AKI in Hospitalized Patients

ACOI 2017

Objectives

1. Define AKI – KDIGO Classification
2. Incidence and consequences of AKI
3. Causes of AKI and workup
4. Prevention of AKI
5. Treatment of AKI

AKI Case

67 yo woman admitted with community acquired pneumonia. She has a history of DM II, CKD Stage 3 and HTN. Her medical treatment consists of metformin and lisinopril. She has a MAP < 65 on presentation with a lactate level of 3.3 and qSOFA of 2. She is treated with 30 ml/kg isotonic fluid and appropriate antibiotics and admitted to the ICU

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Diagnostic criteria Acute Kidney Injury

An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 µmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).

Sustained – prerenal resolves over 72 hours

Definition of Acute Renal Failure

Acute Renal Failure is a decline in renal function (UO and solute clearance) which is abrupt and sustained

Abrupt – over 48 hours

Sustained – for > 24 hours

Severity – AKI Staging

Staging of AKI(KDIGO)

Stage	Serum Creatinine	Urine output
1	1.5-1.9 times baseline within 1 wk or ≥ 0.3 mg/dl increase within 48 hrs	<0.5ml/kg/h for 6-12 hrs
2	2.0-2.9 times baseline	<0.5ml/kg/h for ≥ 12 hrs
3	3.0 times baseline or increase in serum creat to ≥ 4.0 mg/dl or initiation of RRT or in patients < 18 yrs, decrease in eGFR to <35ml/min per 1.73 m^2)	<0.3ml/kg/h for ≥ 24 hrs or Anuria for ≥ 12 hrs

Potential pitfalls of AKI diagnosis based on creatinine and urine criteria

Clinical scenario	Consequence
Administration of drugs which interfere with tubular secretion of creatinine (i.e. cimetidine, trimethoprim)	Misdiagnosis of AKI (rise in serum creatinine without change in renal function)
Reduced production of creatinine (i.e. muscle wasting, liver disease, sepsis)	Delayed or missed diagnosis of AKI
Ingestion of substances which lead to increased generation of creatinine independent of renal function (i.e. creatin, cooked meat)	Misdiagnosis of AKI
Obesity	Overdiagnosis of AKI if using actual weight when applying urine output criteria
Conditions associated with physiologically increased GFR (i.e. pregnancy)	Delayed diagnosis of AKI
Interference with analytical measurement of creatinine (i.e. 5-fluorocytosine, cefoxitin, bilirubin)	Misdiagnosis and delayed diagnosis of AKI (depending on the substance)
Fluid resuscitation and overload	Delayed diagnosis of AKI (dilution of serum creatinine concentration)
Progressive CKD with gradual rise in serum creatinine	Misdiagnosis of AKI
Extrinsic creatinine administration as a buffer in medications (i.e. in dexamethasone, azasetron)	Pseudo-AKI
Oliguria due to acute temporary release of ADH (i.e. post-operatively, nausea, pain) enhanced by maximal sodium reabsorption in the setting of volume/salt depletion	Misdiagnosis of AKI

ARF AKI Staging

- The presence of AKI (even Stage 1) predicts increased mortality, LOS, hospital costs, and need for RRT
- The AKI definition is both sensitive and specific to diagnose ARF (ascertainment bias)
- The worse the stage, the worse the prognosis of the patient, longer hospital LOS, ICU LOS, higher cost and higher mortality

AKI Case

LABS:

BC grow Strep pneumonia

Creatinine: baseline 1.4

admission 1.8

day 1 2.8

Urine output 1000/24 hrs (< 0.5 ml/kg)

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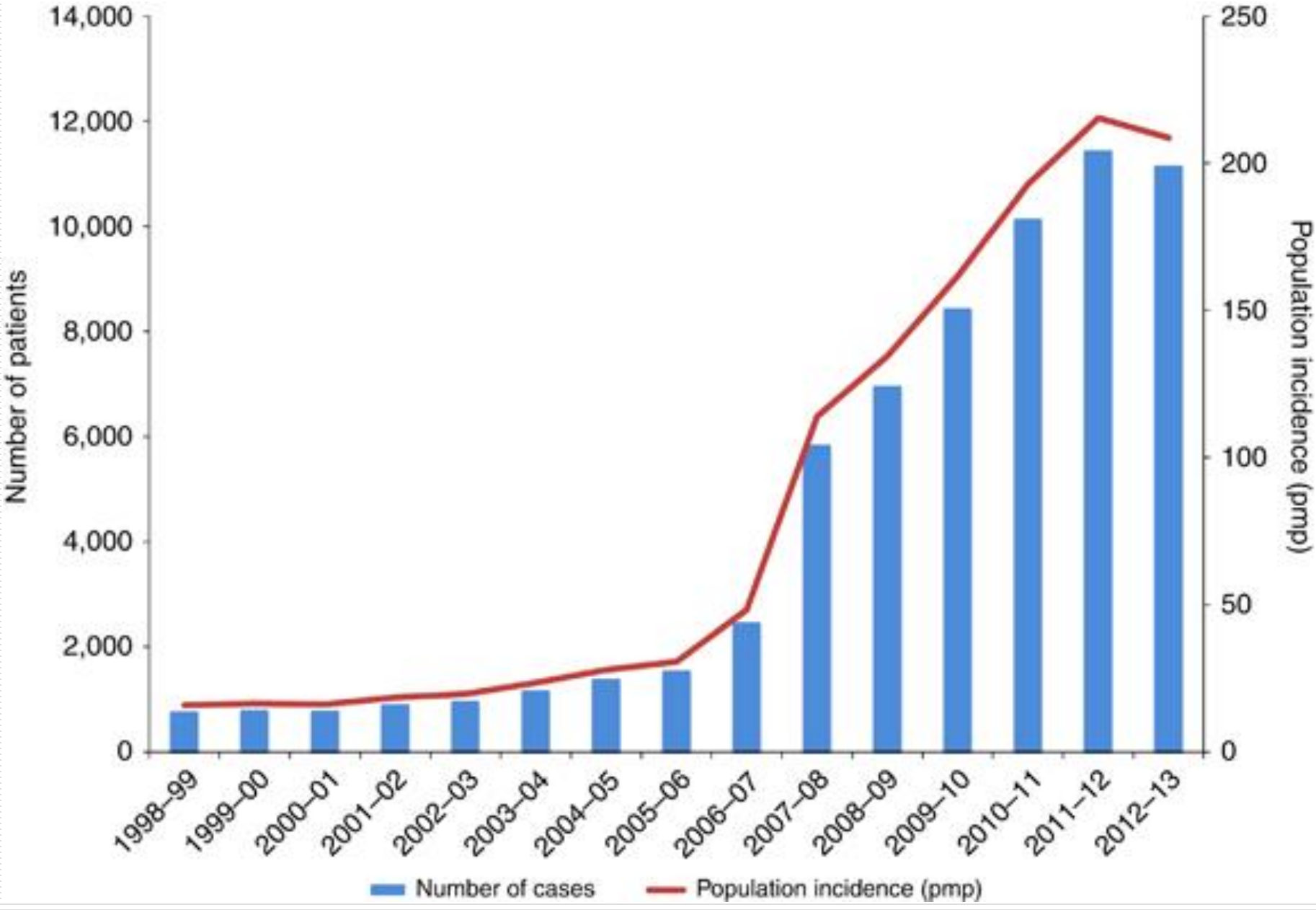
AKI Incidence

20% of hospitalized patients have AKI

50% of ICU patients have AKI

Incidence is increasing

Mortality is static at 33% for all and 50% ICU


14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
Number of patients
250
200
150
100
50
0
Population incidence (pmp)
1998–99
1999–00
2000–01
2001–02
2002–03
2003–04
2004–05
2005–06
2006–07
2007–08
2008–09
2009–10
2010–11
2011–12
2012–13
Number of cases
Population incidence (pmp)

AKI Complications - Immediate

Short term mortality 33% all and 50% ICU

Higher the AKI Stage the higher the mortality

Longer the course the higher the mortality

Patients with AKI are:

more likely to die of sepsis, develop respiratory failure and require long term and short term nursing care

ARF and Mortality – Chertow 2005

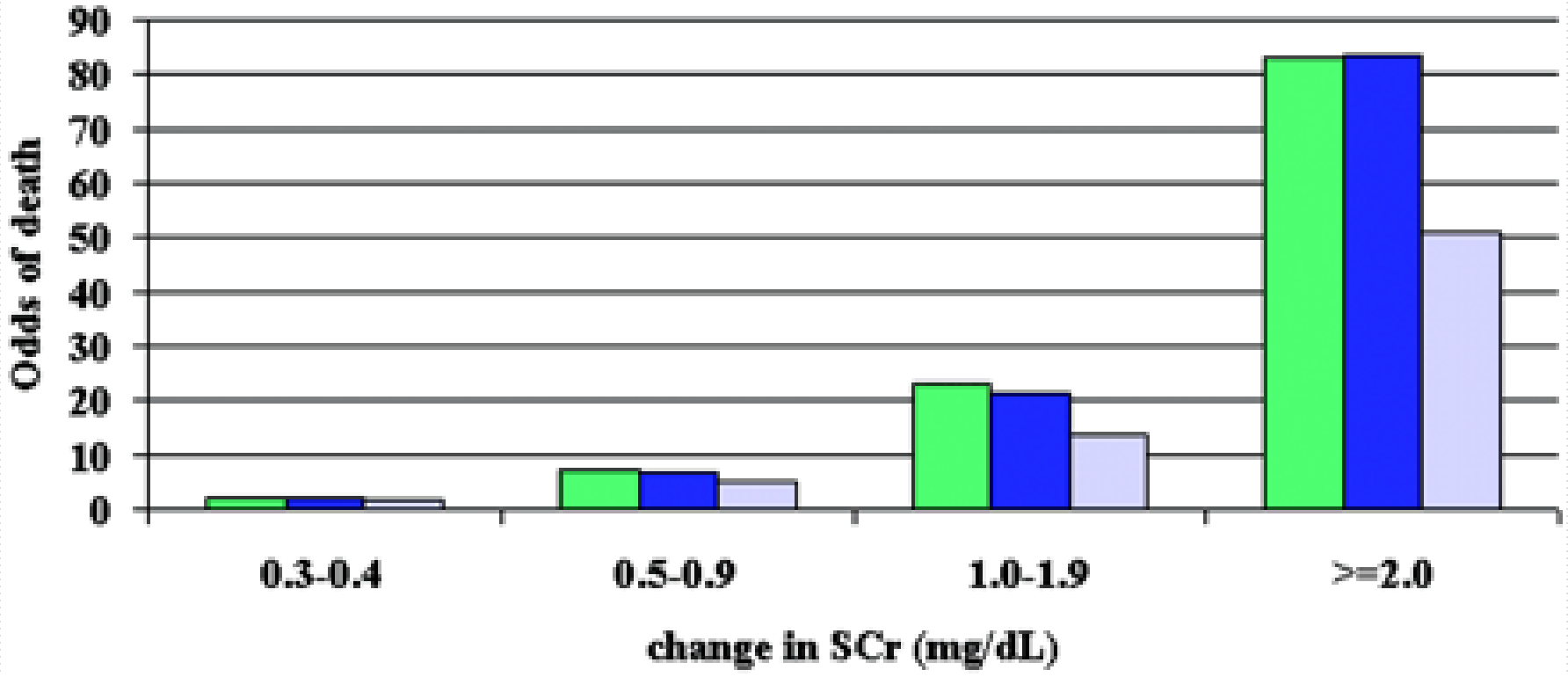


Table 15. Complications of AKI

Complication	Clinical and laboratory findings	Consequence	Treatment
Hyperkalemia	Electrocardiogram abnormalities (high T), tremor	Cardiac dysfunction, arrhythmia	Volume in combination with diuretics, β2 sympathmimetics, calcium, insulin/glucose, bicarbonate, dialysis
Volume overload	Dyspnoe, pulmonary edema, heart insufficiency, hypertension, tissue edema	Impairment of gas exchange, cardiac dysfunction, impairment of wound healing, increased risk of infection	Diuretics, dialysis
Acidosis	Increased respiration, negative base excess	Cardiac dysfunction, hypotension, increased risk of infection	Bicarbonate, dialysis
Encephalopathy/neuropathy	Dizziness, confusion, weakness, paresthesias	Prolonged duration of mechanical weaning	Dialysis
Thrombocytopathy	Bleeding, anemia	Increased blood transfusion	Dialysis
Anemia	Pale skin, decreased hemoglobin	Hemodynamic impairment, increased blood transfusion	Blood transfusion, correct iron deficiency
Decreased immune response	–	Increased risk of infection	Dialysis?
Myopathy	Decreased muscle mass	Prolonged duration of mechanical weaning	
Pleural effusion	Shortness of breath, abnormal chest exam/X-ray	Impairment of gas exchange	Dialysis

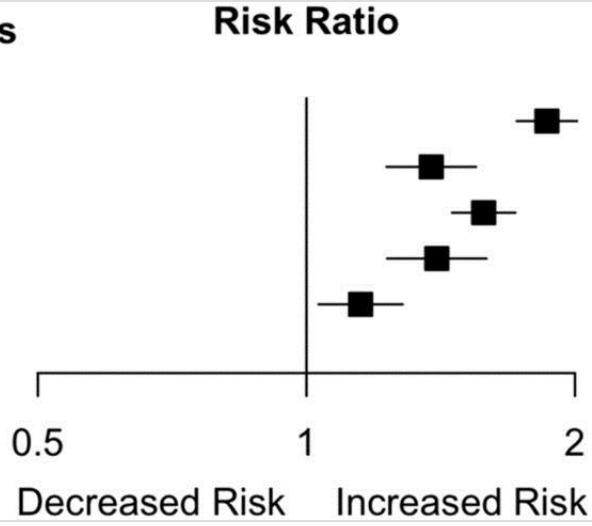
AKI Complications – Long Term

There are long term effects from AKI

- Higher total and CV mortality
- Faster progression of CKD
- Higher rates of ESRD

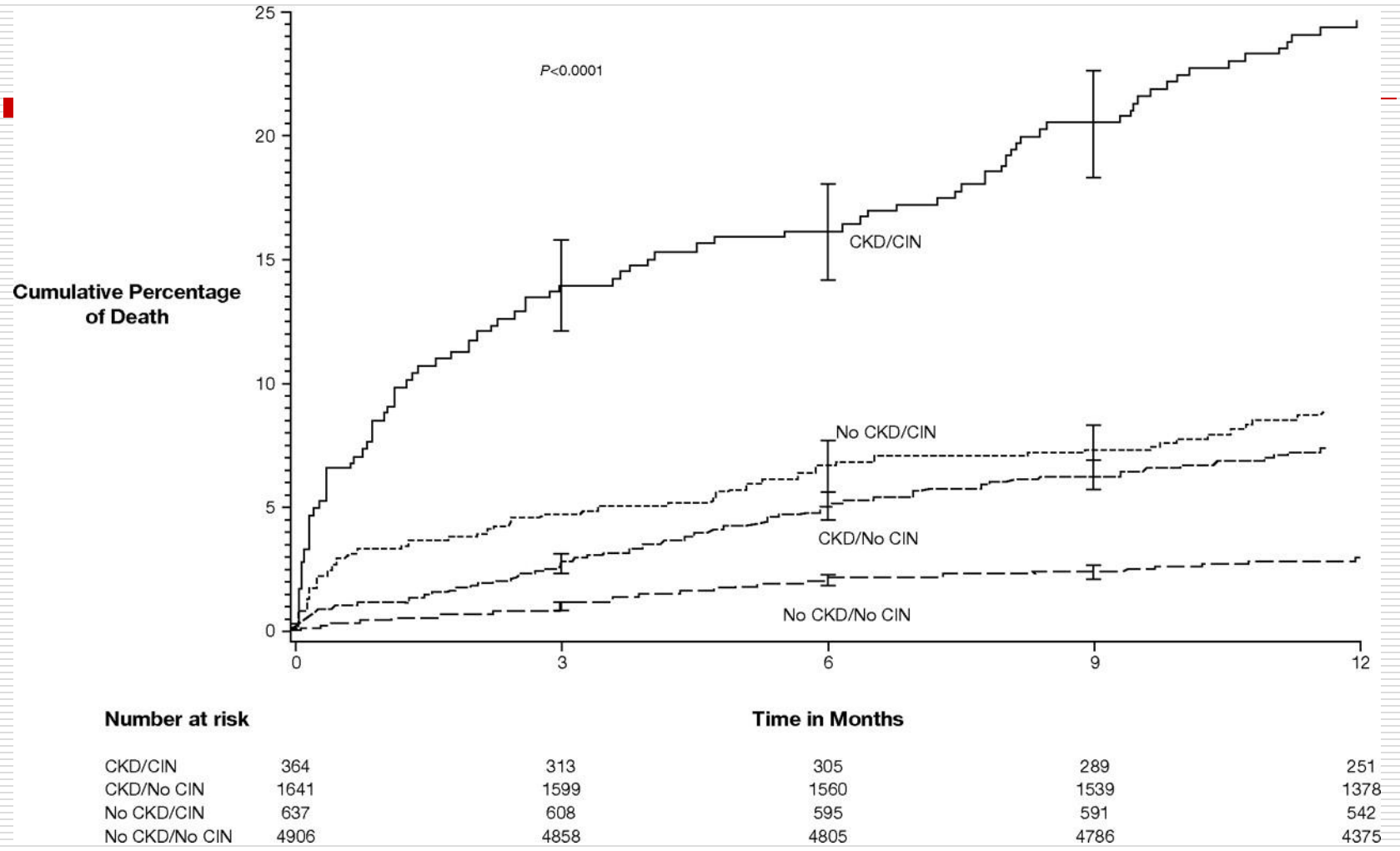
Association between AKI and cardiovascular mortality and cardiovascular events.

