x 12 hours		
Failure	↓GFR >75%	Stage 3	Same as Failure
	↑SCr 3 x baseline		
	↓UO <0.3 ml/kg/hr x 24 hours		Scr >3x Baseline Scr >4 mg/dl Acute ↑Scr >0.5 mg/dl
Loss	RRT > 4 weeks		
ESRD	RRT > 3 months		

11

CREATININE AS A BIOMARKER FOR AKI



- **Not sensitive**
  - Cellular injury without increase in creatinine
- **Not specific**
  - Increased in prerenal state
- **Delayed**
  - May lag 2-3 days
- **Unreliable**
  - Fluids can dilute
  - Muscle mass based
  - Logarithmic relationship to GFR

12

CHARACTERISTICS OF AN IDEAL BIOMARKER

- Increases in the urine or blood within minutes to hours after a renal insult
- Persistent elevation as long as the injury is present
- Correlates quantitatively with the extent of injury
- Decreases as renal recovery takes place

A Possible Option…

LMW proteins that are freely filtered at glomerulus and reabsorbed in proximal tubule therefore presence indicates PT impairment

13

BIOMARKERS TO RECOGNIZE AKI EARLIER

Proximal tubule
- Albumin
- IL-18
- GST-α (urinary)
- Clusterin
- Cystatin C (urinary)
- KIM-1
- α-1 Microglobulin
- β-2 Microglobulin
- NGAL
- HGF
- Netrin-1
- Osteopontin
- NHE-3
- Cyr61
- L-FABP
- Exosomal fetuin-A
- NAG
- RBP
- NHE-3

Glomerulus
- Albumin
- Total protein
- α-1 Microglobulin
- β-2 Microglobulin
- Cystatin C (urinary)

Loop of Henle
- Osteopontin
- NHE-3

Distal tubules
- GST-μ/π
- NGAL
- Osteopontin
- Clusterin
- H-FABP
- Calbindin D-28

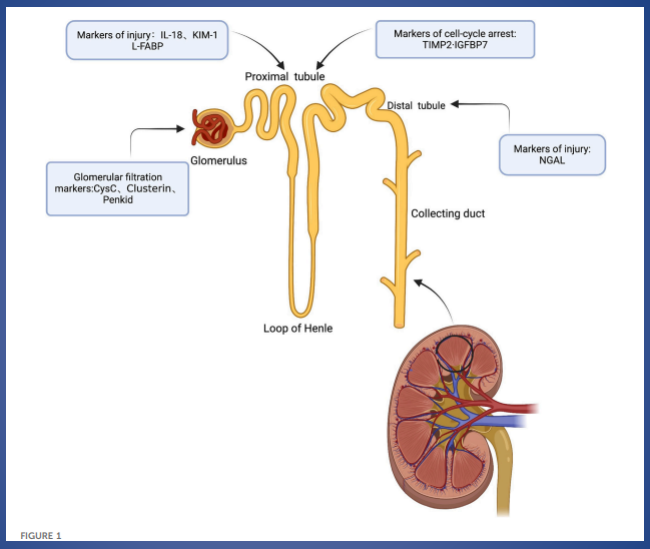
Collecting duct
- Calbindin D-28

Preinjury biomarkers
- IGFBP-7 @
- TIMP-2 @
- DKK1–4 (DKK-3)* (serum, urinary)
- Hemojuvelin (HJV) (urinary)
- Micro-RNAs (U) (urinary)
- Wnt (serum, urinary)

Others
- Cytochrome-C (urinary)
- Epidermal growth factor (urinary)
- Malondialdehyde (urinary)

Bhosale SJ, Kulkarni AP. Biomarkers in Acute Kidney Injury. Indian J Crit Care Med. 2020 Apr;24

14



Zou C, Wang C and Lu L (2022), Advances in the study of subclinical AKI biomarkers. Front. Physiol. 13:960059

15

PROPOSED NEW DEFINITIONS OF AKI

Functional criteria	Stage	Damage criteria
No change or sCr level increase <0.3 mg/dL and no UO criteria	1S	Biomarker positive
Increase of sCr level by ≥0.3 mg/dL for ≤48 h or ≥150% for ≤7 days and/or UO <0.5 mL/kg/h for >6 h	1A	Biomarker negative
	1B	Biomarker positive
Increase of sCr level by >200% and/or UO <0.5 mL/kg/h for >12 h	2A	Biomarker negative
	2B	Biomarker positive
Increase of sCr level by >300% (≥4.0 mg/dL with an acute increase of ≥0.5 mg/dL) and/or UO <0.3 mL/kg/h for >24 h or anuria for >12 h and/or acute KRT	3A	Biomarker negative
	3B	Biomarker positive

Recommendations on AKI Biomarkers From the Acute Disease Quality Initiative Consensus Conference. JAMA Network Open. 2020

16

AKI: EVALUATON

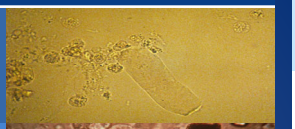
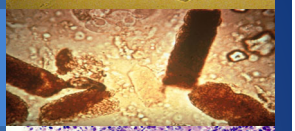
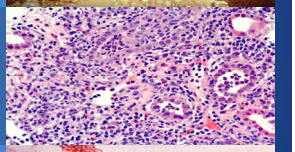
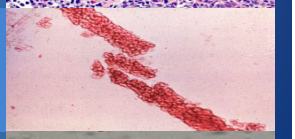
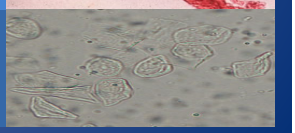
17

EVALUATION OF AKI

- **History**
  - Baseline Renal Function
  - Preexisting Medical Conditions
  - Acute events
- **Chart review**
  - Recent medications
  - Recent contrast dye studies
  - Recent hemodynamic changes, BP drops
  - Review of fluid input and output
- **Physical**
  - Volume status
  - Cardiac exam
  - Abdominal distention, bruits, mass
  - Skin: turgor, rashes
  - Foley patency

18

DIAGNOSTIC TOOLS: URINALYSIS

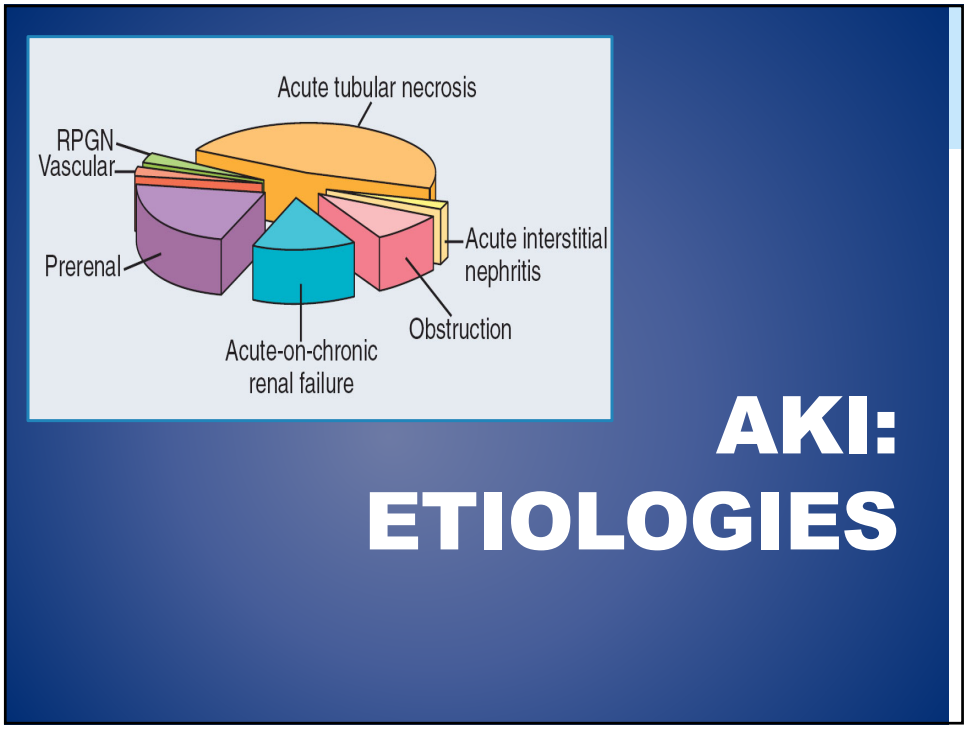
Prerenal	Bland Urine High Specific Gravity >1.015 Hyaline Casts	
ATN	Nonalbumin Proteinuria No Cells Muddy Brown Casts (Granular Casts)	
Interstitial Nephritis	Nonalbumin Proteinuria Possible WBC's & RBC's Eosinophils	
GN	Albuminuria +RBC's & WBC's RBC & WBC Casts	
Post-Renal	Bland Epithelial or Transitional Cells +/- WBC's & RBC's	

19

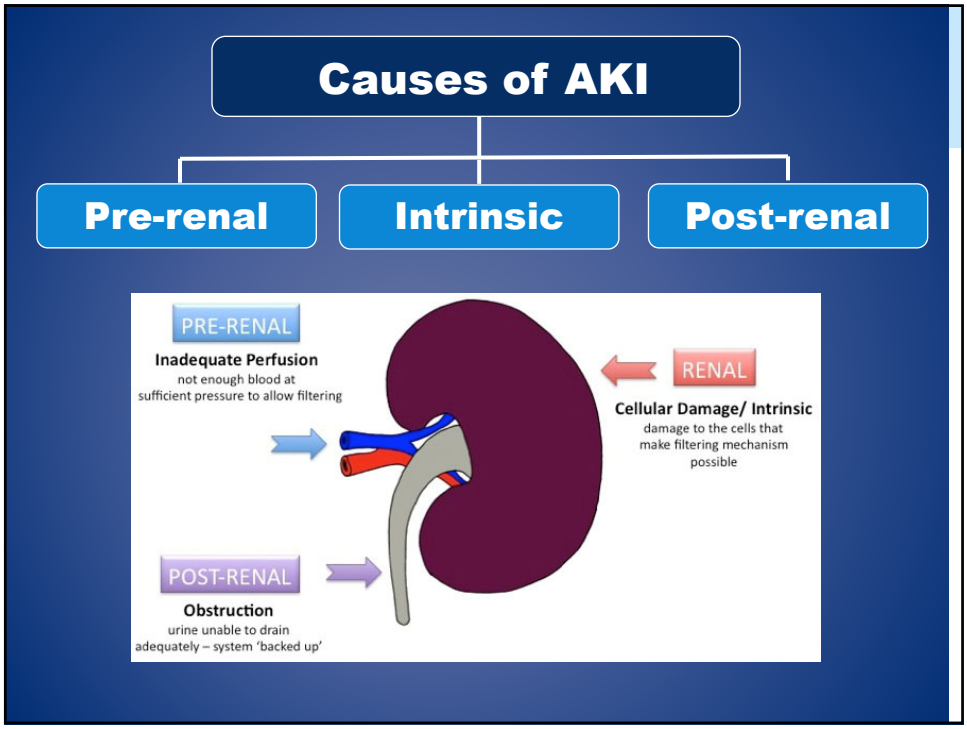
DIAGNOSTIC TOOLS: OTHER CLUES

LABS	PRERENAL	INTRINSIC	POST RENAL
FeNa	<1%	>1%	>1% May be <1
FeUrea	<35%	>35%	>35%
BUN/Cr Ratio	>20	<20	>20
Others	↑Uric Acid Metabolic Alkalosis		↑K+ Metabolic Acidosis

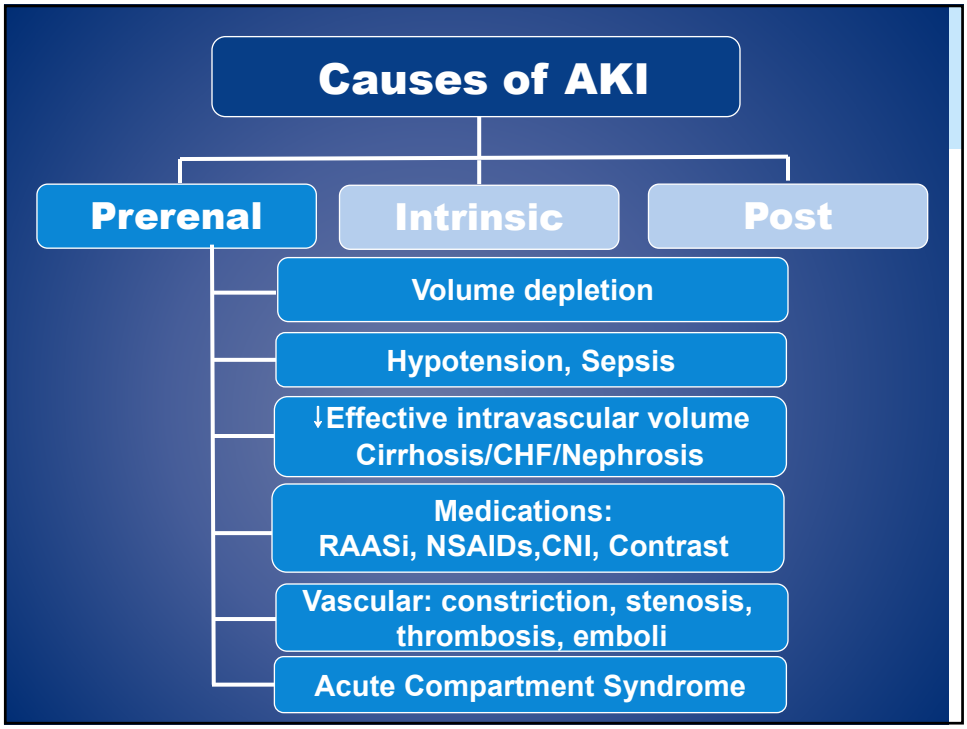
20


Acute tubular necrosis
RPGN
Vascular
Prerenal
Acute interstitial
nephritis
Obstruction
Acute-on-chronic
renal failure
AKI:
ETIOLOGIES

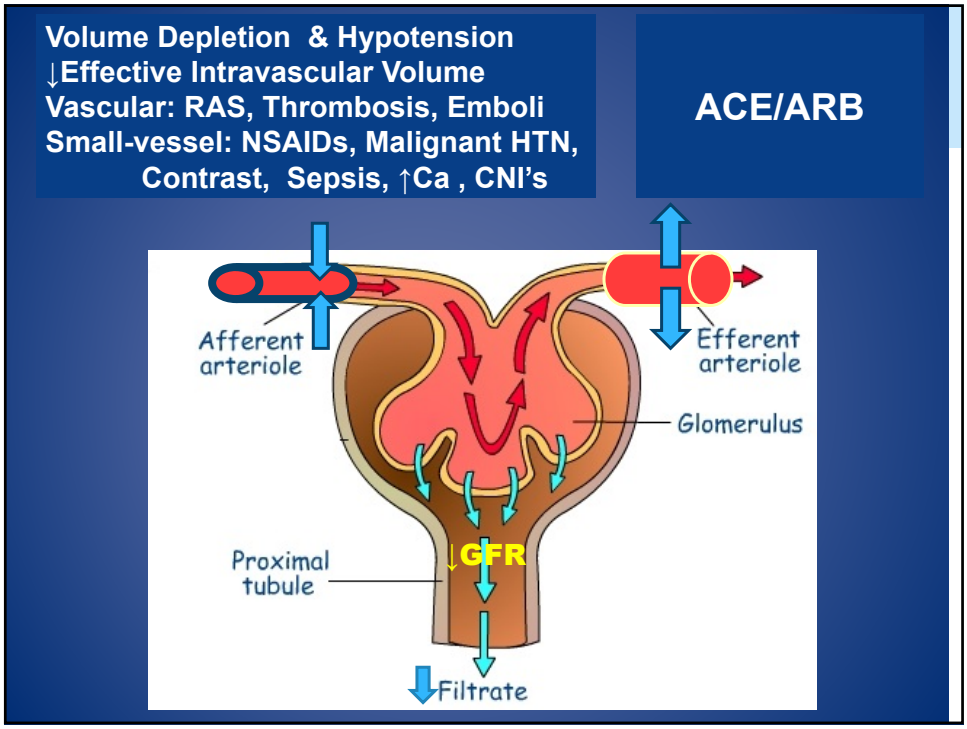
21


Causes of AKI
Pre-renal
Intrinsic
Post-renal
PRE-RENAL
Inadequate Perfusion
not enough blood at
sufficient pressure to allow filtering
RENAL
Cellular Damage/ Intrinsic
damage to the cells that
make filtering mechanism
possible
POST-RENAL
Obstruction
urine unable to drain
adequately – system 'backed up'

22

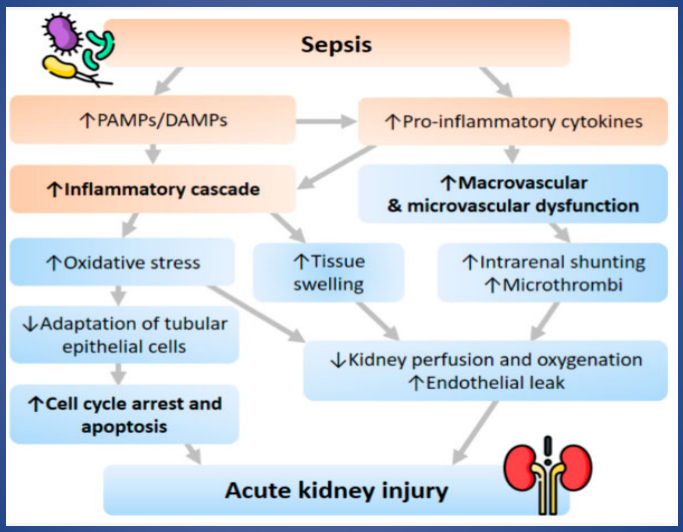

Causes of AKI
Prerenal
Intrinsic
Post
Volume depletion
Hypotension, Sepsis
↓Effective intravascular volume
Cirrhosis/CHF/Nephrosis
Medications:
RAASi, NSAIDs,CNI, Contrast
Vascular: constriction, stenosis,
thrombosis, emboli
Acute Compartment Syndrome

23


Volume Depletion & Hypotension
↓Effective Intravascular Volume
Vascular: RAS, Thrombosis, Emboli
Small-vessel: NSAIDs, Malignant HTN,
Contrast, Sepsis, ↑Ca , CNI's
ACE/ARB
Afferent arteriole
Efferent arteriole
Glomerulus
↓GFR
Proximal tubule
Filtrate