Study	Studies	Participants	Events	RR (95% CI)	I2 (%)
CVD Mortality	6	54641	4195	1.86 (1.72-2.01)	0
MACE	6	40489		1.38 (1.23-1.55)	47
CHF	10	90251	3866	1.58 (1.46-1.72)	10
AMI	10	90498	5057	1.40 (1.23-1.59)	43
Stroke	5	72347	1955	1.15 (1.03-1.28)	0



Ayodele Odutayo et al. JASN 2017;28:377-387

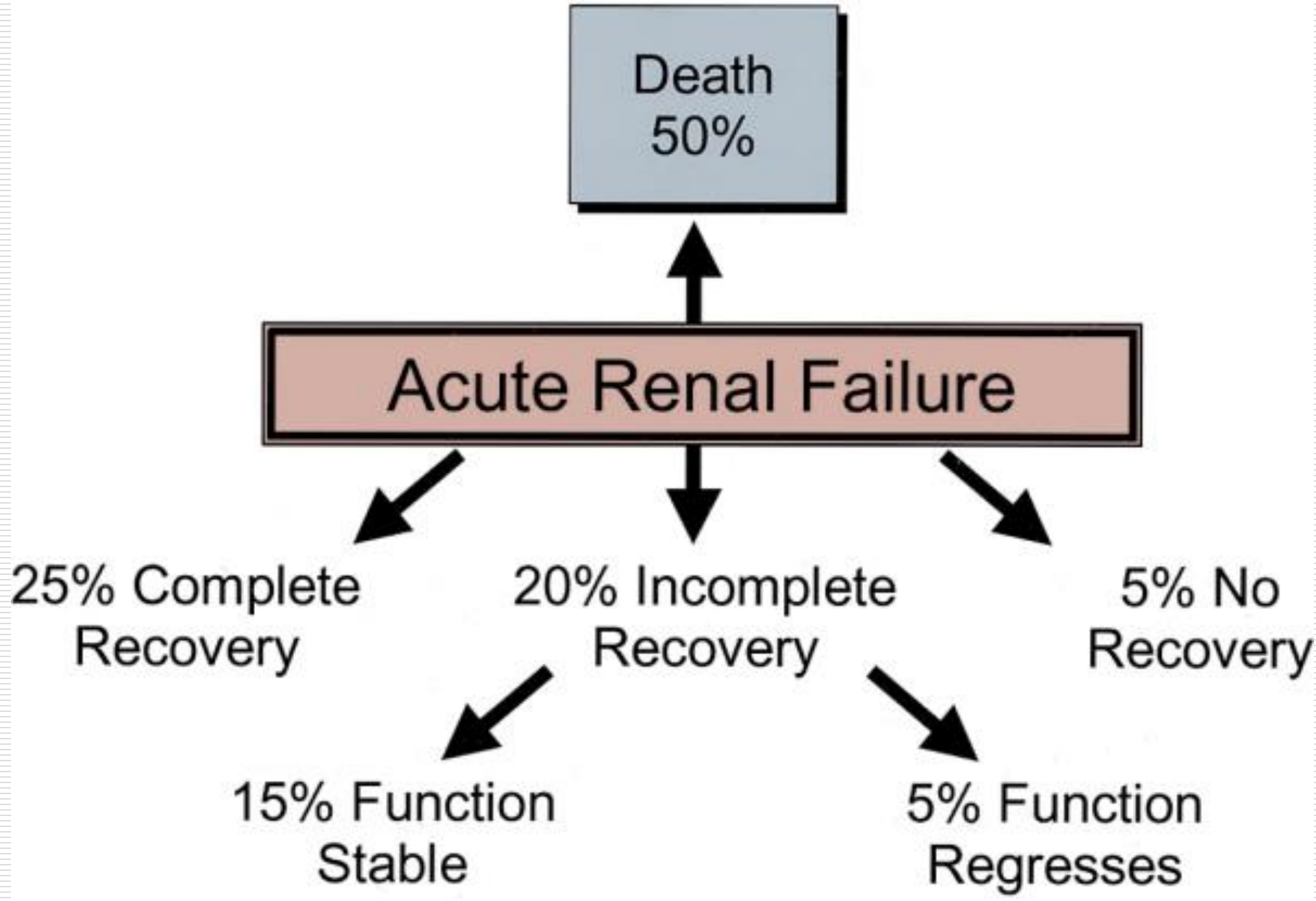
One-year survival after percutaneous coronary intervention in patients with or without CKD and with or without CIN (4).



Number at risk

CKD/CIN	364	313	305	289	251
CKD/No CIN	1641	1599	1560	1539	1378
No CKD/CIN	637	608	595	591	542
No CKD/No CIN	4906	4858	4805	4786	4375

Rudnick M , Feldman H CJASN 2008;3:263-272


Death
50%
Acute Renal Failure
25% Complete
Recovery
20% Incomplete
Recovery
5% No
Recovery
15% Function
Stable
5% Function
Regresses

AKI Case

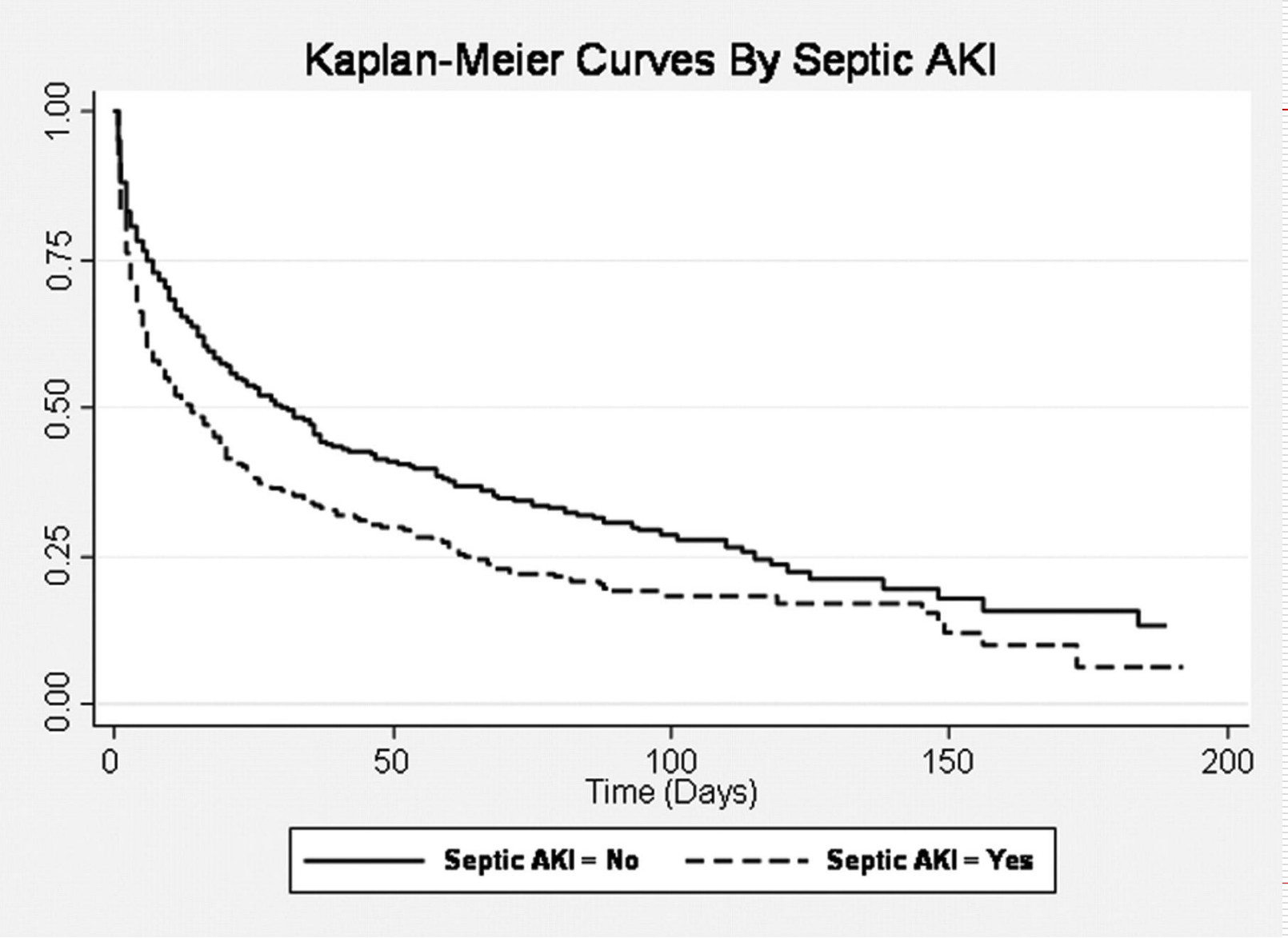
Patient developed respiratory failure requiring mechanical ventilation for 7 days and NSTEMI

Her renal function worsened but she never required dialysis

She was discharge to rehabilitation and then home.

Her GFR is 20 ml/min after 90 days

Kaplan-Meier survival estimates by septic acute kidney injury



Bagshaw, S. M. et al. Clin J Am Soc Nephrol 2007;2:431-439

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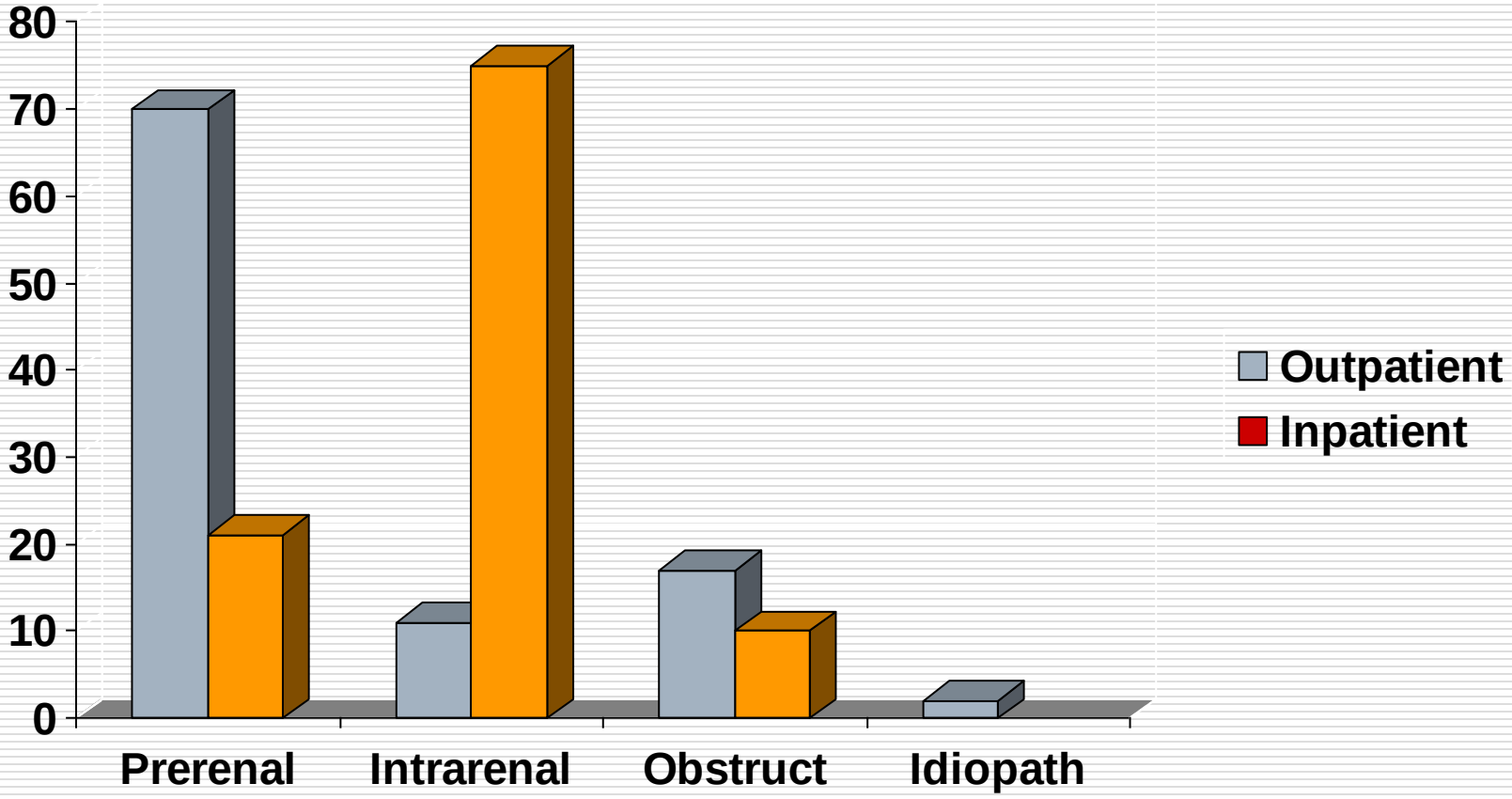
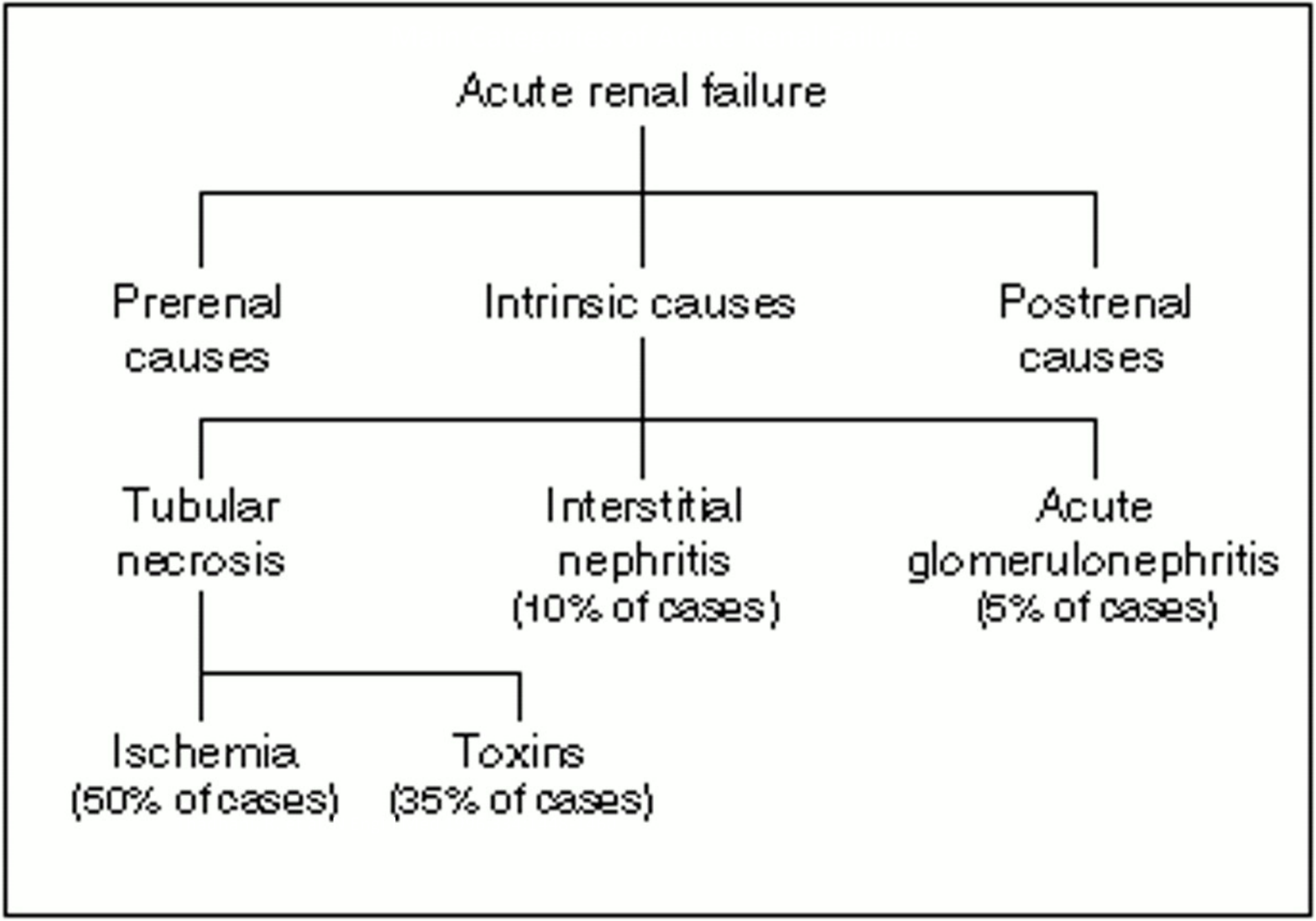
Etiology of AKI