24

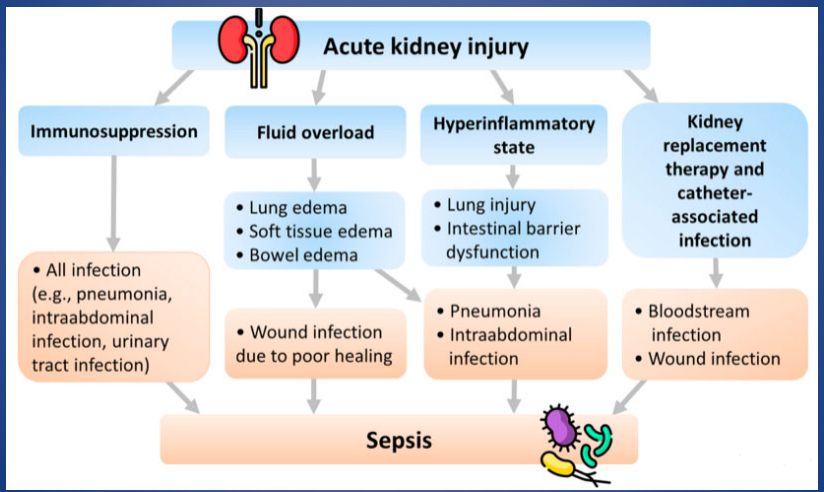
SEPSIS ASSOCIATED AKI



Chang Y et al. Sepsis and Acute Kidney Injury: A Review Focusing on the Bidirectional Interplay Int. J. Mol. Sci. 2022, 23(16), 9159

25

SEPSIS AKI SEQUELAE



26

PREVENTIVE MEASURES: PROVEN EFFICACY

Hemodynamic:

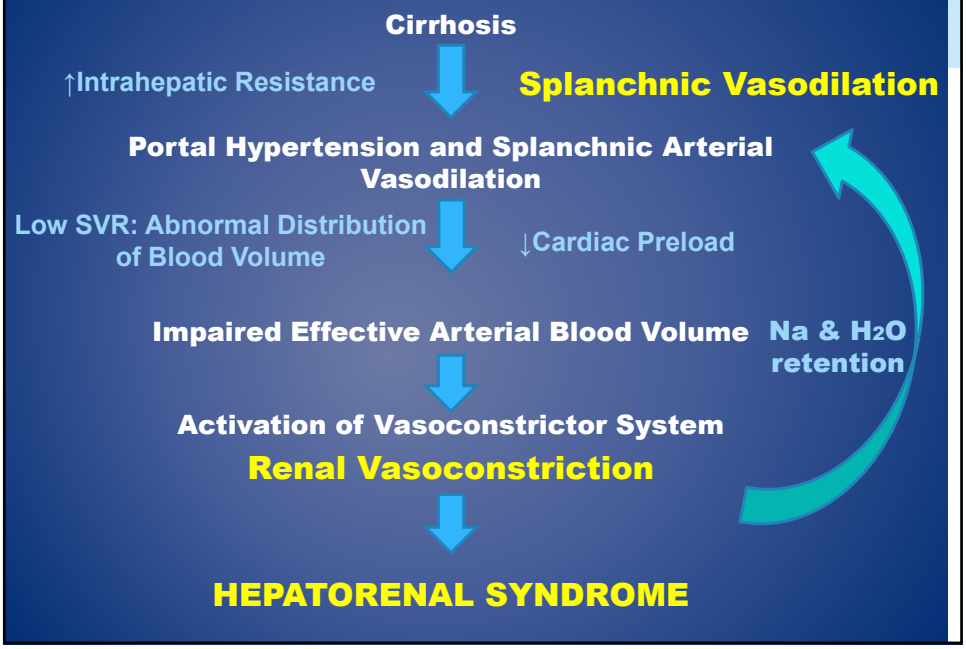
- Volume resuscitation with **Isotonic Fluids**
- Hydration: contrast, cisplatin, rhabdomyolysis and tumor lysis
- Hemodynamic Support with Pressors
- Avoid relative hypotension
- Timely Sepsis Treatment

Clinical modifications

- Avoidance of **Nephrotoxins**
- Single daily dosing of aminoglycosides
- Liposomal Amphotericin
- **Low osmolar Contrast** agents at lowest possible dose

27

HEPATORENAL SYNDROME



28

INTERNATIONAL CLUB OF ASCITES CRITERIA FOR HRS:

- Diagnosis of cirrhosis and ascites
- No response after 48 hours of diuretic withdrawal and albumin 1gm/kg volume expansion
- Absence of Shock
- No current or recent Nephrotoxins
- Absence of macroscopic kidney injury:
  - Proteinuria > 500 mg/day
  - Hematuria >50 RBC/hpf
  - No structural disease on renal US

Boyer et al: REVERSE Gastroenterology 2016

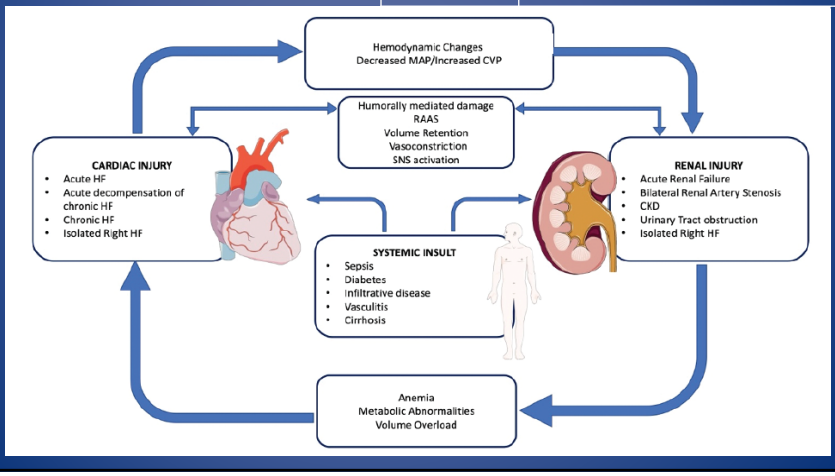
29

HRS	HRS-AKI Type 1 HRS	HRS-NAKI Type 2 AKI
Timeframe	<2 weeks	>2 weeks
Creatinine	Doubling of Scr Cr >2.5 mg/dl	Scr >1.5 mg/dl
Trigger	Acute decompensation	Diuretic resistance
Prognosis	High mortality ~2 weeks	4-6 months
Treatment	Albumin Increase MAP> 65 • Terlipressin • Midodrine Octreotide	Close monitoring Midodrine (Octreotide) Transplant

30

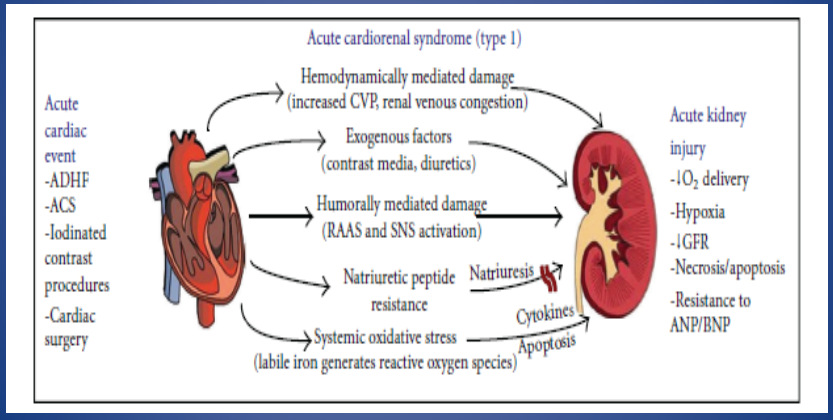
CARDIORENAL SYNDROMES

CRS 1	**AKI due to Acute HF**
CRS 2	CKD due to CHF
CRS 3	**AKI → ACS**
CRS 4	CKD → HF
CRS 5	Systemic disease→ Dual



31

CRS SUBTYPES: ACUTE CARDIORENAL SYNDROME TYPE 1



McCullough P.A. Int J Neph 2010;2011:1-10.

32

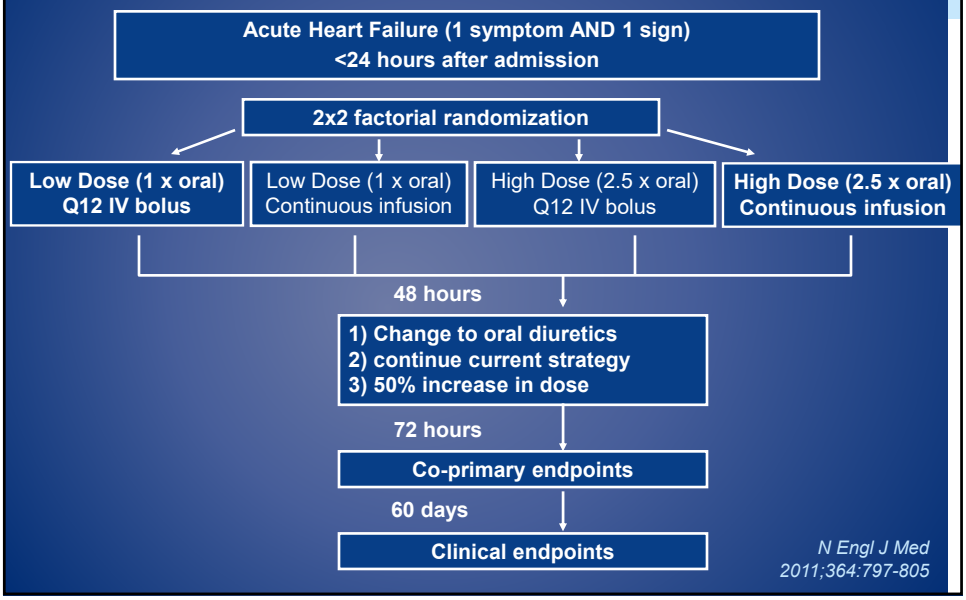
CRS TYPE 1 TREATMENT

- **Mainstay of therapy for CRS1 = diuretics and afterload reduction in order to optimize preload and afterload.**
- **Characteristics of patients with Worsening renal function (WRF) from ESCAPE Trial**
  - ↑SBP, ↑ prevalence of HTN
  - ↑suspicion of ascites
  - ↑use of thiazides
  - ↑weight loss and rate of weight loss
- **Baseline renal function appeared more predictive of long-term outcomes than WRF during hospitalization.**
- **Escape Trial: IAP/PAC monitoring can guide therapy**
  - Vasodilators: nitroglycerin, nesiritide
  - Inotropic Agents: dobutamine, milrinone

Testani et al. Am J Cardiol 2010;106:1763-69

33

DOSE TRIAL: DIURETIC OPTIMIZATION STRATEGIES EVALUATION IN ACUTE HEART FAILURE

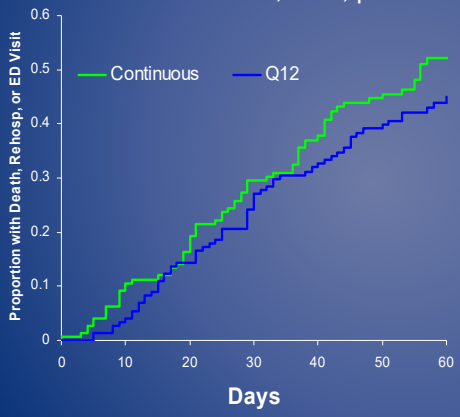


N Engl J Med 2011;364:797-805

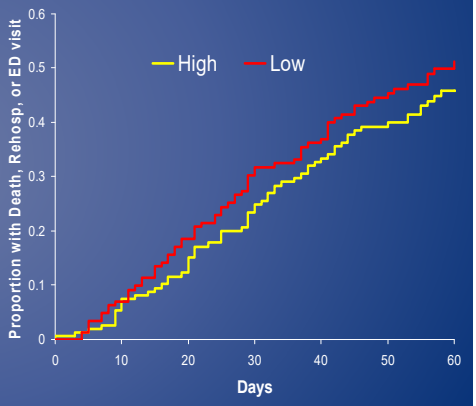
34

DEATH, REHOSPITALIZATION, OR ED VISIT

HR for Continuous vs. Q12 = 1.19
95% CI 0.86, 1.66, p = 0.30



HR for High vs. Low = 0.83
95% CI 0.60, 1.16, p = 0.28



35

CONCLUSIONS

- **Q12hr Bolus vs. Continuous Infusion**
  - There was no statistically significant difference in global symptom relief or change in renal function at 72 hours
  - There was no evidence of benefit for continuous infusion compared to Q12 hour bolus on any secondary endpoint
- **Low intensification vs. High intensification**
  - No difference in symptom relief
  - Despite transient changes in renal function, there was no evidence for higher risk of clinical events at 60 days associated with the high intensification strategy
- **High intensification (2.5 x oral dose) was associated with trends towards greater improvement in :**
  - Symptom relief (global assessment and dyspnea)
  - Weight loss and net volume loss
  - Proportion free from signs of congestion
  - Reduction in NT-proBNP

36

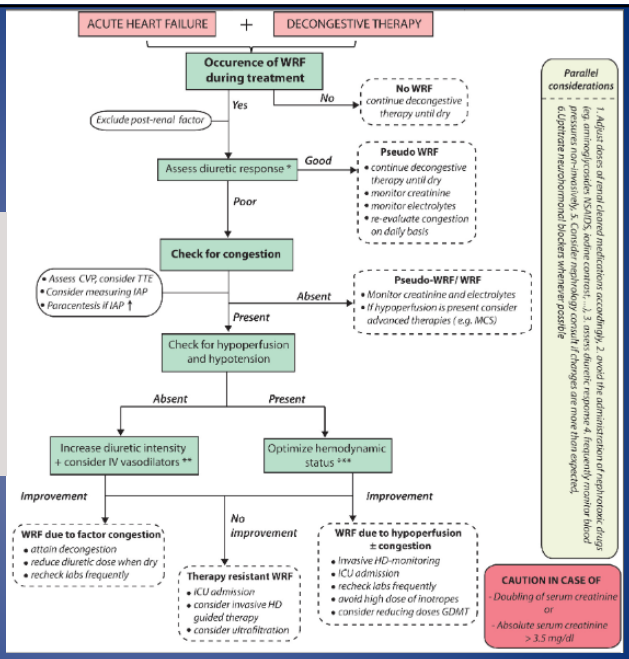
Loop diuretic response HFA-position statement

GOOD loop diuretic response if *:

a. Urinary sodium concentration > 50-70 meq/L 2-hours after diuretic

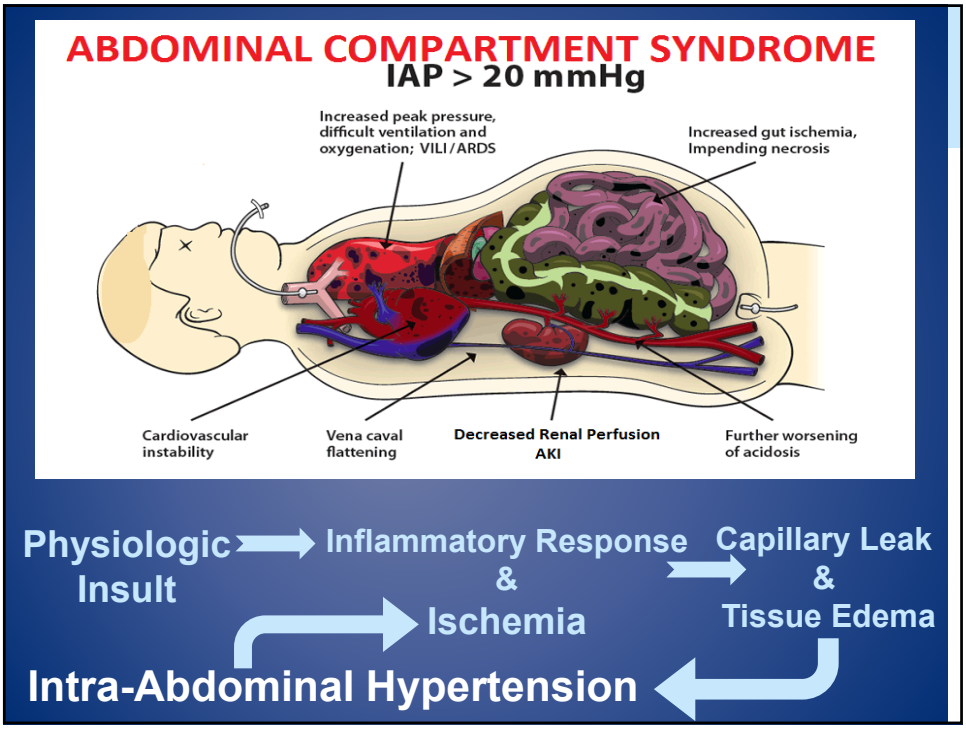
b. Urinary Output >100-150 ml/hour during first 6-hours after diuretic

c. Total diuresis > 3-4 L first 24hours



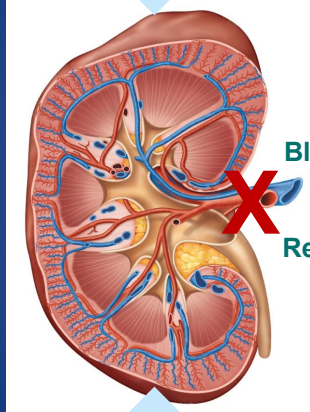
Mullens W et al. Evaluation of kidney function throughout the heart failure trajectory – a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2020

37



38

ABDOMINAL COMPARTMENT SYNDROME



Blood Flow to the Kidneys
&
Renal Congestion and Edema

- Compression of renal veins and IVC
- Reduced cardiac output to kidneys
- Reduced Renal Perfusion

Prerenal AKI

39

HOW COMMON IS INTRA-ABDOMINAL HYPERTENSION & ABDOMINAL COMPARTMENT SYNDROME?