Acute renal failure
Prerenal causes
Intrinsic causes
Postrenal causes
Tubular necrosis
Interstitial nephritis (10% of cases)
Acute glomerulonephritis (5% of cases)
Ischemia (50% of cases)
Toxins (35% of cases)

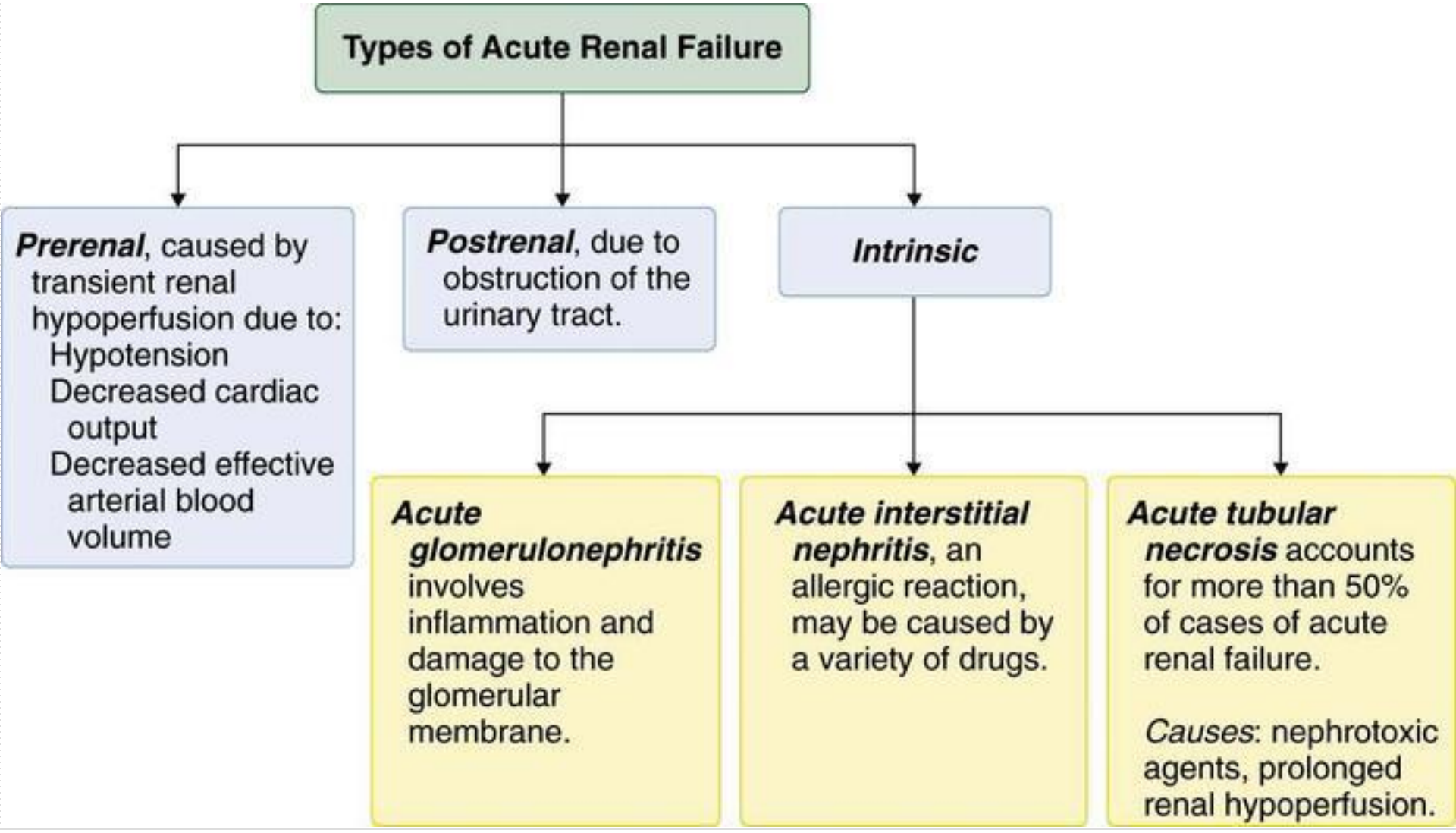
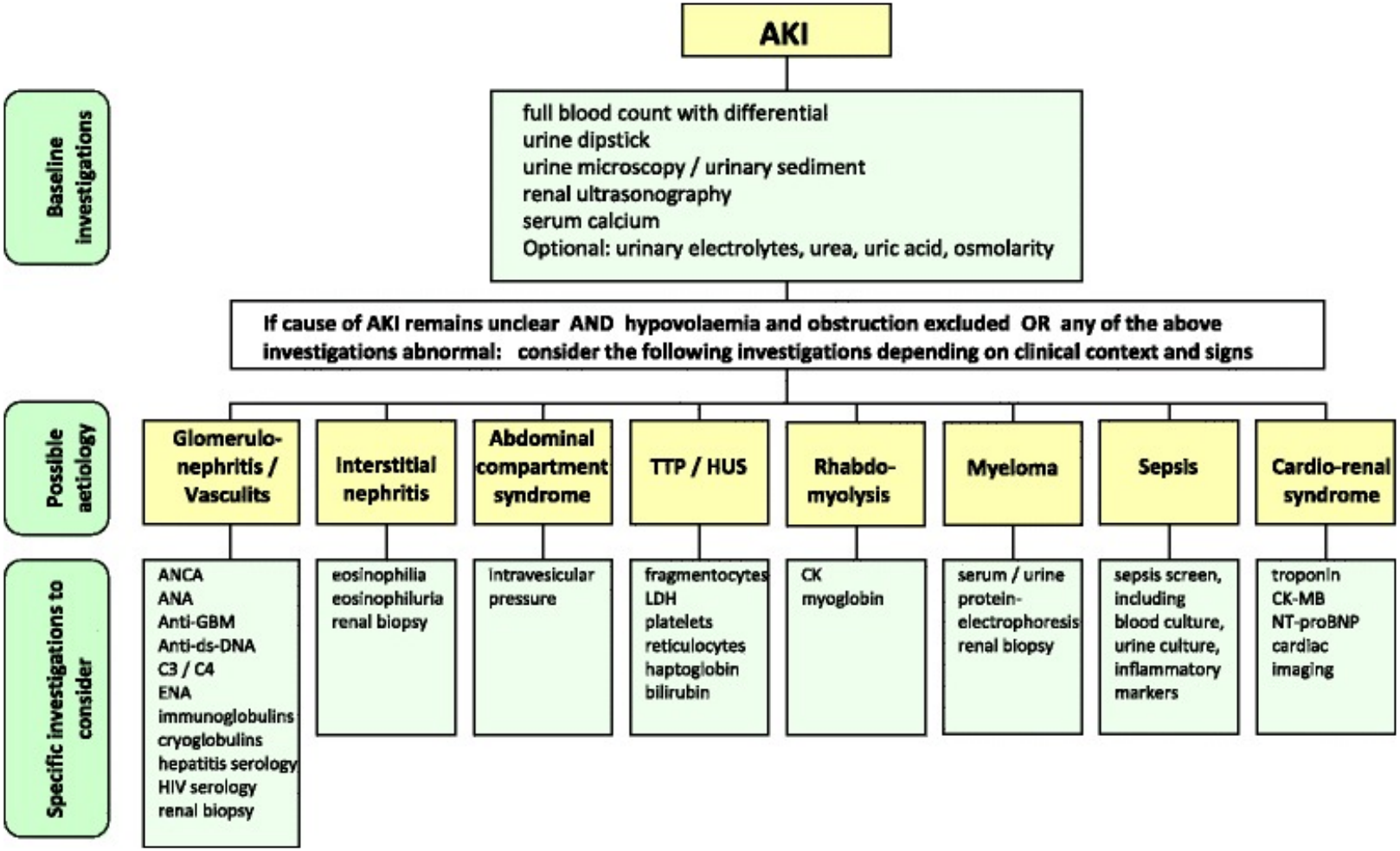

Types of Acute Renal Failure
Prerenal, caused by transient renal hypoperfusion due to:
Hypotension
Decreased cardiac output
Decreased effective arterial blood volume
Postrenal, due to obstruction of the urinary tract.
Intrinsic
Acute glomerulonephritis involves inflammation and damage to the glomerular membrane.
Acute interstitial nephritis, an allergic reaction, may be caused by a variety of drugs.
Acute tubular necrosis accounts for more than 50% of cases of acute renal failure.
Causes: nephrotoxic agents, prolonged renal hypoperfusion.

Table 1

Guidelines for urinary indices whereby established ARF can be distinguished from renal vasoconstriction with intact tubular function (prerenal azotemia)

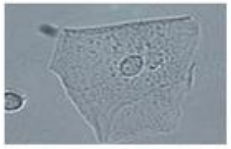
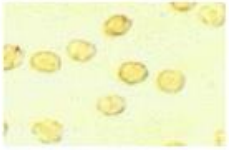
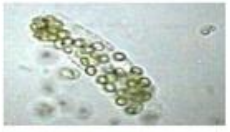
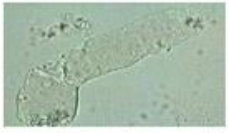
Laboratory test	Prerenal azotemia	ARF
Urine osmolality (mOsm/kg)	>500	<400
Urine sodium level (mEq/l)	<20	>40
Urine/plasma creatinine ratio	>40	<20
Fractional excretion of sodium (%)	<1	>2
Fractional excretion of urea (%)	<35	>35
Urinary sediment	Normal; occasional hyaline or fine granular casts	Renal tubular epithelial cells; granular and muddy brown casts

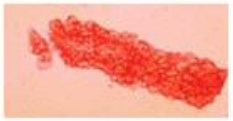
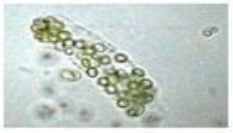
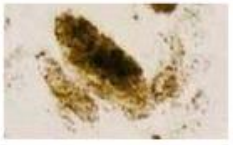
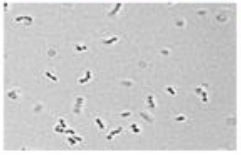
Osm, osmole; Eq, equivalent.

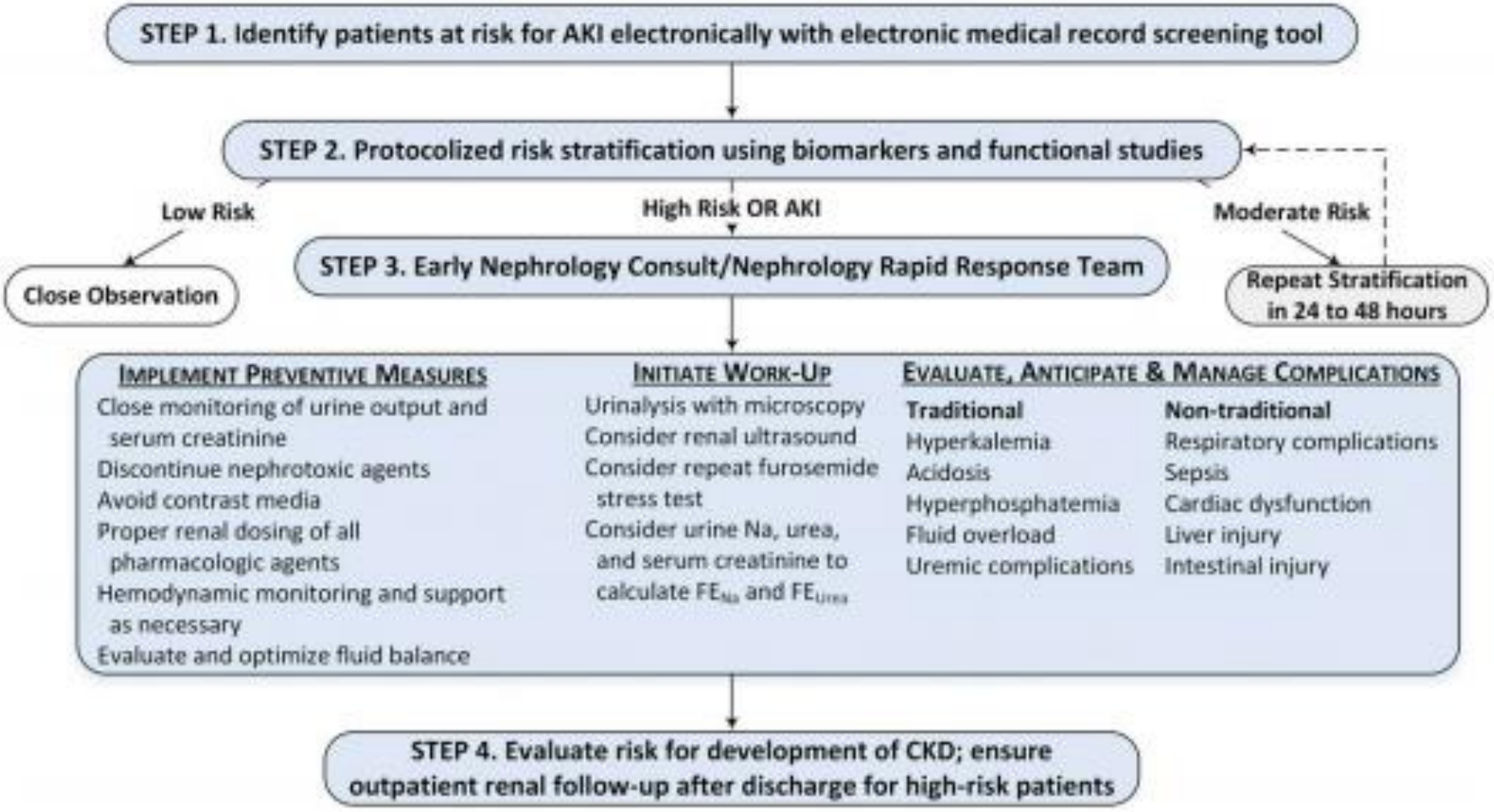


Diagnostic work up. *AKI* acute kidney injury, *ANCA* anti-neutrophil cytoplasmic antibody, *ANA* anti-nuclear antibody, *Anti-ds-DNA* anti-double stranded DNA, *anti-GBM* anti-glomerular basement membrane, *C3* complement component 3, *C4* complement component 4, *CK* creatine kinase, *CK-MB* creatine kinase MB fraction, *ENA* extractable nuclear antigen, *HIV* human immunodeficiency virus, *HUS* haemolytic uraemic syndrome, *LDH* lactate dehydrogenase, *NT-proBNP* N-terminal pro-brain natriuretic peptide, *TTP* thrombotic thrombocytopenic purpura

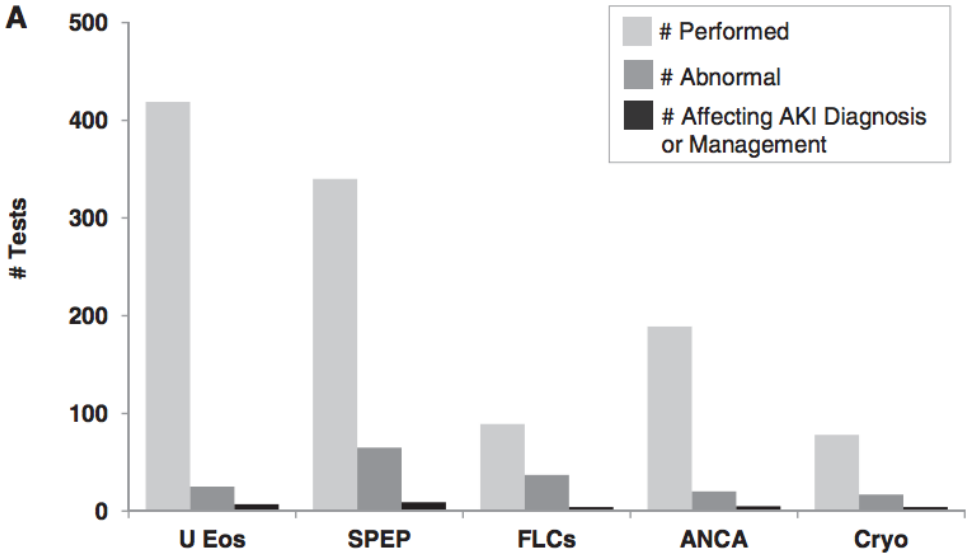
Interpretation of urine microscopy findings

Microscopy finding	Example	Significance
Epithelial cells		Normal
Renal tubular cells		Acute tubular injury
Non-dysmorphic red cells		Non-glomerular bleeding from anywhere in the urinary tract
Dysmorphic red cells		Glomerular disease, but can also be seen if urine sample is not fresh at time of microscopy
Red cell casts		Diagnostic of glomerular disease
Leukocytes		Up to 3 per high-power field = normal; >3 per high-power field = inflammation in urinary tract
White cell casts		Renal infection
Hyaline casts		Any type of renal disease
Granular casts		More significant renal disease