Abdominal pressure	Total Prevalence	MICU Prevalence	SICU Prevalence
IAP>12 *Intra-abdominal Hypertension*	**58.8%**	**54.4%**	**65%**
IAP > 15	**28.9%**	**29.8%**	**27.5%**
IAP > 20 *Acute Compartment Syndrome*	**8.2%**	**10.5%**	**5.0%**

Malbrain, Intensive Care Medicine (2004)

40

ABDOMINAL COMPARTMENT SYNDROME: TREATMENT

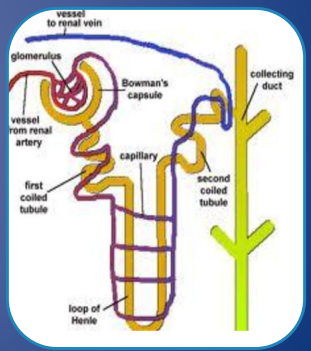
- **Optimize abdominal perfusion pressure**
  - Supine body
  - Sedation
- **Evacuate abdominal contents**
  - Paracentesis
  - Abscess & Hematoma drainage
  - NG suction, Rectal decompression
- **Fluid Management**
  - Colloids instead of crystalloids
  - Diuretics
  - HD/UF
- **Maintain abdominal perfusion pressure**
- **DECOMPRESSIVE LAPAROTOMY**

41

Causes of AKI

Pre-renal | **Intrinsic** | **Post-renal**

- **ATN:** Prerenal, Sepsis, Nephrotoxic
- **Acute Interstitial Nephritis:** Allergic, Infectious, Autoimmune
- **Vasculitis** Thrombotic, Embolic
- **Glomerulonephritis** RPGN



42

Causes of ATN

Ischemic

- Prolonged prerenal state
- Hypotension
- Hypovolemic
- Sepsis
- CP arrest
- CP bypass

Drug Induced

- Contrast agents
- Aminoglycosides
- Vancomycin
- Amphotericin B
- Cisplatin
- Acetaminophen

Pigment

- Hemoglobin
- Myoglobin

43

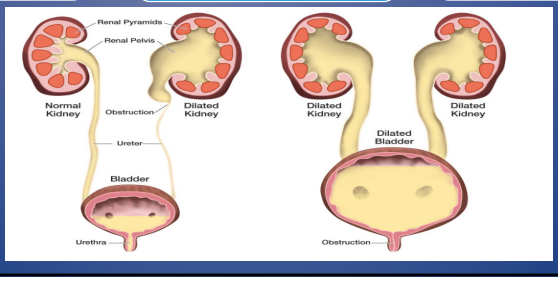
Causes of AKI

Pre

Intrinsic

Post

- **Extrinsic**
- **Inraluminal**
- **Intramural**



44

STRUCTURAL & FUNCTIONAL ETIOLOGIES OF OBSTRUCTION

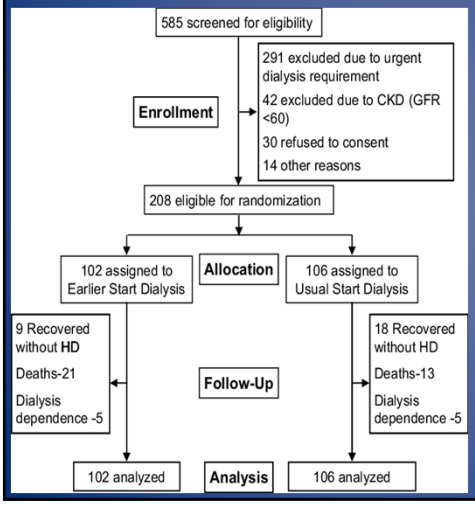
EXTRINSIC	INTRALUMINAL	INTRAMURAL
Tumor/Mass	Stones	Neurologic: DM, spinal cord injury, MS Medications: anti-cholinergics
BPH	Crystals: Uric acid in TLS	Strictures: TB, Radiation, Post-surgical
Retroperitoneal Fibrosis	Drugs: acyclovir, indinavir, MTX, sulfanamides	Schistosomiasis
Vascular	Papillary Necrosis	TCC
(Pregnancy)	Blood clots	Anti-cholinergics
	BJ proteins in MM	

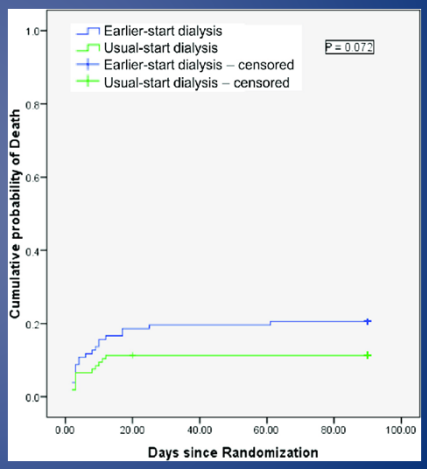
45

46

EARLY VS LATE START DIALYSIS IN AKI

Early start: BUN 70 mg/dl and/or Cr 7 mg/dl
Late Start: Fluid/Na restriction, bicarbonate therapy, diuretics, correction of hyperkalemia

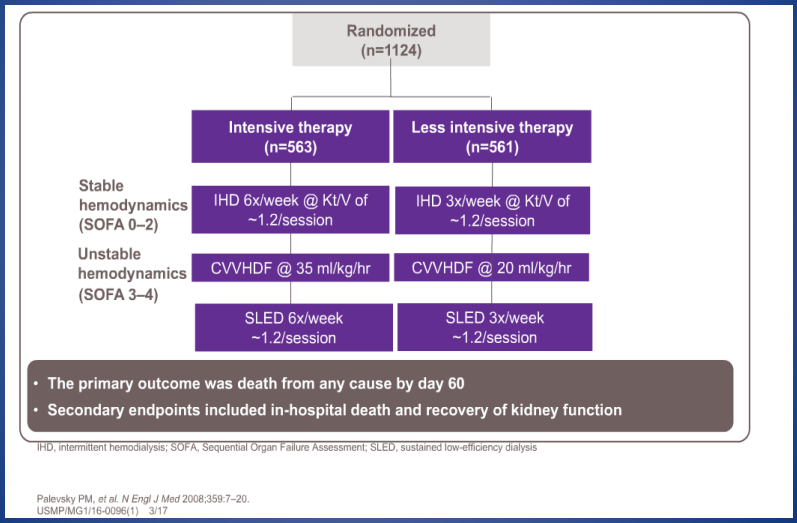




Jamale T et al. AJKD 2013

47

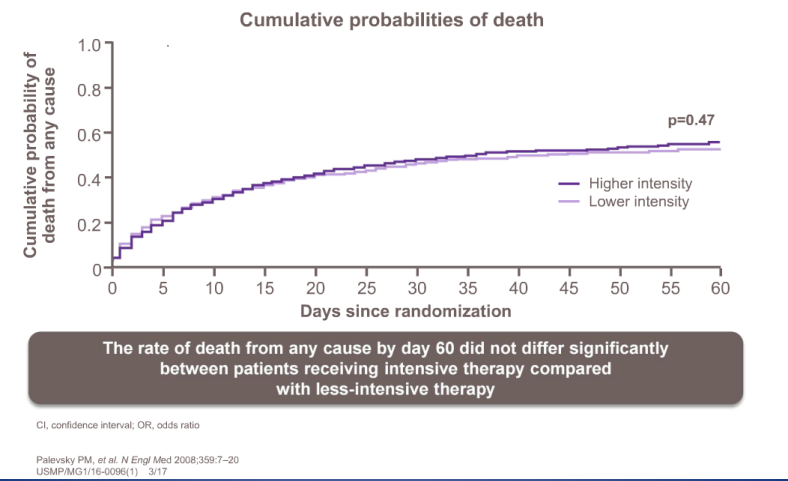
ATN TRIAL 2008



Palevsky PM, *et al. N Engl J Med* 2008;359:7–20.
USMP/MG1/16-0096(1) 3/17

48

ATN TRIAL OUTCOMES



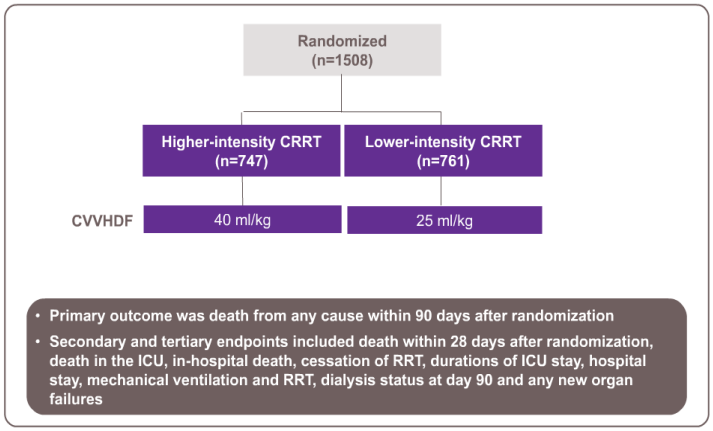
The rate of death from any cause by day 60 did not differ significantly between patients receiving intensive therapy compared with less-intensive therapy

CI, confidence interval; OR, odds ratio

Palevsky PM, *et al. N Engl Med* 2008;359:7–20
USMP/MG1/16-0096(1) 3/17

49

RENAL TRIAL 2009

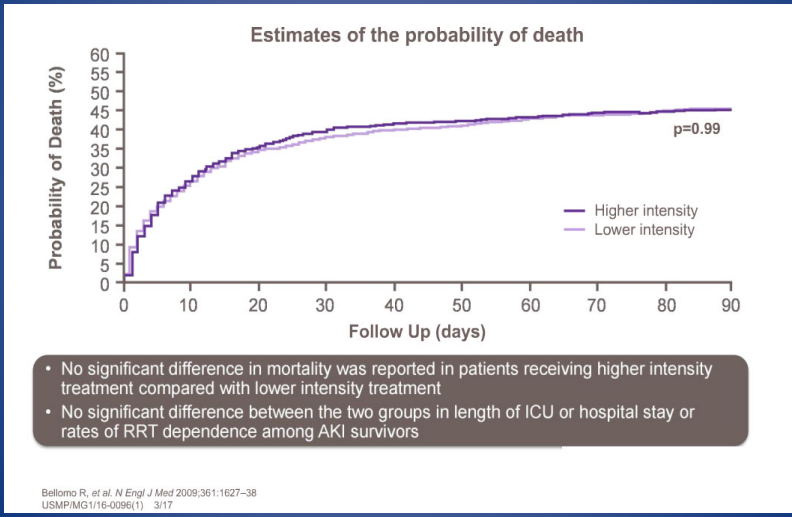


- Primary outcome was death from any cause within 90 days after randomization
- Secondary and tertiary endpoints included death within 28 days after randomization, death in the ICU, in-hospital death, cessation of RRT, durations of ICU stay, hospital stay, mechanical ventilation and RRT, dialysis status at day 90 and any new organ failures