Non-dysmorphic red cells		Non-glomerular bleeding from anywhere in the urinary tract
Dysmorphic red cells		Glomerular disease, but can also be seen if urine sample is not fresh at time of microscopy
Red cell casts		Diagnostic of glomerular disease
Leukocytes		Up to 3 per high-power field = normal; >3 per high-power field = inflammation in urinary tract
White cell casts		Renal infection
Hyaline casts		Any type of renal disease
Granular casts		More significant renal disease
"Muddy brown cast"		Necrotic tubular cells aggregated with tamm horsfall protein indicating acute tubular injury
Crystals		Some crystals can be found in healthy individuals; "abnormal" crystals may indicate metabolic disorders or excreted medications
Bacteria		Urinary tract infection; contamination

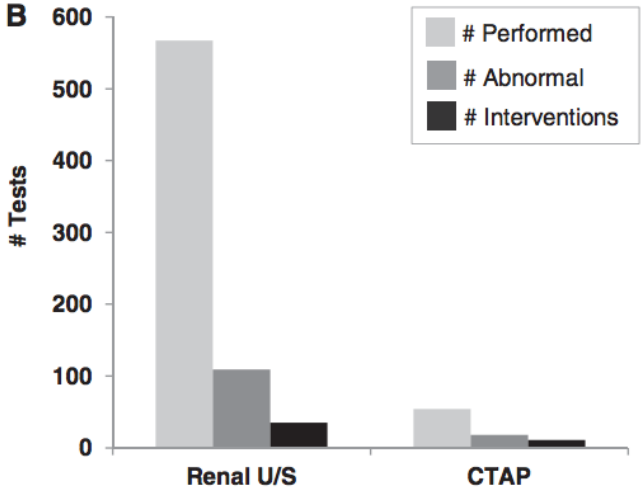

STEP 1. Identify patients at risk for AKI electronically with electronic medical record screening tool
STEP 2. Protocolized risk stratification using biomarkers and functional studies
Low Risk
High Risk OR AKI
Moderate Risk
Close Observation
STEP 3. Early Nephrology Consult/Nephrology Rapid Response Team
Repeat Stratification in 24 to 48 hours
IMPLEMENT PREVENTIVE MEASURES
Close monitoring of urine output and serum creatinine
Discontinue nephrotoxic agents
Avoid contrast media
Proper renal dosing of all pharmacologic agents
Hemodynamic monitoring and support as necessary
Evaluate and optimize fluid balance
INITIATE WORK-UP
Urinalysis with microscopy
Consider renal ultrasound
Consider repeat furosemide stress test
Consider urine Na, urea, and serum creatinine to calculate FE_{Na} and FE_{Urea}
EVALUATE, ANTICIPATE & MANAGE COMPLICATIONS
Traditional
Hyperkalemia
Acidosis
Hyperphosphatemia
Fluid overload
Uremic complications
Non-traditional
Respiratory complications
Sepsis
Cardiac dysfunction
Liver injury
Intestinal injury
STEP 4. Evaluate risk for development of CKD; ensure outpatient renal follow-up after discharge for high-risk patients

A



	U Eos	SPEP	FLCs	ANCA	Cryo
#Tests	419 / 29 / 7	340 / 65 / 9	89 / 37 / 4	189 / 20 / 5	78 / 17 / 2
% of Total	--- / 6.9 / 1.7	--- / 19.1 / 2.6	--- / 41.6 / 4.5	--- / 10.6 / 2.6	--- / 21.8 / 2.6

B



	Renal U/S	CTAP
#Tests	567 / 109 / 35	54 / 18 / 11
% of Total	---- / 19.2 / 6.2	---- / 33.3 / 20.4

Furosemide Stress Test

Furosemide 1 mg/kg for naïve patients or 1.5 mg/kg in furosemide is given IV

+ test - UO is < 200 ml over subsequent 2 hours

+ test predicts AKI progression, need for RRT and mortality

Furosemide Stress Test and Biomarkers for the Prediction of AKI Severity

Table 5.

Prediction of the composite of AKIN stage 3 and death

Biomarker	AUC±SEM	*P* Value for Biomarker Alone	*P* Value Compared With FST alone	AUC of Biomarker and FST±SEM	*P* Value for Biomarker and FST Compared With FST Alone
FST (2-hr UOP)	0.81±0.06	<0.0001	NA	NA	NA
Urine NGAL	0.69±0.06	0.006	0.07	0.82±0.06	0.89
Urine IL-18	0.63±0.07	0.07	0.009	0.82±0.06	0.87
Urine KIM-1	0.64±0.06	0.04	0.04	0.82±0.06	0.81
Uromodulin	0.54±0.07	0.58	0.004	0.85±0.06	0.31
Urine IGFBP-7	0.65±0.08	0.07	0.19	0.79±0.08	0.80
Urine TIMP-2	0.66±0.08	0.06	0.18	0.80±0.08	0.75
Urine IGFBP-7×TIMP-2	0.68±0.08	0.03	0.27	0.78±0.08	0.93
Urine Creatinine	0.54±0.07	0.56	0.007	0.83±0.06	0.23
Urine ACR	0.50±0.07	0.96	0.002	0.82±0.06	0.32
FeNa	0.49±0.07	0.84	0.009	0.80±0.06	0.31
Plasma NGAL	0.69±0.08	0.03	0.27	0.80±0.08	0.76

Furosemide Stress Test and Biomarkers for the Prediction of AKI Severity

Table 3.

AUCs for prediction of receipt of inpatient RRT

Biomarker	AUC±SEM	*P* Value for Biomarker Alone	*P* Value Compared With FST alone	AUC of Biomarker and FST±SEM	*P* Value for Biomarker and FST Compared With FST Alone
FST (2-hr UOP)	0.86±0.08	0.0001	NA	NA	NA
Urine NGAL	0.50±0.08	0.96	0.0006	0.88±0.06	0.35
Urine IL-18	0.61±0.07	0.26	0.03	0.85±0.09	0.70
Urine KIM-1	0.61±0.10	0.27	0.05	0.85±0.09	0.77
Uromodulin	0.55±0.11	0.60	0.07	0.89±0.06	0.65
Urine IGFBP-7	0.57±0.12	0.61	0.05	0.90±0.06	0.29
Urine TIMP-2	0.62±0.12	0.33	0.17	0.83±0.09	0.57
Urine IGFBP-7×TIMP-2	0.61±0.13	0.37	0.10	0.89±0.07	0.23
Urine creatinine	0.64±0.11	0.19	0.24	0.84±0.09	0.90
Urine ACR	0.67±0.09	0.13	0.28	0.86±0.08	0.51
FeNa	0.64±0.09	0.18	0.11	0.85±0.09	0.27
Plasma NGAL	0.52±0.13	0.88	0.07	0.80±0.13	0.92

- NA, not applicable; ACR, albumin-to-creatinine ratio.

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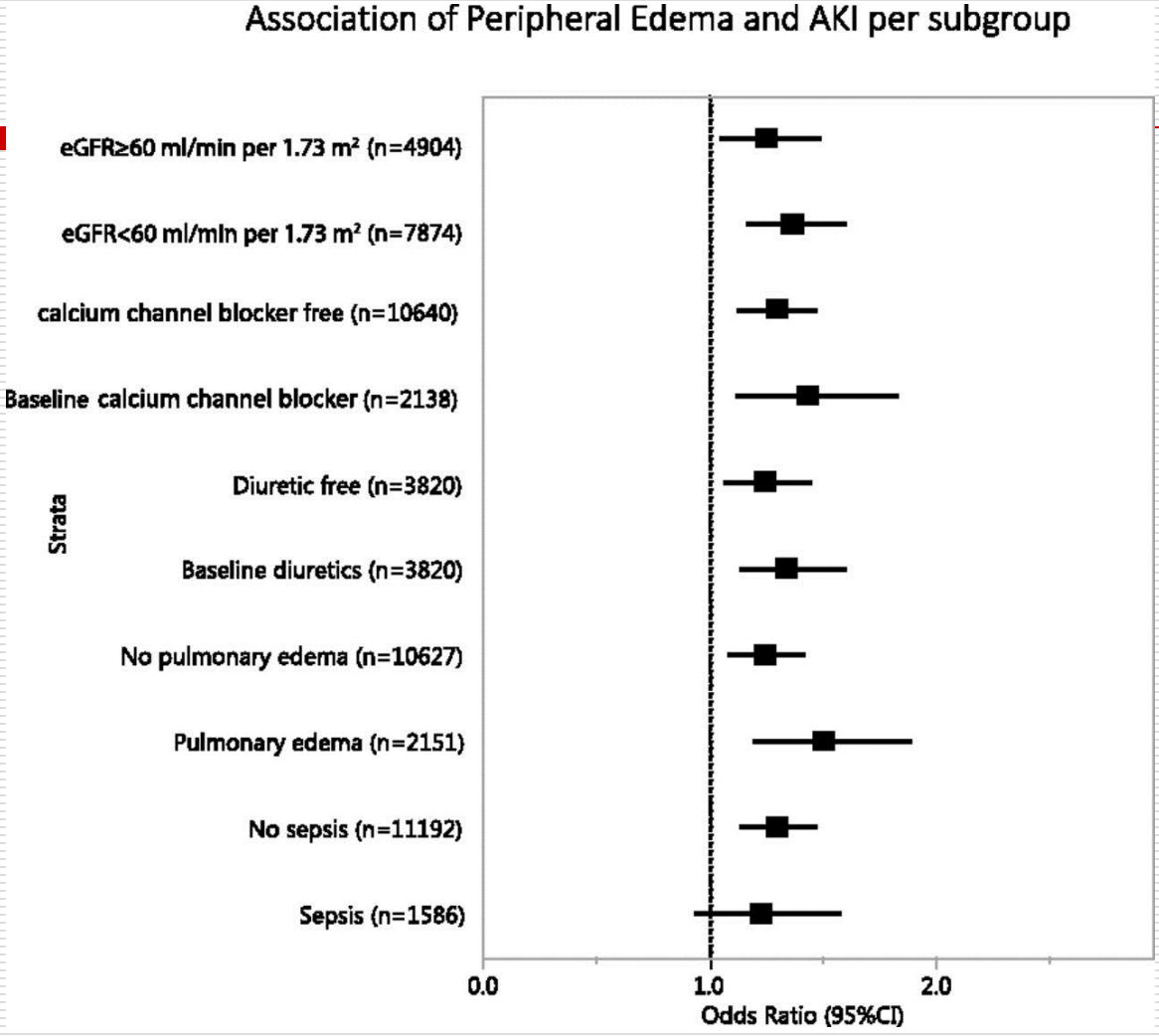
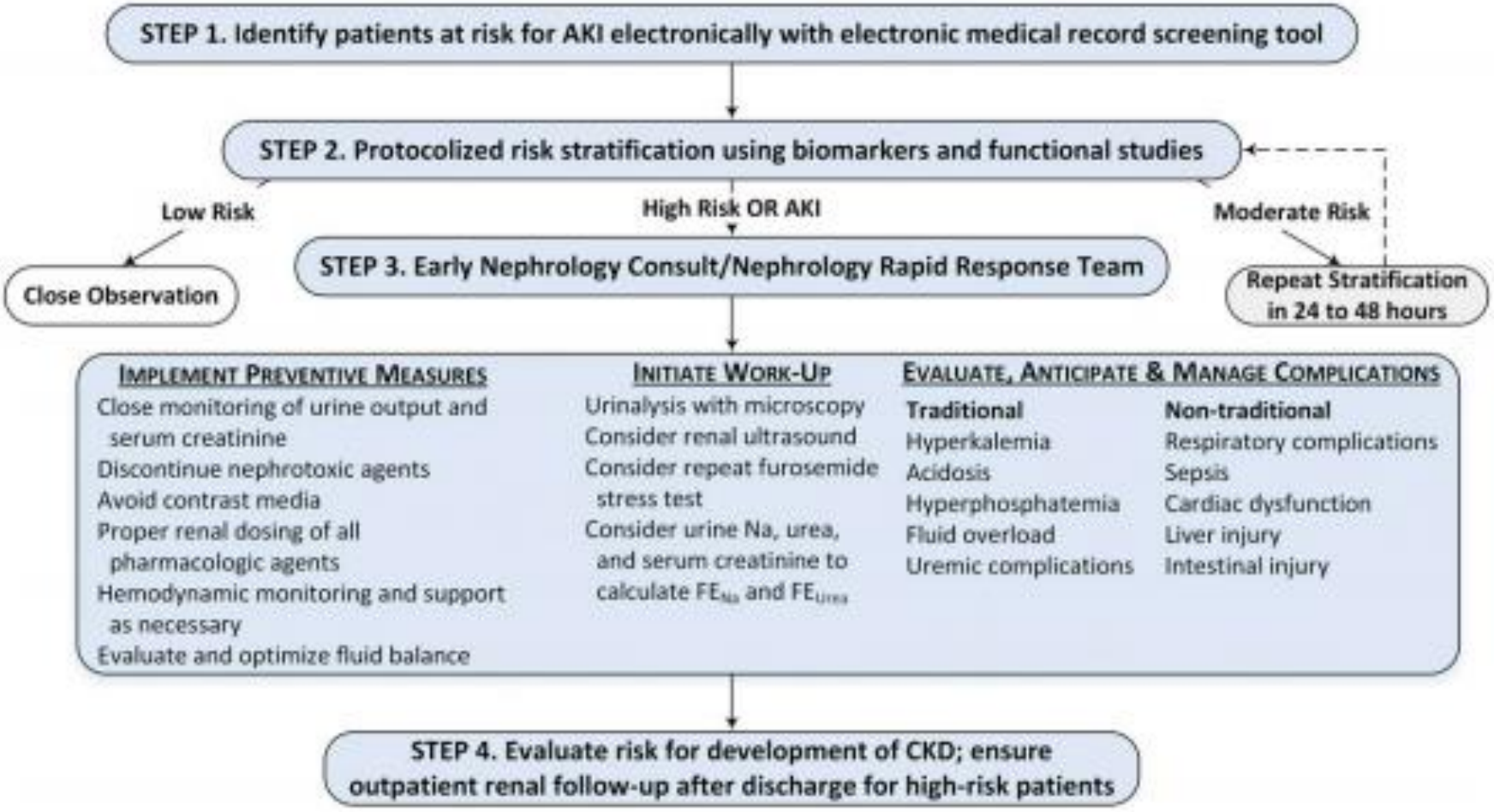
Primary prevention of AKI

Baseline risks	Acute clinical conditions	Nephrotoxic agents
Advanced age	Sepsis	Contrast media
Diabetes mellitus	Hypotension/shock	Antimicrobial agents
CKD	Volume depletion	Chemotherapeutic agents
Heart failure	Rhabdomyolysis	NSAIDs
Liver failure	Cardiac/vascular surgery	
Male gender	Non-renal solid organ transplantation	
Race & genetic variation	Abdominal compartment syndrome	
Hypoalbuminemia	Mechanical ventilation	
Arterial vascular disease		

Forest plot for risk of peripheral edema and AKI per subgroup.



Kenneth P. Chen et al. CJASN 2016;11:602-608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IMPLEMENT PREVENTIVE MEASURES
Close monitoring of urine output and serum creatinine
Discontinue nephrotoxic agents
Avoid contrast media
Proper renal dosing of all pharmacologic agents
Hemodynamic monitoring and support as necessary
Evaluate and optimize fluid balance
INITIATE WORK-UP
Urinalysis with microscopy
Consider renal ultrasound
Consider repeat furosemide stress test
Consider urine Na, urea, and serum creatinine to calculate FE_{Na} and FE_{Urea}
EVALUATE, ANTICIPATE & MANAGE COMPLICATIONS
Traditional
Hyperkalemia
Acidosis
Hyperphosphatemia
Fluid overload
Uremic complications
Non-traditional
Respiratory complications
Sepsis
Cardiac dysfunction
Liver injury
Intestinal injury
STEP 4. Evaluate risk for development of CKD; ensure outpatient renal follow-up after discharge for high-risk patients

Contrast Induced Nephropathy

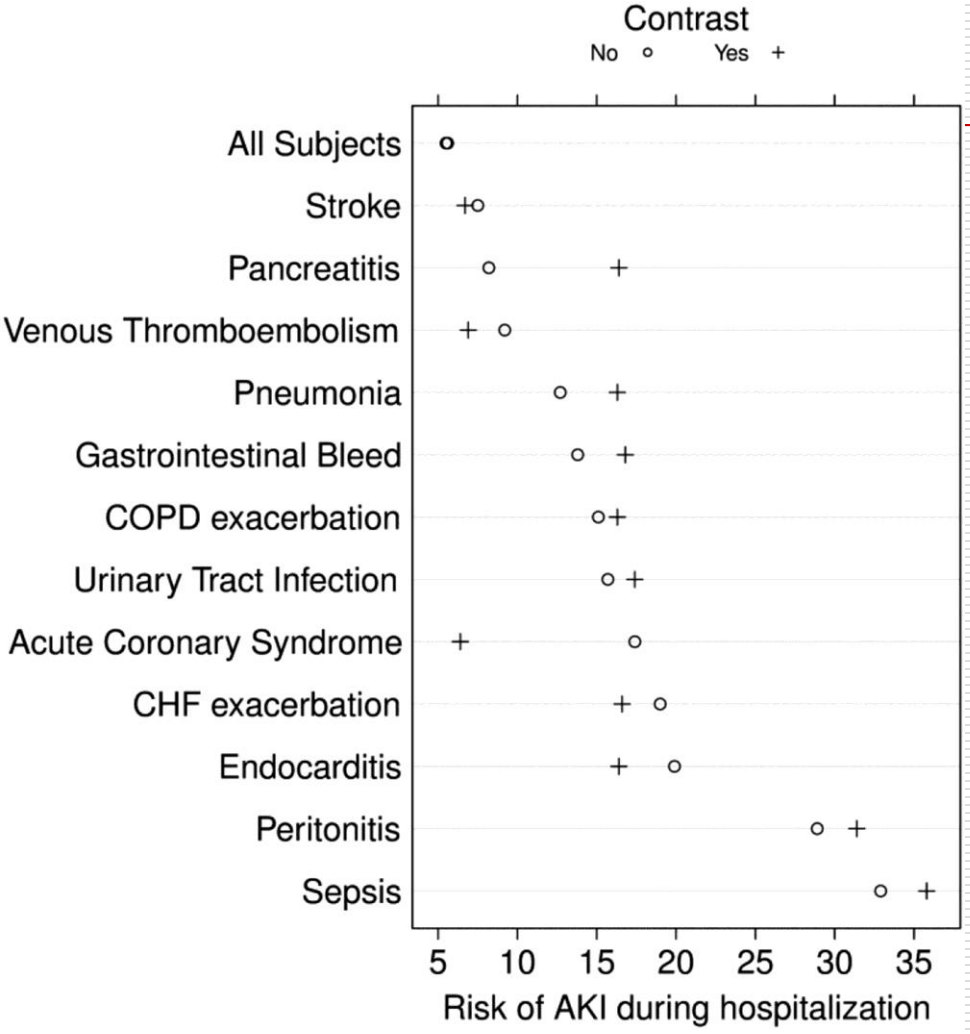
Traditionally IV contrast has been thought to cause AKI

Incidence unclear but seemed to be based on pre contrast risks (GFR etc), dose and route of administration(IV VS IA)

Recent observational data suggests much less common than thought

Prophylaxis and discretion still recommended for now

The variable relationship between contrast administration and AKI across the examined disease states.



Emilee Wilhelm-Leen et al. JASN 2017;28:653-659

Remote Ischemic Preconditioning

Transient ischemia protects cells from later ischemic events locally (heart, brain, kidney)

Transient local ischemia also has remote protective effects

Inducing brachial (local) ischemia has been shown to prevent CIN. Data for CV surgery is mixed

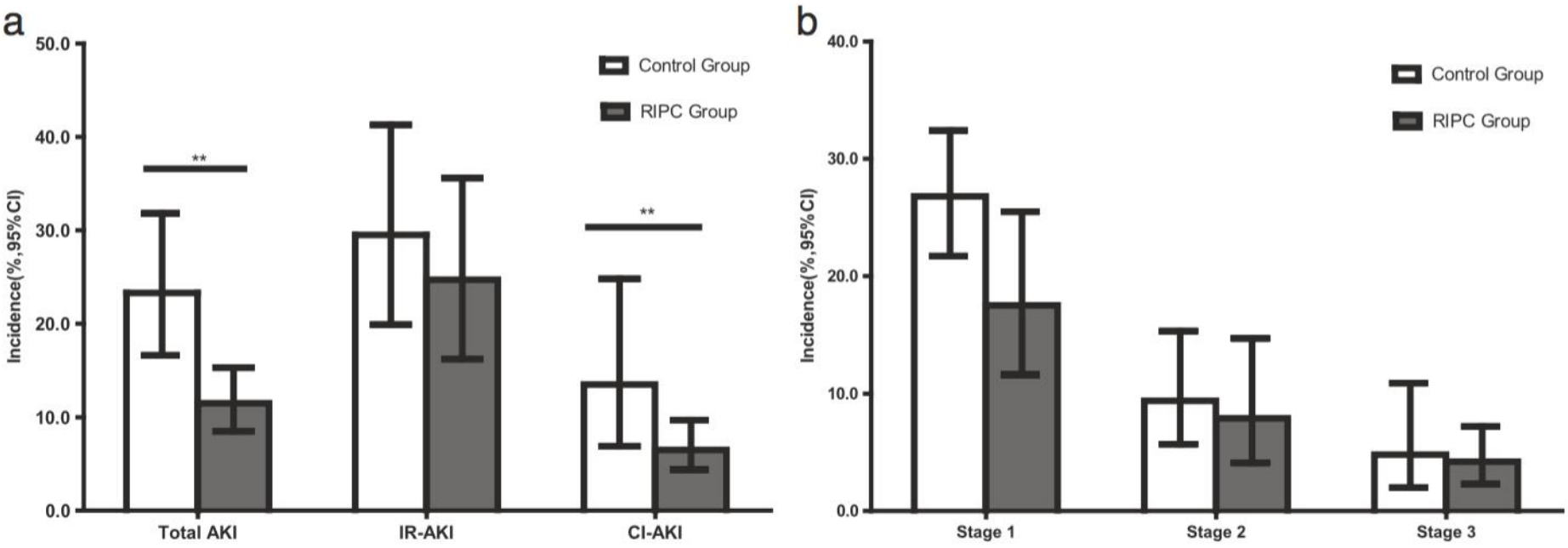


Fig. 2 Effects of remote ischemic preconditioning (RIPC) on the incidence of acute kidney injury (AKI). (**a**) Effects of RIPC on total AKI, ischemia/reperfusion-induced AKI (IR-AKI) and contrast-induced AKI (CI-AKI). (**b**) Effects of RIPC on every stage of AKI. $^{**}P < 0.01$

AKI Prevention

Identification of patients at risk

Protocolized comprehensive management plans for sepsis, CV and vascular surgery etc (ASA postop CPB)

Avoidance of nephrotoxins or potentially nephrotoxic events

Table 6. Phenotypes of therapeutic drug-induced AKI

	Tubular	Interstitial	Glomerular	Crystal Induced
Type of injury	Cytopathic or toxic injury	Inflammatory	Nephritic or nephrotic syndrome, TMA	Intracellular deposition or intratubular obstruction
Mechanisms	Mitochondrial damage	Hypersensitivity reaction	Podocyte or endothelial cell damage	Osmotic, obstructive, or epithelial cell toxicity
Common agents	Aminoglycosides, contrast, vancomycin	Penicillin, PPI	Bisphosphonates, hydralazine, calcineurin inhibitors	Phosphate, orlistat, sulpha, indinavir

From: **Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults**

JAMA. 2012;308(15):1566-1572. doi:10.1001/jama.2012.13356

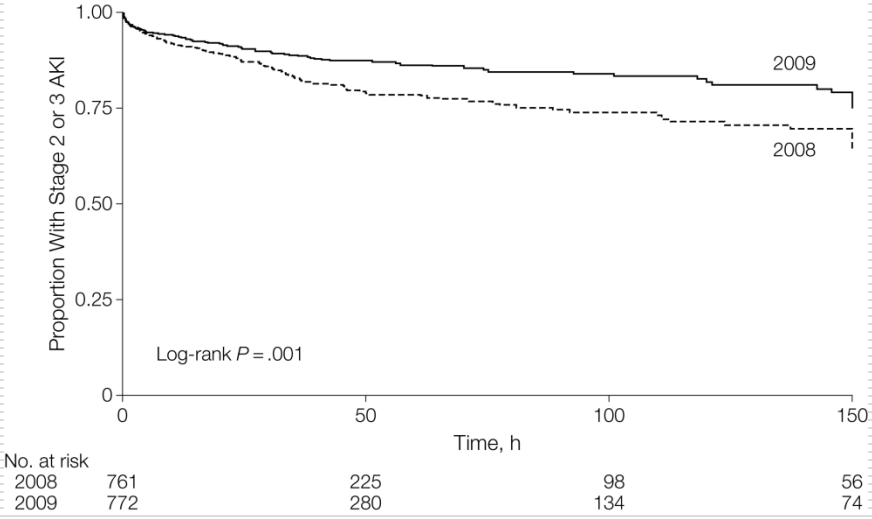
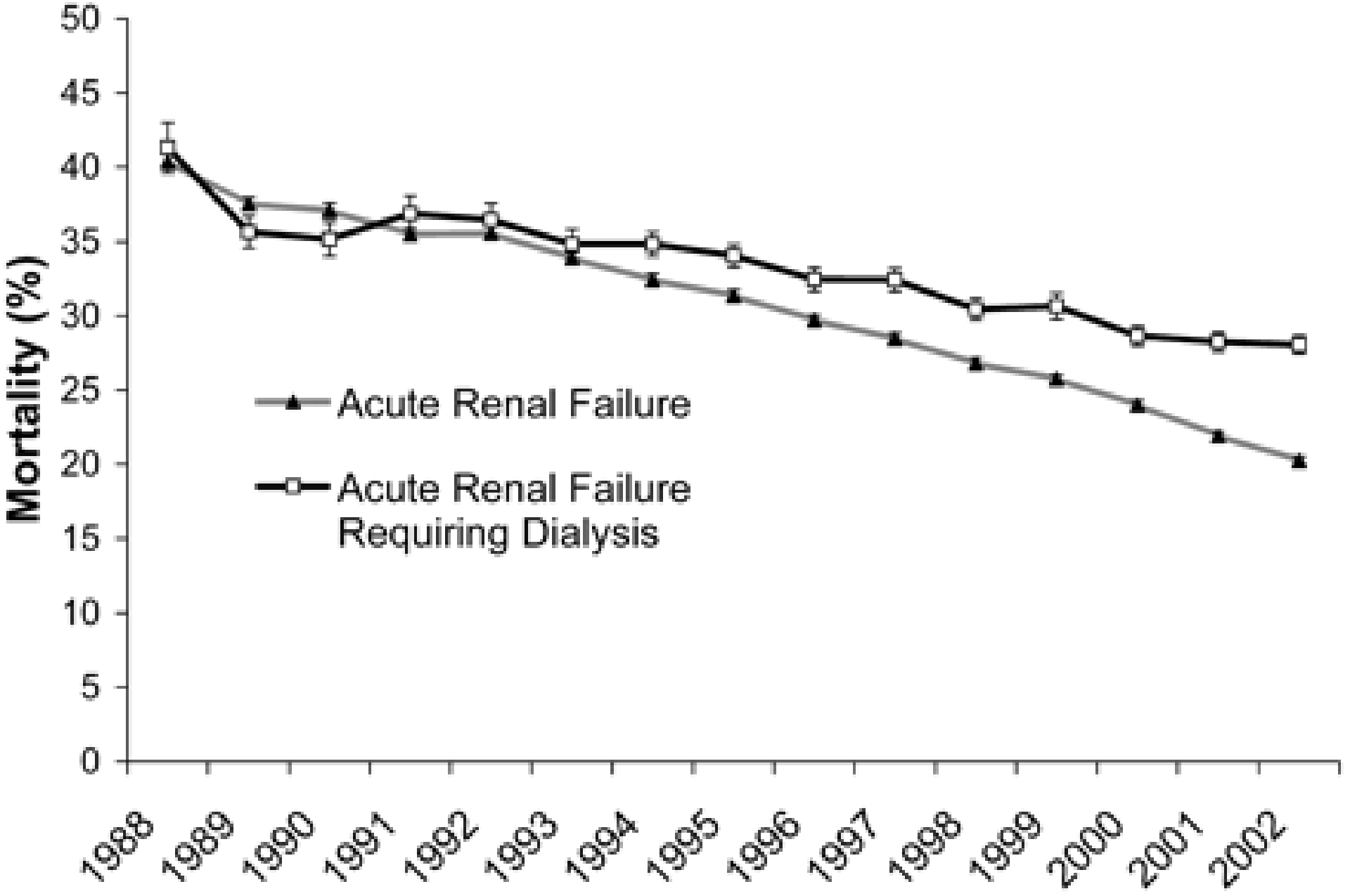


Figure Legend:

Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

Objectives

1. Define AKI – KDIGO Classification
2. Incidence and consequences of AKI
3. Causes of AKI and workup
4. Prevention of AKI
5. Treatment of AKI
6. Cases


Mortality (%)
50
45
40
35
30
25
20
15
10
5
0
Acute Renal Failure
Acute Renal Failure Requiring Dialysis
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002

Management of AKI

1. Remove or treat offending agent
2. Dx – US, UA, Urinary indices
3. Improve hemodynamics – if wet – dry, if not wet – wet
4. Make non-oliguric. Fix electrolytes
5. Avoid nephrotoxins
6. Adjust meds for eGFR
7. RRT

Derby Hospitals NHS Foundation Trust

AUDITS - The Acute Kidney Injury Care Bundle

Patient sticker

Date .....

Time .....

Ward.. .....

This care bundle applies to initial care of those admitted with Acute Kidney Injury (AKI)

Action		Parameter	Sign
A	**A**ssess History & examine **(VENUS)**	• **V**olume depletion • **E**soteric history - 3H &3R (Haemoptysis, Haemolysis, Hypercalcemia, Rash, Recent vascular intervention, raised CK) • **N**ephrotoxins – check medications • **U**rinary symptoms – outflow obstruction, haematuria, oliguria, colic • **S**epsis	
U	**U**rine dispstick	• No blood or protein – Pre renal • Blood & protein – Renal • Only blood – post renal or renal	
D	Clinical **D**iagnosis	• Think cause of AKI as Pre renal, Renal and Post renal • Classify and document AKI as per AKIN stage.	
I	**I**nvestigations	• U+E, bicarbonate, Glucose, ANCA, SEP, ECG, CXR, MSU or blood & urine cultures depending on clinical suspicion.	
		• USS to r/o post renal cause.	
T	**T**reatment - **PUMP**	• **P**erfusion – ensure euvolemic status, ionotropes if required	
		• **U**nderlying cause – – remove nephrotoxins, antibiotics for sepsis	
		• **M**onitor – EWS, volume status, Daily U+Es	
		• **P**revent complications - fluid overload, adjust doses of medications, sepsis including removal of potential sources of sepsis.	
S	**S**eek advice	Seek renal advice (bleep 8121) for all AKI stage 3 and, if esoteric cause for AKI is suspected - as per the Trust guideline. *Refer to "DONUT" on the website* Consider HDU/ITU according to severity	