Bellomo R, *et al. N Engl J Med* 2009;361:1627–38
USMP/MG1/16-0096(1) 3/17

50

RENAL TRIAL OUTCOMES



- No significant difference in mortality was reported in patients receiving higher intensity treatment compared with lower intensity treatment
- No significant difference between the two groups in length of ICU or hospital stay or rates of RRT dependence among AKI survivors

Bellomo R, *et al. N Engl J Med* 2009;361:1627–38
USMP/MG1/16-0096(1) 3/17

51

CASE:
65M WITH AKI DUE TO CRS TYPE 1

- **Diuretic Therapy**
  - 1-2 times home dose/24 hours
  - If naive, 20-40 mg furosemide
  - If suboptimal response: add 2nd diuretic: chlorthiazide, metolozone
- **Early Response Monitoring**
  - Strict I/O's: check UOP response after 6 hours, goal >100 ml/hr
  - Una at 2 hrs post IV diuretic, goal >50-70 meq/L
- **Close assessment of hemodynamics: HR, RR, O2, EKG, weight and signs of hypoperfusion**
- **Other: Continue GDMT, consider MRA especially if hypoK**
- **If not responsive: assess CVP, TTE, consider IAP, vasodilators or inotropic agents, Ultrafiltration/HD**

52

SUMMARY

- Early recognition of AKI, limitations of Creatinine
- Understanding individual risk factors
- Accurate evaluation and diagnosis of AKI
- Proven beneficial therapeutic options:
  - *Sepsis: Optimal fluid management, early antibiotics, hemodynamic stability*
  - *HRS: albumin, octreotide, vasopressin, midodrine, paracentesis*
  - *CRS: diuresis, close monitoring, vasodilators, inotropes*
  - *Avoid nephrotoxins*
- No benefit of early dialysis initiation or high dose of dialysis
- Follow up after AKI and appropriate transition of care

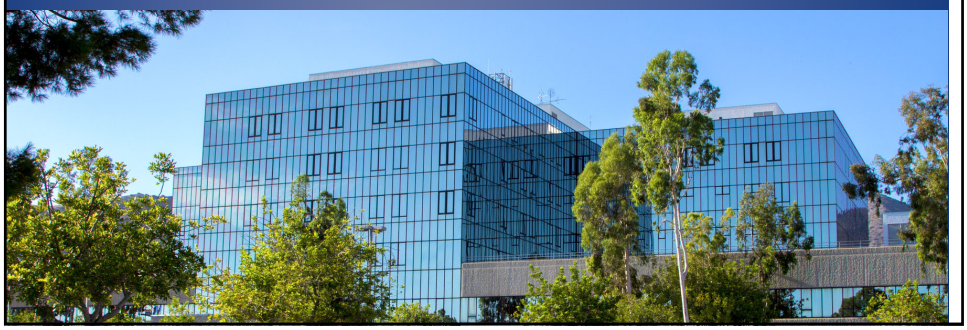
53

QUESTIONS

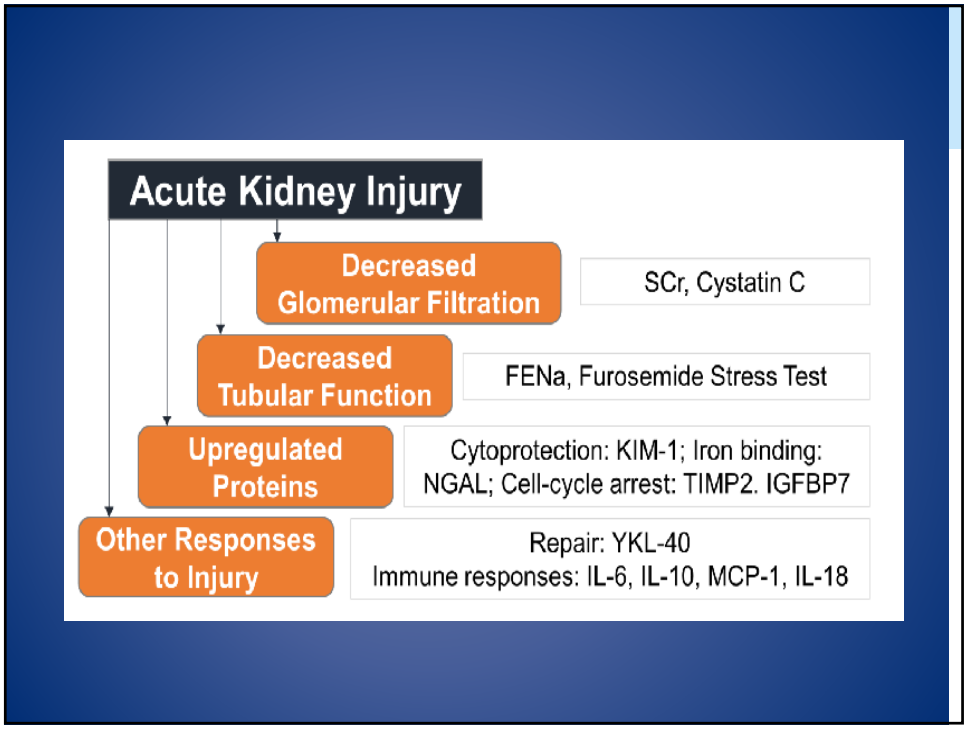
Golriz Jafari

gjafari@dhs.lacounty.gov

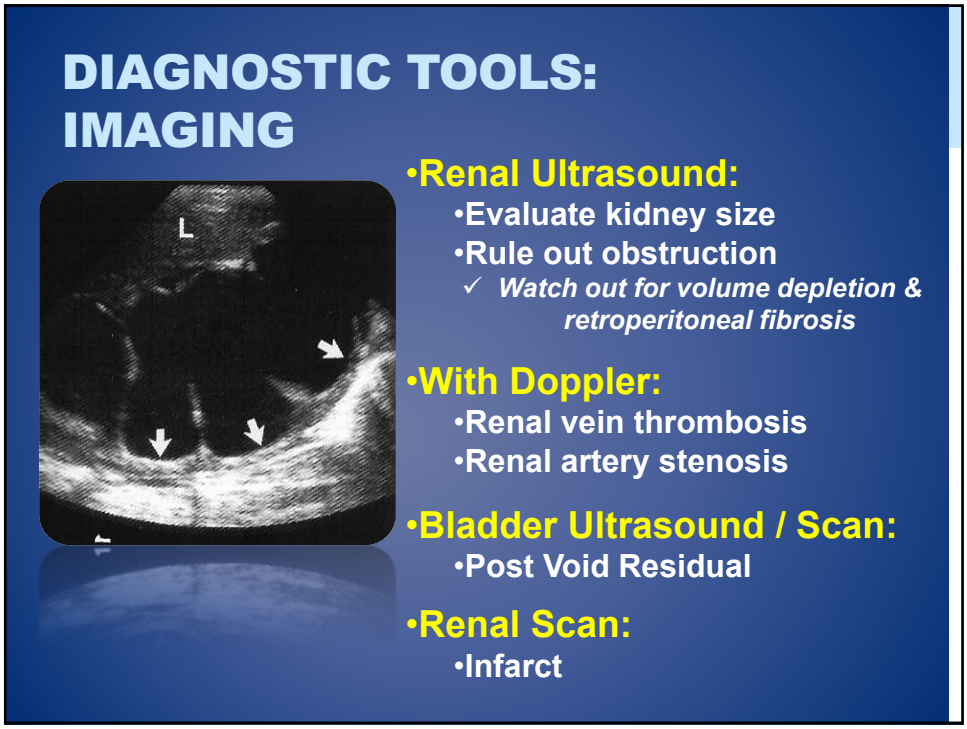
https://www.uclaoliveview.org/nephrology



54


Acute Kidney Injury
Decreased Glomerular Filtration
SCr, Cystatin C
Decreased Tubular Function
FENa, Furosemide Stress Test
Upregulated Proteins
Cytoprotection: KIM-1; Iron binding: NGAL; Cell-cycle arrest: TIMP2. IGFBP7
Other Responses to Injury
Repair: YKL-40
Immune responses: IL-6, IL-10, MCP-1, IL-18