AKI Care Bundle

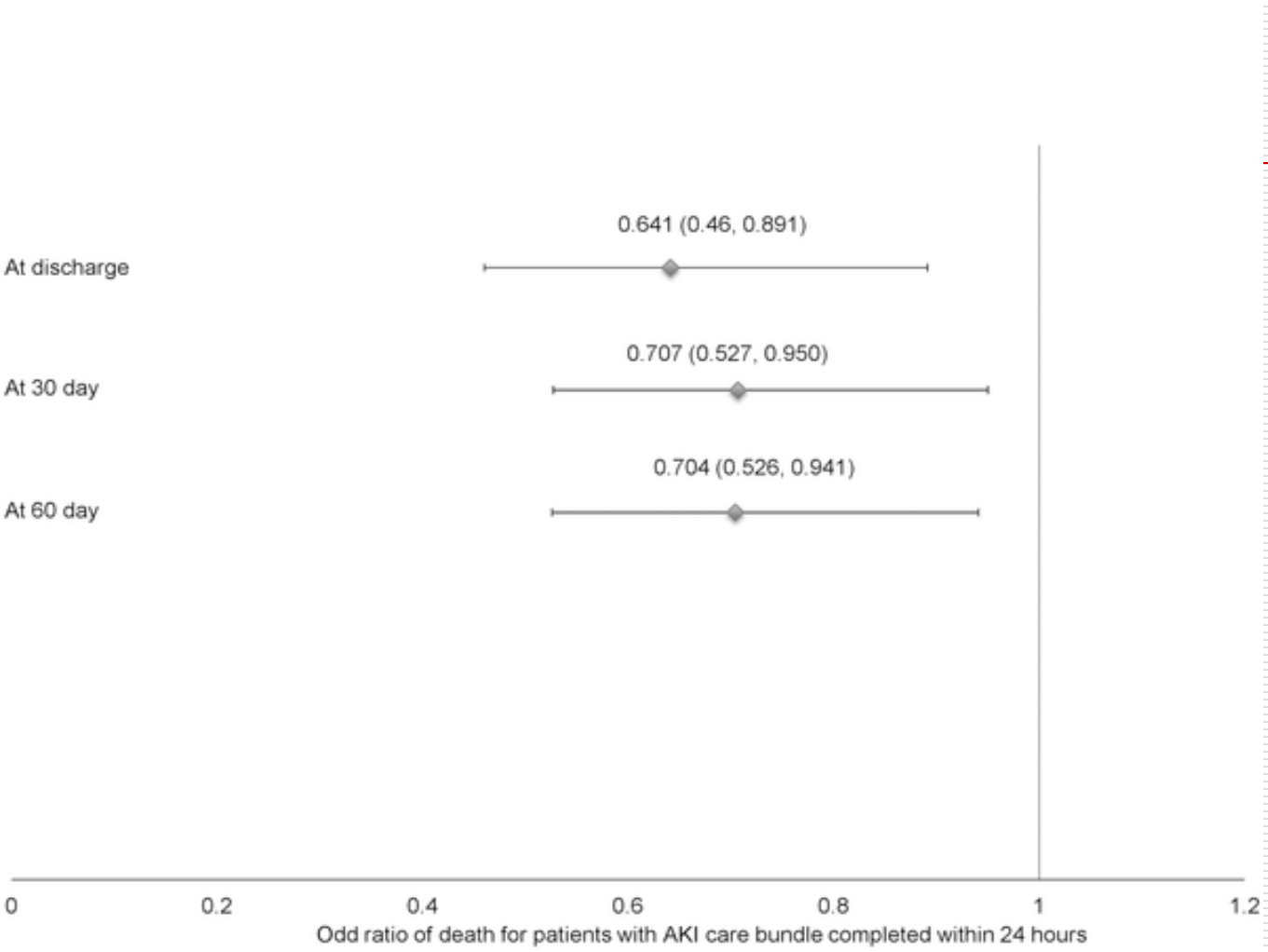
Entered:_____

Completed:_____

Instructions

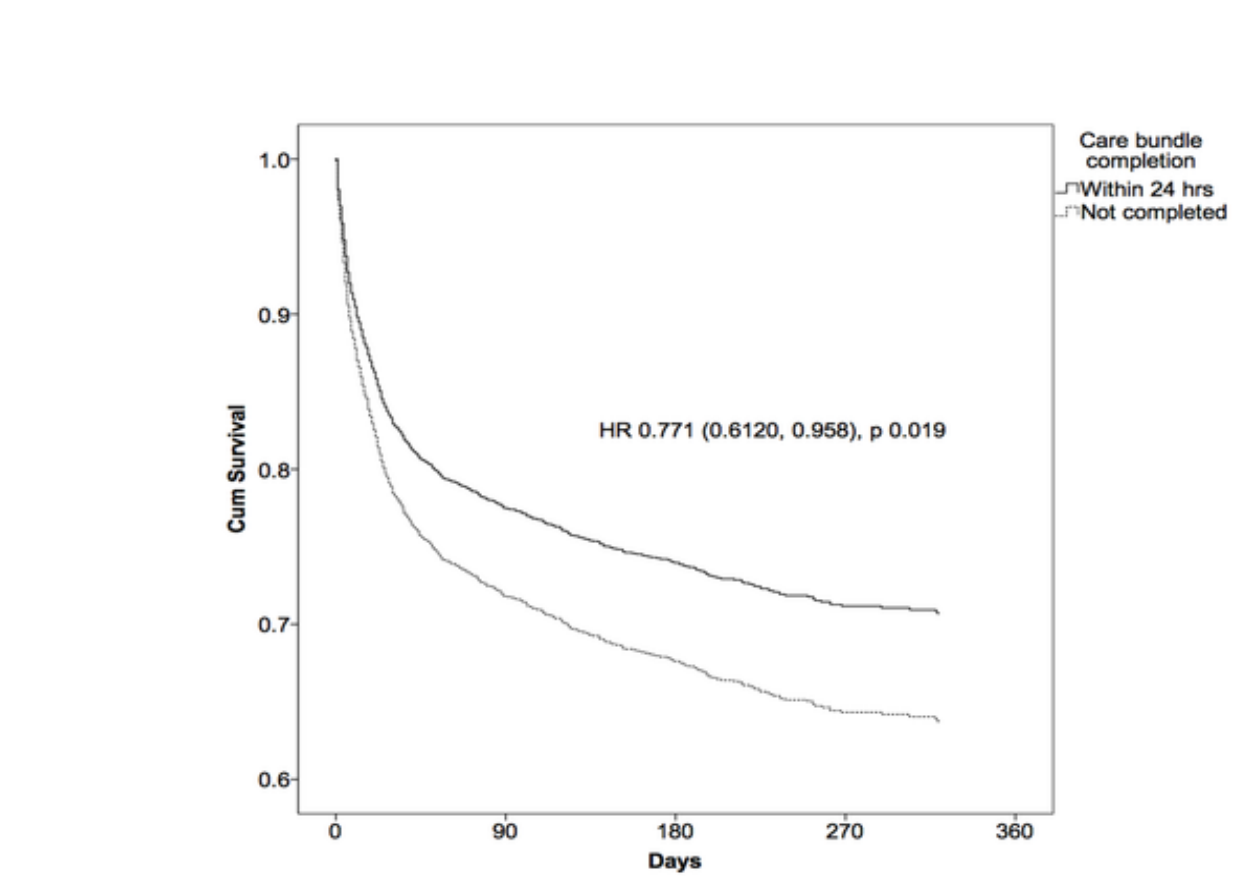
1. Attach patient label and fill in Box A
2. Detach square sticker, and place in notes and follow.
3. Detach round sticker, and place in front of notes folder.
4. File this backing sheet (with patient label) in designated audit tray.

Fig 2. Odd ratios and 95% confidence interval of death for AKI episodes which had AKI Care Bundle completed within 24 hours.



Kolhe NV, Staples D, Reilly T, Merrison D, Mcintyre CW, et al. (2015) Impact of Compliance with a Care Bundle on Acute Kidney Injury Outcomes: A Prospective Observational Study. PLOS ONE 10(7): e0132279. https://doi.org/10.1371/journal.pone.0132279
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0132279

Fig 3. Adjusted survival curve stratified by timing of completion of AKI Care Bundle.



Kolhe NV, Staples D, Reilly T, Merrison D, Mcintyre CW, et al. (2015) Impact of Compliance with a Care Bundle on Acute Kidney Injury Outcomes: A Prospective Observational Study. PLOS ONE 10(7): e0132279. https://doi.org/10.1371/journal.pone.0132279
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0132279

Assessment of Volume

Bedside – 50% of ICU patients are volume responsive.

Dynamic vs. Static

Static

- CVP and PAOP

Dynamic

- IVC collapse
- Pulse pressure and SBP variation
- Passive straight leg raise
- Lactate clearance

Assessment of Volume Responsiveness

Our clinical exam predicts volume responsiveness 50% of the time

Adding CVP measurements -50%

Adding IVC assessment – 60%

Dynamic measurements – PPV, PSLR or stroke volume variation predictive value > 80%

To avoid volume overload – use dynamic measurements

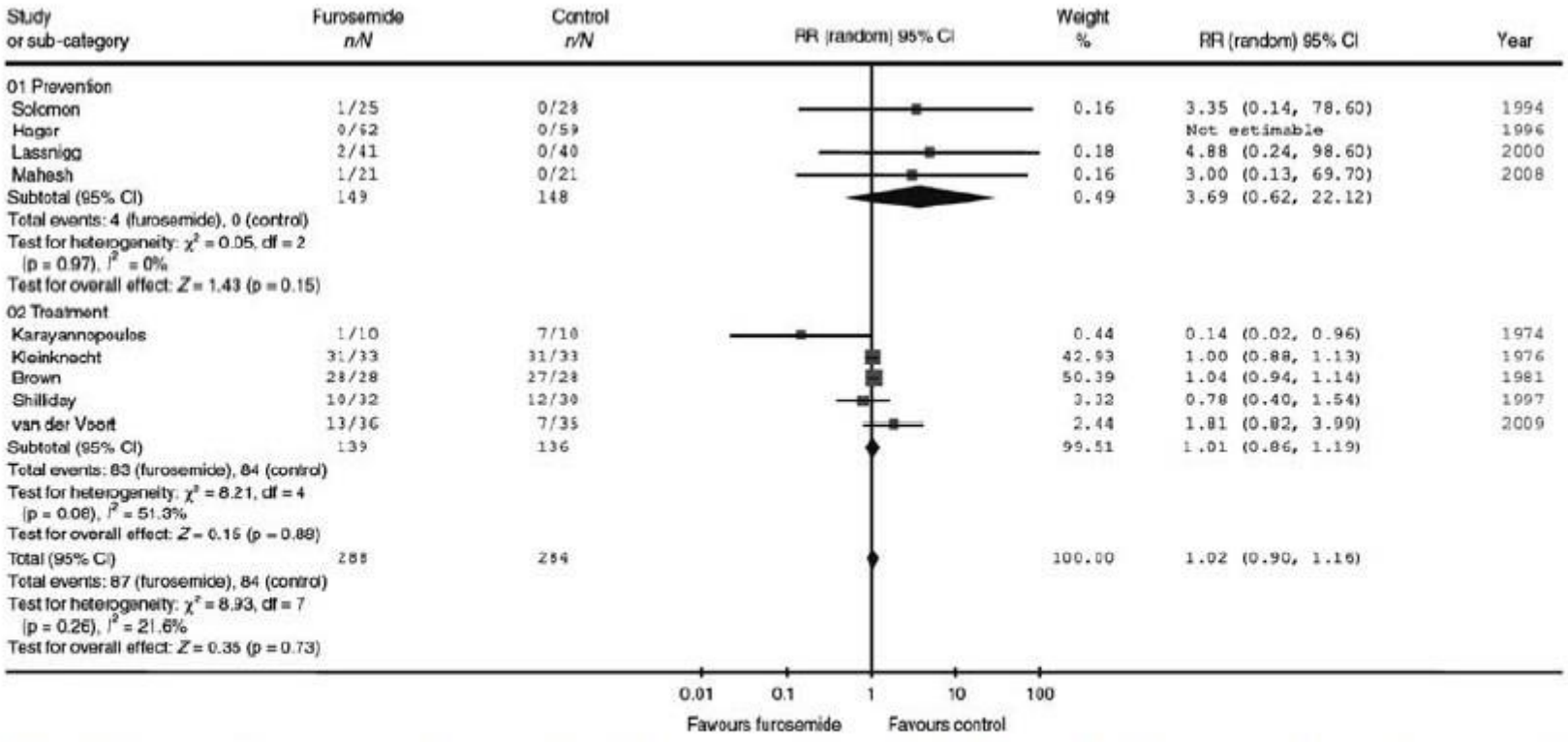


Figure 10 | Effect of furosemide vs. control on need for RRT. Reprinted from Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010; 65: 283–293 with permission from John Wiley and Sons[193]; accessed http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2009.06228.x/full

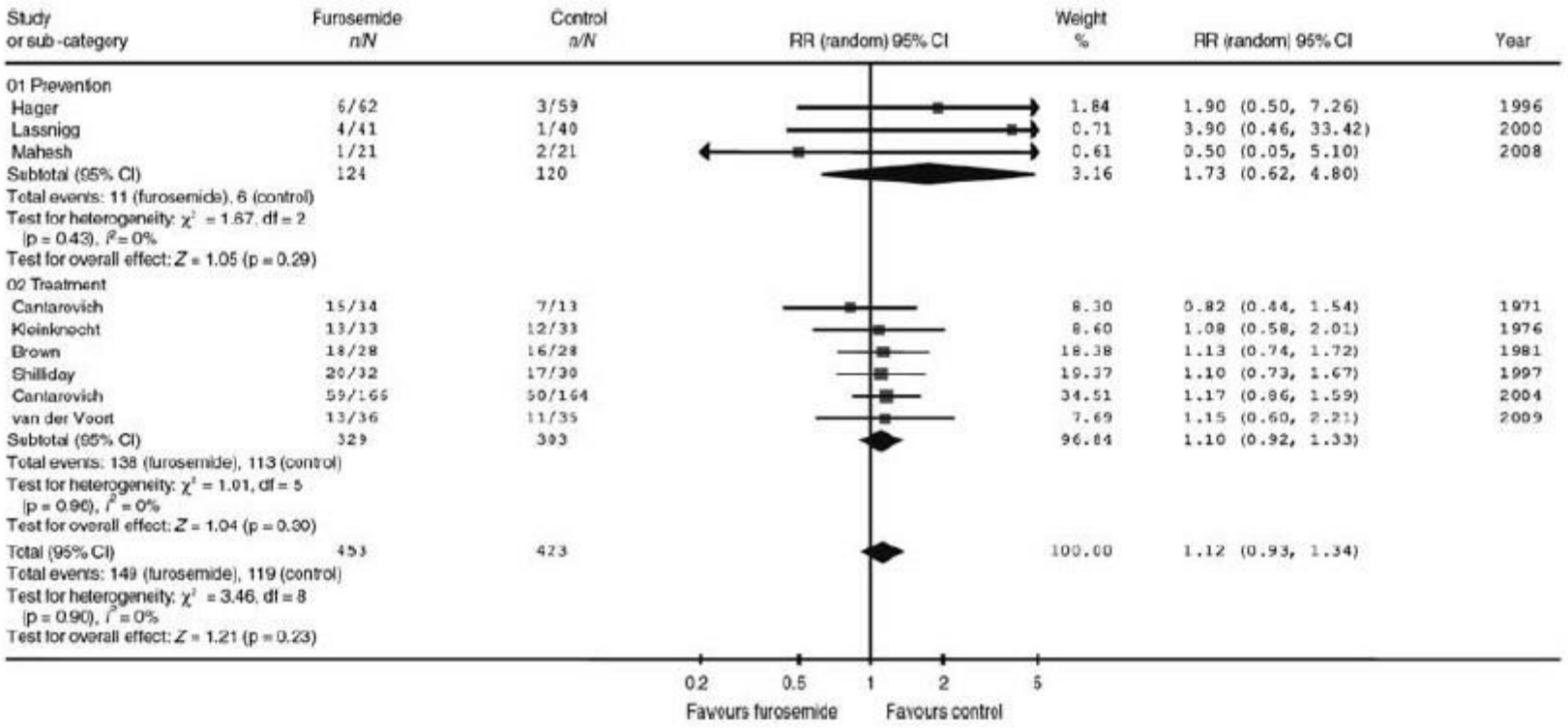


Figure 9 | Effect of furosemide vs. control on all-cause mortality. Reprinted from Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010; 65: 283–293 with permission from John Wiley and Sons[193]; accessed http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2009.06228.x/full

Indications for RRT in AKI

- Volume overload unresponsive to diuretics
- Metabolic acidosis refractory to medical management
- Intoxication with dialyzable drug or toxin
- Uremic symptoms
  - Encephalopathy
  - Pericarditis
  - Uremic bleeding
- Progressive azotemia in the absence of specific symptoms

Indications are open to interpretations

How volume overloaded?

What should potassium level be?

How severe for metabolic acidosis?

What is the definition of diuretic resistance?

Types of Renal Replacement Therapy

Table 22| Theoretical advantages and disadvantages of CRRT, IHD, SLED, and PD

Modality	Potential setting in AKI	Advantages	Disadvantages
IHD	Hemodynamically stable	Rapid removal of toxins and low-molecular-weight substances Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation Lower costs than CRRT	Hypotension with rapid fluid removal Dialysis disequilibrium with risk of cerebral edema Technically more complex and demanding
CRRT	Hemodynamically unstable Patients at risk of increased intracranial pressure	Continuous removal of toxins Hemodynamic stability Easy control of fluid balance No treatment-induced increase of intracranial pressure User-friendly machines	Slower clearance of toxins Need for prolonged anticoagulation Patient immobilization Hypothermia Increased costs
SLED	Hemodynamically unstable	Slower volume and solute removal Hemodynamic stability Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation	Slower clearance of toxins Technically more complex and demanding
PD	Hemodynamically unstable Coagulopathy Difficult access Patients at risk of increased intracranial pressure Under-resourced region	Technically simple Hemodynamic stability No anticoagulation No need for vascular access Lower cost Gradual removal of toxins	Poor clearance in hypercatabolic patients Protein loss No control of rate of fluid removal Risk of peritonitis Hyperglycemia Requires intact peritoneal cavity Impairs diaphragmatic movement, potential for respiratory problems

Are you considering RRT for this patient?

☐ **YES** *(continue with next question)* ☐ **NO** *(move on to indications to start RRT)*

What is your estimate of mortality during hospitalization:

☐ Unlikely (<25%) ☐ Possible (25-74%) ☐ Very certain (75-94%) ☐ Almost certain (>95%)

Do you think RRT would be futile for this patient?

☐ **YES because of**:

- ☐ No meaningful chance of recovery from non-renal illness:
  - ☐ Metastatic cancer
  - ☐ Overwhelming lactic acidosis (10mmol/L)
  - ☐ Overwhelming sepsis (3 pressors, SBP<90, evidence of infection)
- ☐ Profound, irreversible neurologic impairment
- ☐ Other: _____

☐ **NO** *move on to indications to start RRT*

Will you still proceed with RRT?

☐ **YES, because:**

- ☐ Discussion with MICU team
- ☐ Patient's goal of care
- ☐ Time-limited trial
- ☐ Family decision
- ☐ Other: _____

☐ **NO**

	Indications to start RRT		Non-urgent characteristics
	MORE URGENT	LESS URGENT	
Acid-base	☐ Metabolic acidosis; pH<7.2	☐ pH 7.2-7.3	☐ pH >7.3 // Not available
Electrolytes	☐ K>6.5 or EKG changes	☐ K= 6.0-6.5	☐ K<6.0
Ingestion	☐ Toxin: _____		☐ N/A
Overloaded	☐ Massive anasarca ☐ Hypoxemic respiratory failure, FIO2>0.7	☐ 2-3+ edema ☐ Hypoxemia, FIO2= 0.5-0.7	☐ ≤1+ edema
	☐ Urine output <100 ml/24 hr	☐ Urine output 100-500 ml/24 hr	☐ Urine output >500 ml/24 hr
Uremia	☐ Uremic Symptoms ☐ Altered mental status	☐ BUN 60-130	☐ BUN<60

If ANY checked: → *SCAMP recommends* **RRT**

≥3 checked

1-2 checked → *SCAMP recommends* **No RRT**

If ALL checked

Please Circle your Plan

RRT

Reasons for starting RRT against SCAMP recommendation:

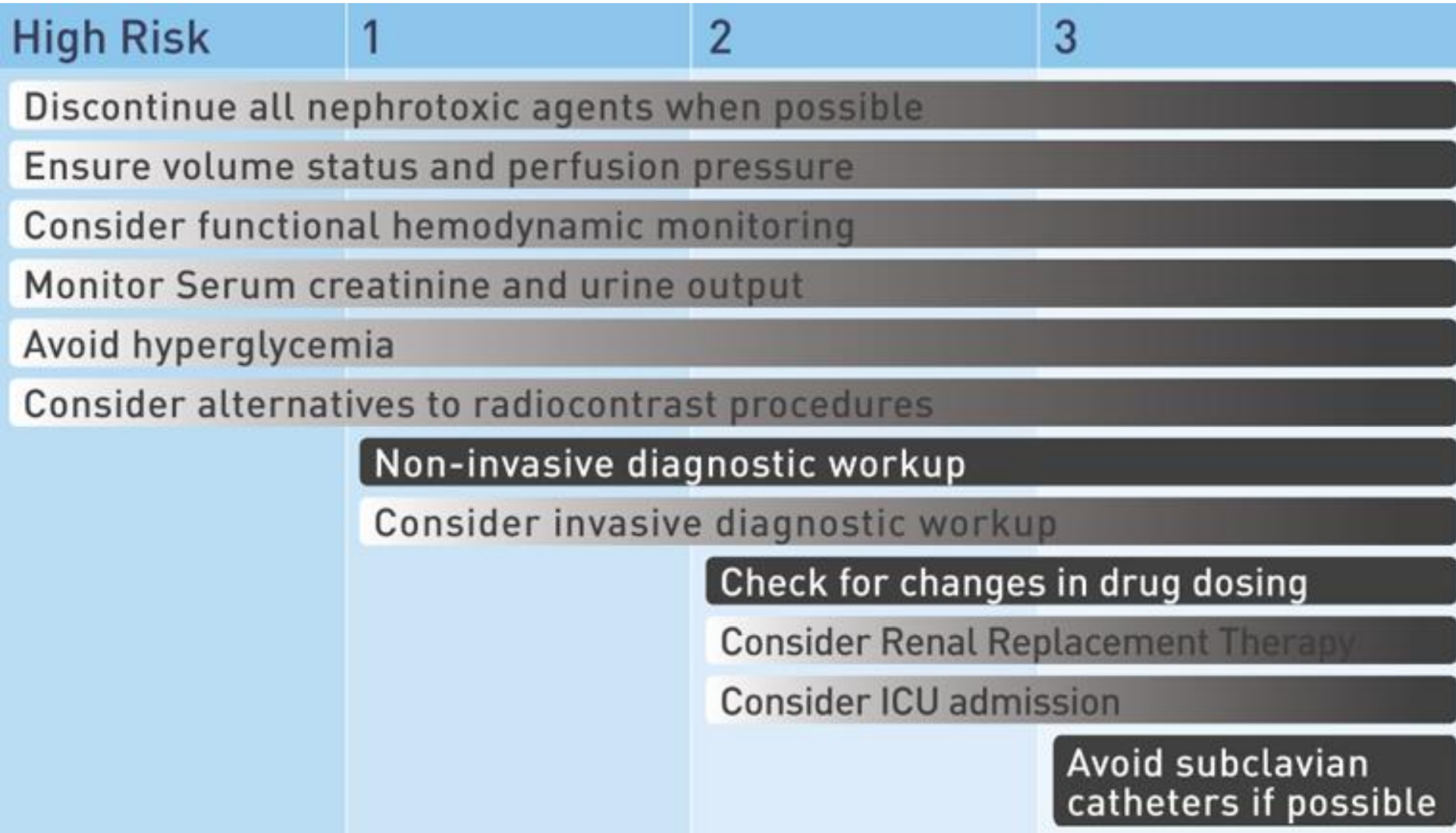
- ☐ Volume overload (not yet life-threatening)
- ☐ Anticipate worsening renal function
- ☐ Hyperkalemia (but K<6)
- ☐ Other: _____

No RRT

Reasons for NOT starting RRT against SCAMP recommendation:

- ☐ Could hasten demise
- ☐ Not consistent with goals of care
- ☐ Expected renal recovery because: _____
- ☐ Futile, because:
  - ☐ No meaningful chance of recovery from non-renal illness:
    - ☐ Metastatic cancer
    - ☐ Overwhelming sepsis
    - ☐ Overwhelming lactic acidosis
  - ☐ Profound, irreversible neurologic impairment
  - ☐ Other: _____
- ☐ Other: _____

	Indication to continue RRT	Indication to discontinue RRT
Urine output	☐ <500 mL/24 hr	☐ >500 mL/24 hr
	↓	↓
	If checked *SCAMP recommends to:*	**If checked** *SCAMP recommends to:*
Please CIRCLE your plan:	**Continue RRT**	**Discontinue RRT**
	Reasons for continuing RRT if SCAMP recommends discontinuing:	**Reasons for discontinuing RRT if SCAMP recommends continuing:**
	☐ Remains volume overloaded ☐ Worsening creatinine ☐ Remains uremic ☐ I do not agree with SCAMP recommendation because: _____ _____ ☐ Other: _____	☐ Medical futility ☐ I do not agree with SCAMP recommendation because: _____ ☐ Other: _____


High Risk
1
2
3
Discontinue all nephrotoxic agents when possible
Ensure volume status and perfusion pressure
Consider functional hemodynamic monitoring
Monitor Serum creatinine and urine output
Avoid hyperglycemia
Consider alternatives to radiocontrast procedures
Non-invasive diagnostic workup
Consider invasive diagnostic workup
Check for changes in drug dosing
Consider Renal Replacement Therapy
Consider ICU admission
Avoid subclavian catheters if possible

AKI Treatment Summary

Perfusion – IVF, diuretics, inotropes

Underlying cause – remove, reverse, treat

Monitor – volume status, electrolytes, urine

Prevent complications – volume overload, electrolytes, medication adjustment

Objectives

1. Define AKI – KDIGO Classification
2. Incidence and consequences of AKI
3. Causes of AKI and workup
4. Prevention of AKI
5. Treatment of AKI
6. Cases

Case Cardio-Renal Syndrome

65 yo gentleman with long standing HTN admitted for ADHFpEF and 10 kg weight gain. Creatinine 1.8 and eGFR 49. He is treated with high dose loop diuretics with a loss of 5 kg and stable eGFR. On day 4 his creatinine was noted to be 2.5 and diuretics were discontinued. The next day his creatinine was 3.0

Cardiorenal Syndromes

Definition – Negative effects of heart or kidney dysfunction on the other organ

CRS 1 - rapid worsening of cardiac function leading to AKI

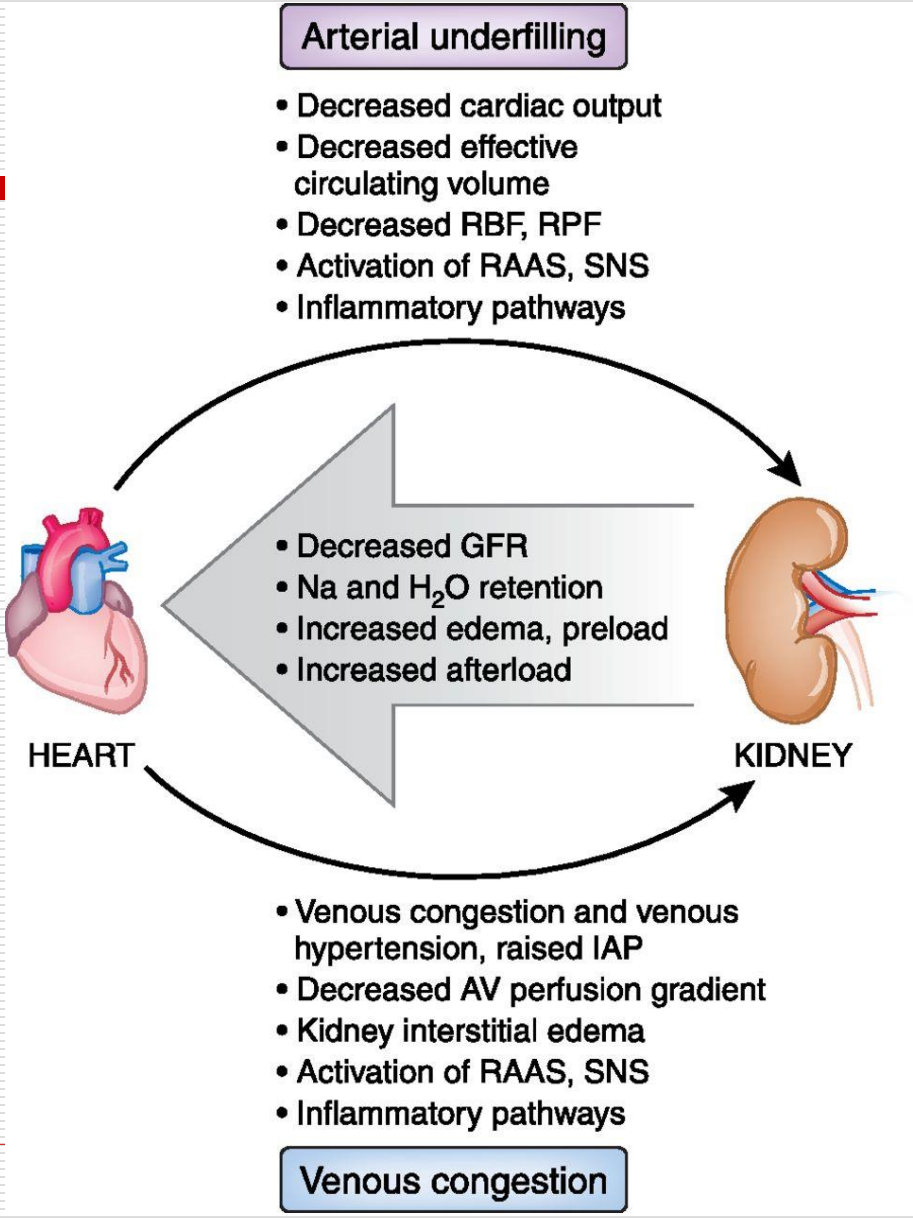
CRS 2 – chronic cardiac dysfunction leads to CKD

CRS 3 – AKI leads to cardiac dysfunction

CRS 4 – CKD and cardiovascular disease

CRS 5 – Systemic illness affecting heart and kidney

Dual hemodynamic pathways for acute cardiorenal syndrome.



House A A CJASN 2013;8:1808-1815

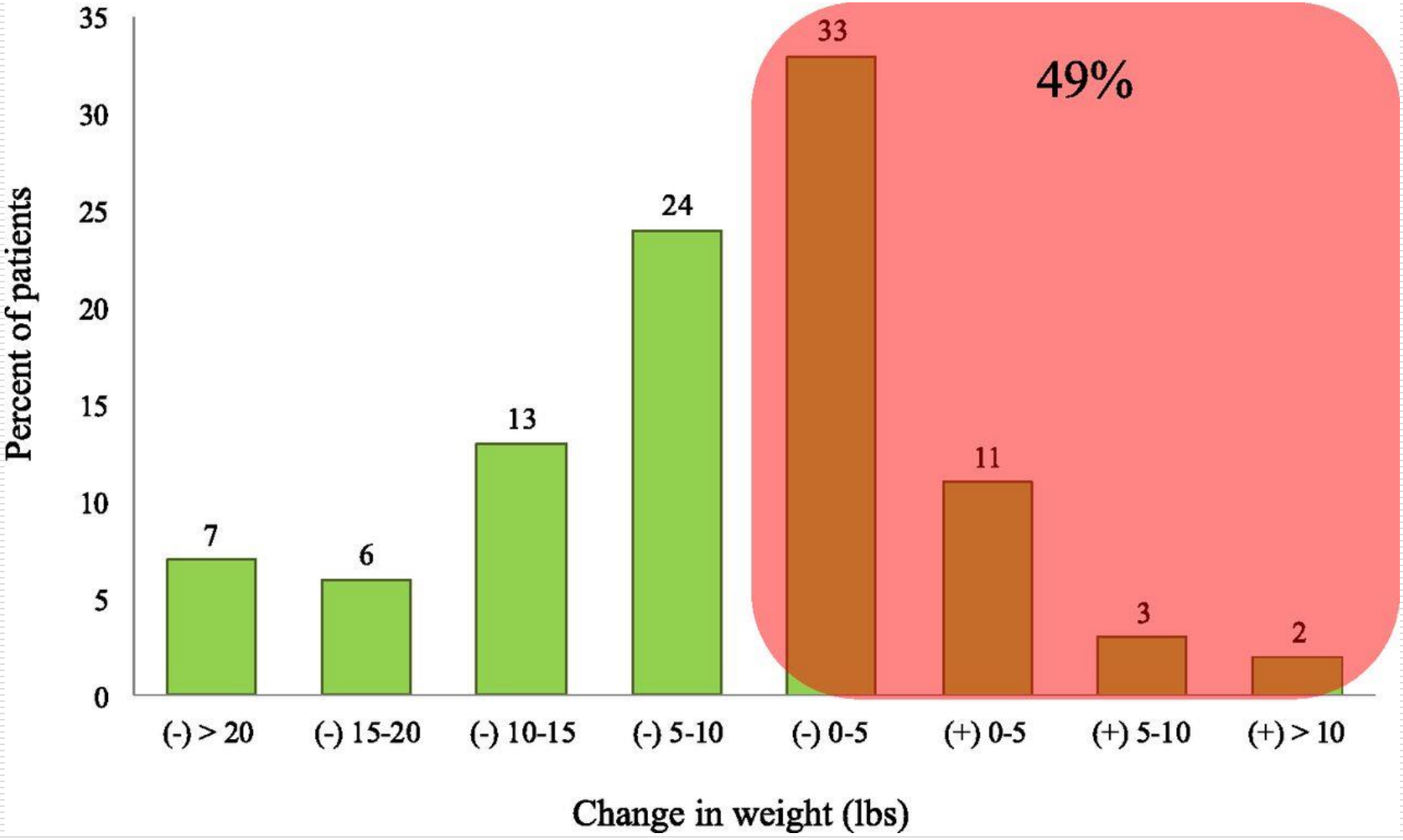
Case CRS

High percentage of CKD with ADHF (30-40%)

AKI is called worsening renal function (WRF) in CHF literature and uses same KDIGO criteria and associated with increased mortality

Most patients with ADHF are under diuresed

Change in body weight at discharge based on Acute Decompensated Heart Failure National Registry database.



Kazory A CJASN 2013;8:1816-1828

CRS Patterns of AKI

1. AKI on admission improving with treatment

2. AKI which worsens daily from admission Flash pulmonary edema

3. Stable GFR which worsens as diuresis progresses

CRS Case

Our patient has pattern 3.

75% of these patient have high RAP and may also have low MAP

The venous congestion leads to AKI and treatment is decongestion (diuresis)

Typically eGFR improves as patient is diuresed

Case HRS

31 yo man with a hx of "psychiatric disease" is admitted for recent onset of jaundice, weakness and swelling

Hx of heavy ETOH use over the past several years. + peripheral edema. Liver large and tender. No abdominal tenderness

Last drink 1 week ago

Case HRS

Labs: ALT and AST 5X nl ALT/AST ratio 2, bilirubin 49, albumin 2.5, and INR 1.4. WBC 20K

Creatinine 1.4 on admission rising to 3 over several days. UA – negative except bilirubin

He makes < 0.3 ml/kg/hr urine

US ABD – minimal ascites, no hydronephrosis

Box 1. Diagnostic criteria of hepatorenal syndrome (HRS) type of acute kidney injury (AKI) in patients with cirrhosis

HRS-AKI

- Diagnosis of cirrhosis and ascites
- Diagnosis of AKI according to ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g per kg of body weight
- Absence of shock
- No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc.)
- No macroscopic signs of structural kidney injury*, defined as:
  - absence of proteinuria (>500 mg/day)
  - absence of microhaematuria (>50 RBCs per high power field),
  - normal findings on renal ultrasonography

*Patients who fulfil these criteria may still have structural damage such as tubular damage. Urine biomarkers will become an important element in making a more accurate differential diagnosis between HRS and acute tubular necrosis.