55

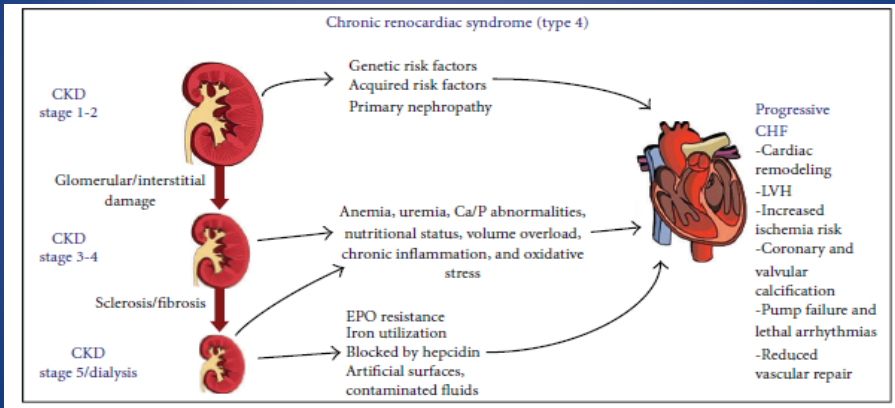

DIAGNOSTIC TOOLS: IMAGING
L
•Renal Ultrasound:
•Evaluate kidney size
•Rule out obstruction
✓ Watch out for volume depletion & retroperitoneal fibrosis
•With Doppler:
•Renal vein thrombosis
•Renal artery stenosis
•Bladder Ultrasound / Scan:
•Post Void Residual
•Renal Scan:
•Infarct

56

AKI EVALUATION	ACUTE	CHRONIC
History	Acute onset	Malaise Vague
Hemoglobin	Normal	Low
Potassium	High	Normal-High
Calcium	Normal	Low
Urinalysis	Active sediment: WBC's, RBC's, Casts	Bland Hyaline/Broad/Waxy Casts
Osteopenia	No	Yes
Kidney Size (Imaging)	Normal	Small-Normal

57

CRS SUBTYPES: CHRONIC RENOCARDIAC SYNDROME TYPE 4



McCullough P.A. Int J Neph 2010;2011:1-10.

58

PRIMARY ENDPOINTS

Efficacy

-Patient Global Assessment over 72 hours

Safety

-Change in SCr from baseline to 72 hours

59

SECONDARY ENDPOINTS

Change in weight over 24, 48, 72, 96 hours

Freedom from signs and symptoms of congestion at 72 hours

Change in SCr and weight at 72 hours

Dyspnea over 24, 48 and 72 hours

Change in SCr at 24, 48, 96 hrs, day 7 (or discharge), and day 60

Change in cystatin C at 72 hours, day 7 (or discharge) and day 60

Persistent or worsening heart failure

Development of worsening renal function (increase in SCr > 0.3 mg/dL at any time during initial 72 hours)

Treatment failure (persistent HF, worsening renal failure, or death)

Index hospitalization length of stay

Death, rehospitalization, or ED visit w/i 60 days

60

INCLUSION-EXCLUSION CRITERIA

INCLUSION (≥18 years old)

Prior clinical dx of HF w/ daily home loop diuretic x ≥ 1mo
Daily oral furosemide ≥ 80 mg & ≤240 mg (or equivalent)
Identified within 24 h of admission
HF defined by ≥ 1 symptom & 1 sign
Anticipated need for IV loop diuretics x ≥ 48 h

EXCLUSION

Received or planned IV vasoactive treatment (inotropes, vasodilators) or ultra-filtration for HF
SBP <90 mmHg
SCr >3.0 mg/dl at baseline or renal replacement therapy
BNP <250 ng/ml or NT-proBNP <1000 mg/ml
ACS within 4 weeks
Anticipated coronary angio/procedures using IV contrast

61

BASELINE CHARACTERISTICS (1)

Characteristic	N = 308
Age, yrs (mean, SD)	66 (14)
Male, % (N)	73% (226)
Race, % white, (N)	72% (222)
Baseline furosemide dose, mg/day, mean (SD)	131 (52)
Ejection fraction, %, mean (SD)	35 (18)
Prior HF hosp in last 12 mos, % (N)	74% (225)
Ischemic etiology, % (N)	57% (176)
Atrial fibrillation or flutter, % (N)	53% (162)
Diabetes mellitus, % (N)	51% (158)

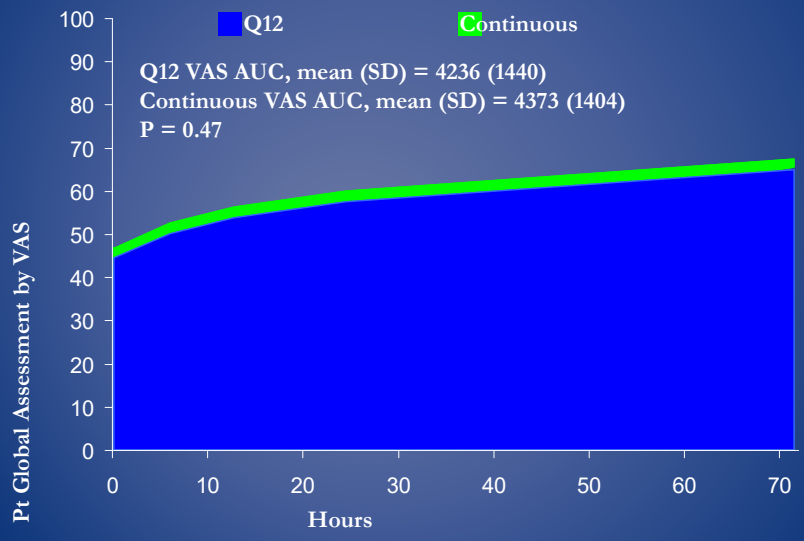
62

BASELINE CHARACTERISTICS (2)

Characteristic	N = 308
ACE or ARB, %, (N)	64% (197)
Beta blocker, % (N)	83% (256)
Aldosterone antagonist % (N)	28% (86)
Systolic blood pressure, mg, mean (SD)	119 (20)
Heart rate, beats/min, mean (SD)	78 (16)
Jugular venous pulse > 8 cm H_20, % (N)	91% (267)
Rales, % (N)	58% (178)
Sodium, mg/dL, mean (SD)	138 (4)
Creatinine, mg/dL, mean (SD)	1.6 (0.5)
NT-proBNP, pg/mL, mean (SD)	7439 (7319)

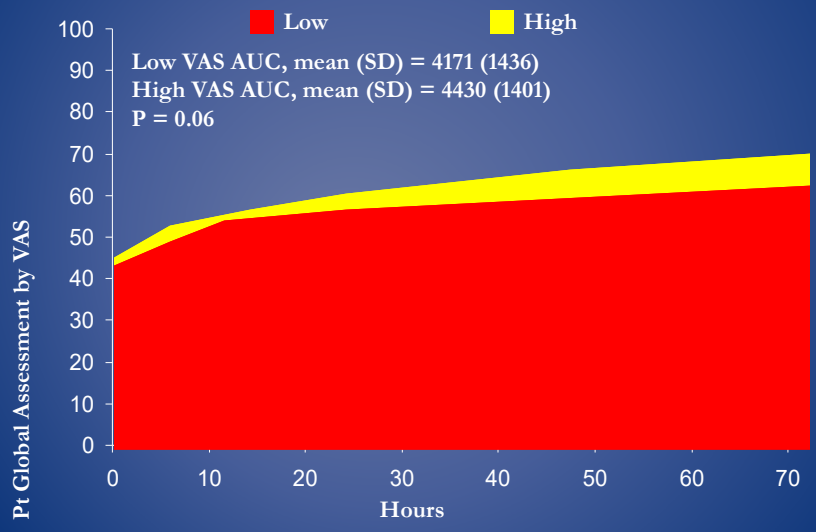
63

PATIENT GLOBAL ASSESSMENT VAS AUC: Q12 VS. CONTINUOUS



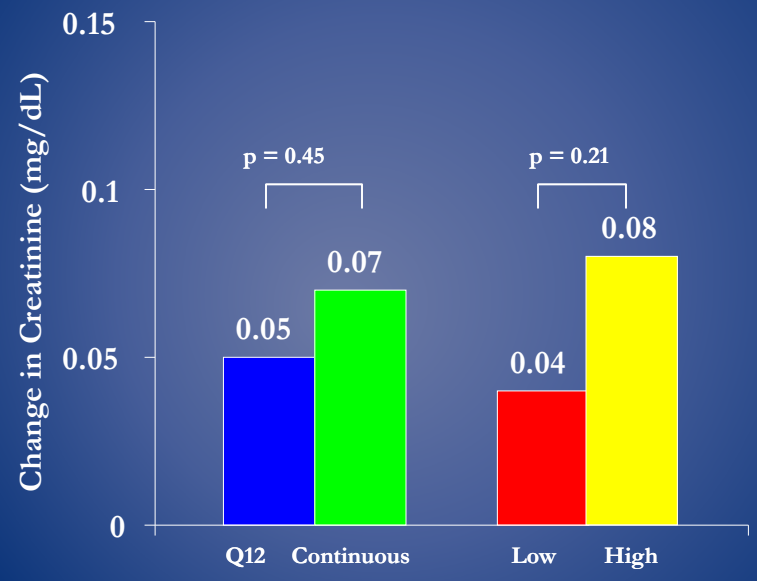
64

PATIENT GLOBAL ASSESSMENT VAS AUC: LOW VS. HIGH INTENSIFICATION



65

CHANGE IN CREATININE AT 72 HOURS



66

SECONDARY ENDPOINTS: Q12 VS. CONTINUOUS

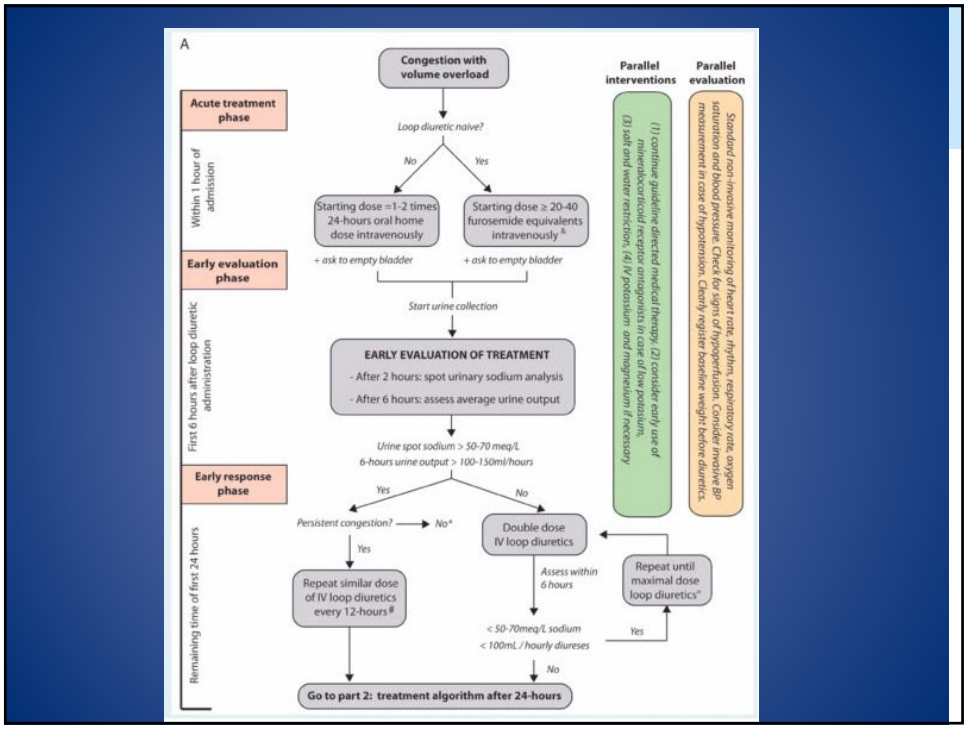
	Q12	Continuous	P value
Dyspnea at 72 hrs	4456	4699	0.36
% free from congestion at 72 hrs	14%	15%	0.78
Change in weight at 72 hrs	-6.8 lbs	-8.1 lbs	0.20
Net volume loss at 72 hrs	4237 mL	4249 mL	0.89
Change in NTproBNP at 72 hrs (pg/mL)	-1326	-1773	0.44
% treatment failure	38%	39%	0.88
% with Cr increase > 0.3 mg/dL within 72 hrs	17%	19%	0.64
Length of stay, days (median)	5	5	0.97

67

SECONDARY ENDPOINTS: LOW VS. HIGH INTENSIFICATION

	Low	High	P value
Dyspnea at 72 hours	4478	4668	0.041
% free from congestion at 72 hrs	11%	18%	0.091
Change in weight at 72 hrs	-6.1 lbs	-8.7 lbs	0.011
Net volume loss at 72 hrs	3575 mL	4899 mL	0.001
Change in NTproBNP at 72 hrs (pg/mL)	-1194	-1882	0.06
% Treatment failure	37%	40%	0.56
% with Cr increase > 0.3 mg/dL within 72 hrs	14%	23%	0.041
Length of stay, days (median)	6	5	0.55

68



69

RISK FACTORS FOR ABDOMINAL COMPARTMENT SYNDROME

Increased Capillary Leak	Fluid Resuscitation	Increased Abdominal Contents	Decreased Abdominal Wall Compliance
Sepsis	Massive IVF's	Ascites	Ventilator dyssynchrony
		Pancreatitis Peritonitis	Burns with eschars
Burns	Blood Products	Bleeding	
		Tumor	Tight abdominal wall closures
Trauma	Oliguria	Gastric distension Ileus	
		Enteral Feeding	Retroperitoneal Bleeding
		Obesity	

70

DIAGNOSTIC CRITERIA

- Signs/Symptoms: Tense abdomen, ↓Tidal volume, ↑CVP, ↓Cardiac Index, Oliguria

Measurement of intra-abdominal pressure via transduction of bladder pressure

- Intra-abdominal pressure ≥20 mm Hg
- At least one organ failure

71

CONTRAST INDUCED NEPHROPATHY: RISK FACTORS

- **Patient related:**
  - Age
  - CKD
  - DM (+ CKD)
  - Hypotension
  - CHF
  - Anemia
  - Concomitant nephrotoxins
- **Procedure-related:**
  - Increased volume contrast
  - Multiple sequential procedures
  - High osmolal contrast
  - ?Intra-arterial administration

Table 2: Contrast-Induced Nephropathy Risk Assessment Tool

Risk Factor	Points
Systolic BP <80mm Hg	5
Intra-aortic balloon pump	5
Chronic CHF	5
Age >75 years	4
Anemia (Hct <39 men, <36 women)	3
Diabetes	3
Contrast media volume	1 point per 100 cc³ of contrast used
Serum creatinine >1.5 mg/dL	4
or Est GFR 40-59 mL/min	2
or Est GFR 20-39 mL/min	4
or Est GFR <20 mL/min	6

Total Points	CIN Risk	Dialysis Risk
less than 5	7.50%	0.04%
6 to 10	14.00%	0.12%
11 to 16	26.10%	1.09%
more than 16	57.30%	12.60%

SOURCE: Adapted from Mehran R, et al..

72

PREVENTION: CONTRAST INDUCED AKI

INEFFECTIVE	UNCLEAR BENEFIT	EFFECTIVE
CCB	NAC: Inconclusive ASN 2010: Rx: 1200 mg po bid x 2 days	**IVF** **Isotonic saline or NaHCO3** **Clear dose not defined, suggested: 1 cc/kg/hr ~6 hours pre & post procedure as tolerated**
Hemofiltration	Theophylline Aminophylline	
Loop diuretics	ANP	Low contrast osmolarity
Dopamine	Statins	
Mannitol	Ascorbic acid	Lowest possible contrast dose
Fenoldopam	Stop ACE/ARB	
Hemodialysis		

Weisbord S. ASN Nov, 2010

73

ACUTE INTERSTITIAL NEPHRITIS

Drugs :

Antimicrobials: Ampicillin, Ciprofloxacin, Methicillin, PCN, Rifampicin, Sulfonamides, Clotrimoxazole, Vancomycin

NSAIDs: ASA, Fenoprofen, Ibuprofen, Indomethacin, Naproxen, Piroxicam, Tolmetin

Acid suppressors: PPI's, Cimetidine

Others: Phenytoin, Triamterene, Furosemide, Allopurinol, Phenindione

Infections:

Direct infiltration: Leptospirosis, CMV, Candidiasis, Tuberculosis

Reactive to systemic infections: Strep, Diphtheria, Hantavirus, HIV

Systemic diseases :

Metabolic diseases: Urate, Hypercalcemic and Oxalate Nephropathy

Immunologic reactions: Transplant rejection, SLE, Sarcoidosis, Cryoglobulinemia, TINU

Neoplastic diseases : Lymphoproliferative diseases

74

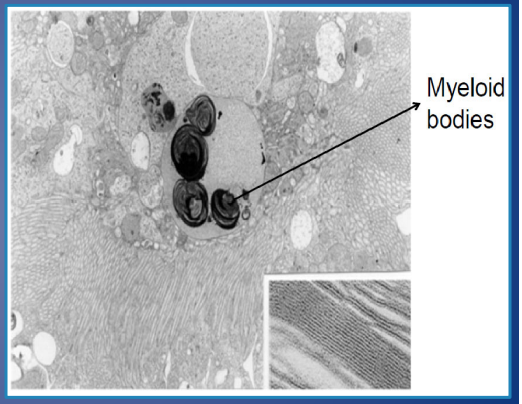
DRUG INDUCED INTERSTITIAL NEPHRITIS

TUBULAR	INTERSTITIAL	GLOMERULAR	CRYSTAL
Amino-glycosides Vancomycin Contrast	Penicillin PPI	Bisphosphonates NSAIDs Hydralazine CNI	Indinavir Acyclovir Phosphate Sulpha Ethylene Glycol
MECHANISM			
Mitochondrial Damage Tubular Toxicity	Hypersensitivity Inflammatory	Podocyte and Endothelial Cell Injury Nephrotic Syndrome TMA	Osmotic Obstructive Obstruction

75

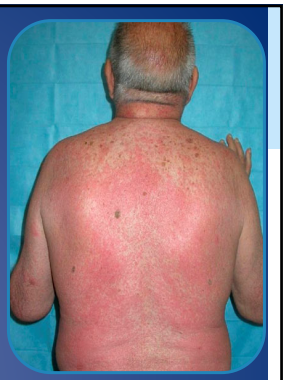
AMINOGLYCOSIDES

- Reduced GFR usually **7-10 days** after initiating treatment
- **Proximal Tubule** mitochondrial damage
- **Risk factors**:
  - Prolonged treatment
  - Hypotension
  - Volume depletions
  - Other nephrotoxins
  - CKD
  - Hypokalemia
  - Elderly
- UNa>20 meq/L, FeNA>2
- Usually reversible
- Monitor drug levels and creatinine



76

DRUG INDUCED AIN



- Usually within 3 weeks
- Not Dose Dependent
- 1/3 require dialysis
- Tubular proteinuria 1-2 gm,
- +WBC's, +RBC's, +/- Eosinophils
- Only 10% with Triad: Rash, Fever, Eos >1%
- Treatment: stop offending drug, treat underlying disease/infection, supportive care, +/- steroids

Kidney International (2010) 77, 956–961

77