ICA, International Club of Ascites; NSAIDs, non-steroidal anti-inflammatory drugs; RBCs, red blood cells.

Table 2. International Club of Ascites (ICA-AKI) new definitions for the diagnosis and management of AKI in patients with cirrhosis.

Subject	Definition		
Baseline sCr	A value of sCr obtained in the previous 3 months, when available, can be used as baseline sCr. In patients with more than one value within the previous 3 months, the value closest to the admission time to the hospital should be used. In patients without a previous sCr value, the sCr on admission should be used as baseline.		
Definition of AKI	• Increase in sCr ≥0.3 mg/dl (≥26.5 μmol/L) within 48 hours; or, • A percentage increase sCr ≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days		
Staging of AKI	• **Stage 1**: increase in sCr ≥0.3 mg/dl (26.5 μmol/L) or an increase in sCr ≥1.5-fold to 2-fold from baseline • **Stage 2**: increase in sCr >2-fold to 3-fold from baseline • **Stage 3**: increase of sCr >3-fold from baseline or sCr ≥4.0 mg/dl (353.6 μmol/L) with an acute increase ≥0.3 mg/dl (26.5 μmol/L) or initiation of renal replacement therapy		
Progression of AKI	**Progression** Progression of AKI to a higher stage and/or need for RRT	**Regression** Regression of AKI to a lower stage	
Response to treatment	**No response** No regression of AKI	**Partial response** Regression of AKI stage with a reduction of sCr to ≥0.3 mg/dl (26.5 μmol/L) above the baseline value	**Full response** Return of sCr to a value within 0.3 mg/dl (26.5 μmol/L) of the baseline value

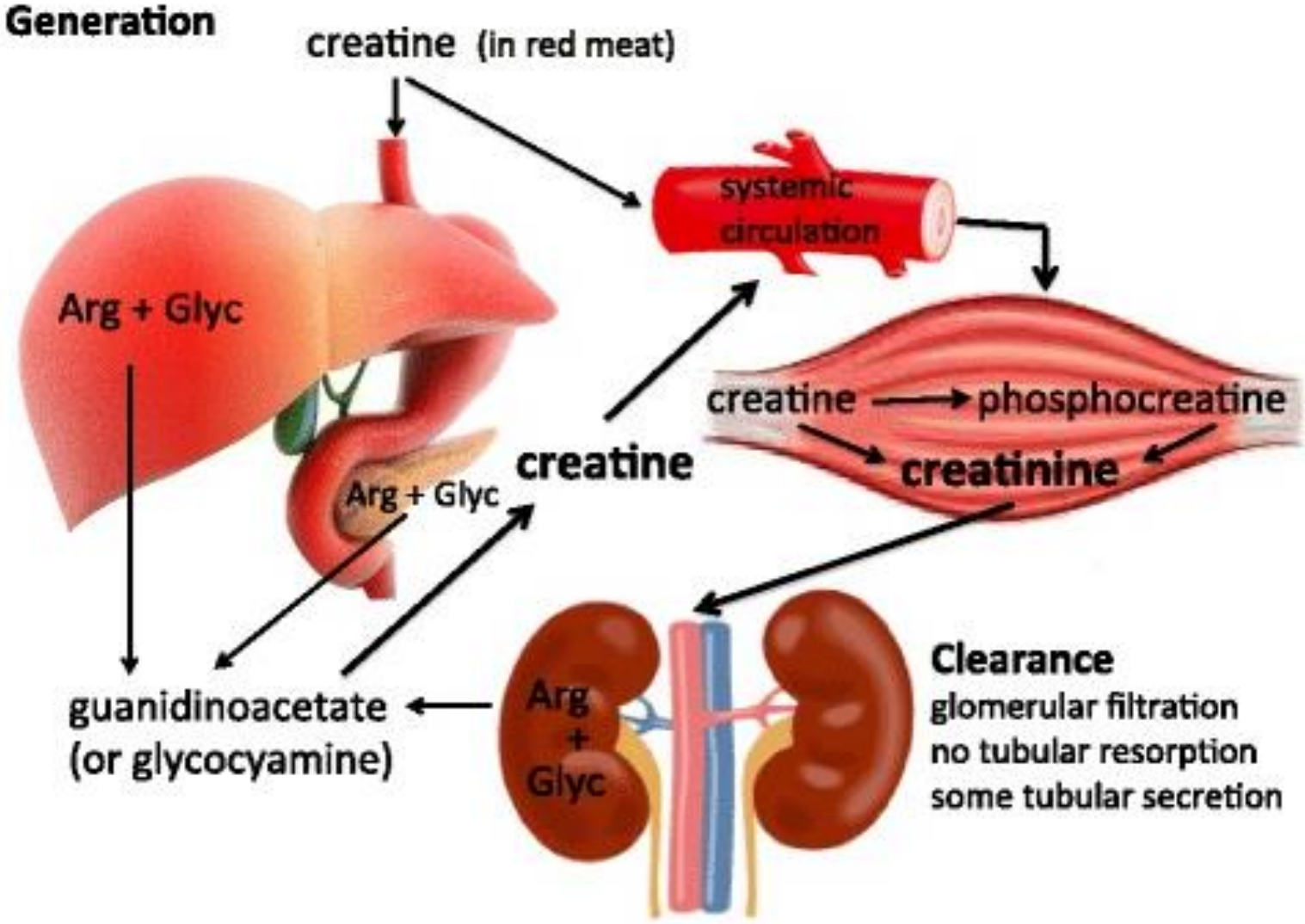
AKI, acute kidney injury; RRT, renal replacement therapy; sCr, serum creatinine.

Assessing kidney function in pts with cirrhosis

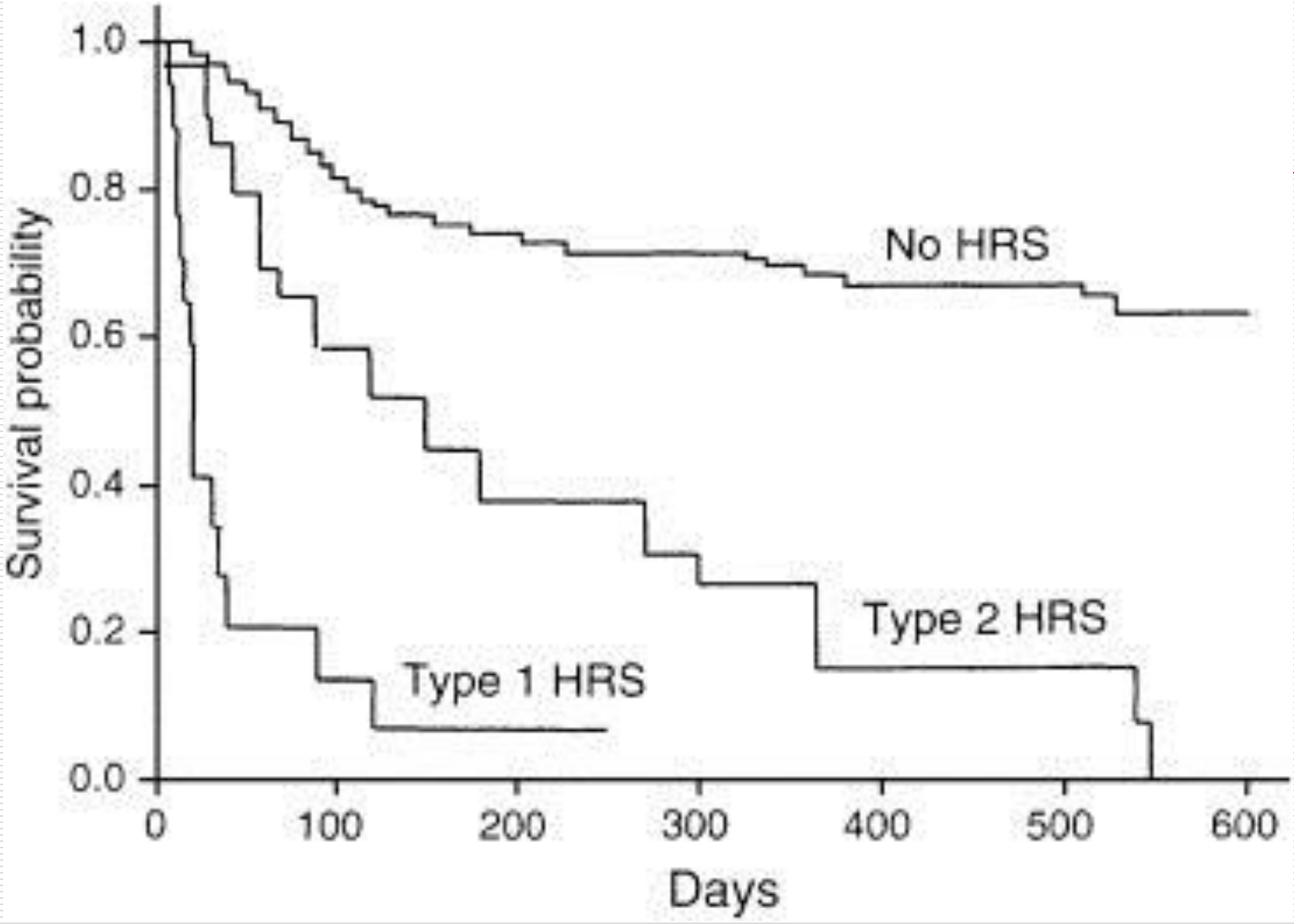
Serum creatinine levels should be used to estimate GFR in cirrhosis with the following conditions:

- There is decreased muscle and hepatic production of creatinine. Malnutrition
- The edematous state that complicates end-stage liver disease leads to large distribution of Cr in the body and lower serum Cr concentration
- Formula that use creatinine to estimate GFR will overestimate
- Cystatin C has same problems

Proulx et al. Nephrology Dialysis Transplantation 2005

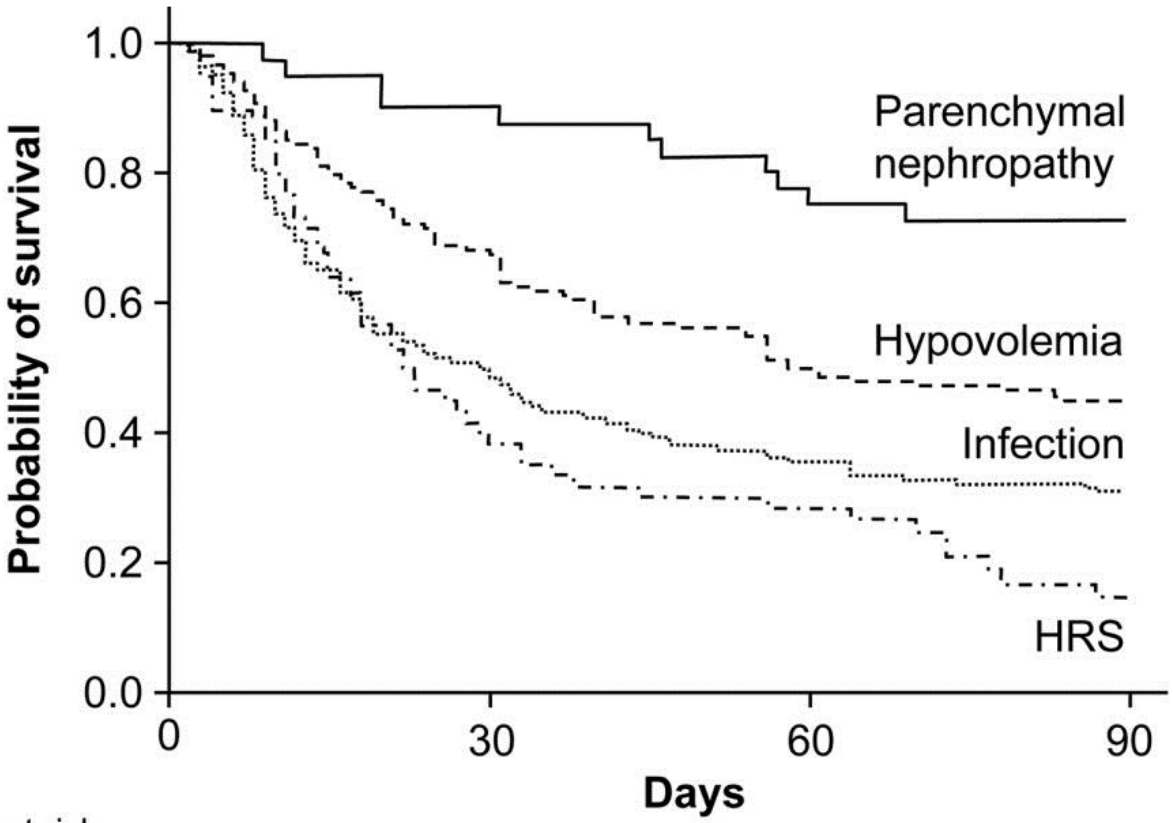


Generation and clearance of creatinine. *Arg* arginine, *Glyc* glycine



Munoz S. Medical Clinics of North America July 2008

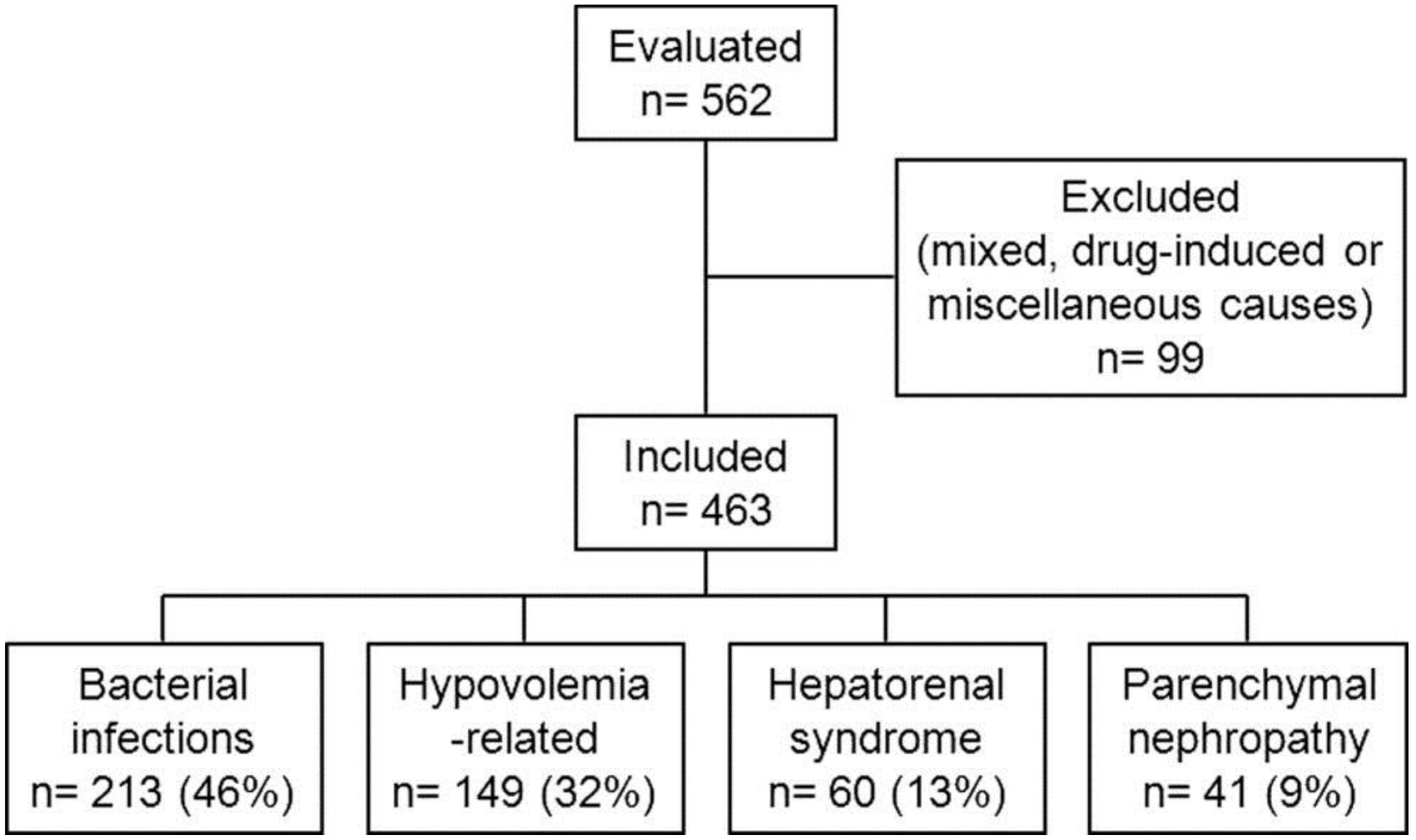
Causes & Outcomes of Renal Failure



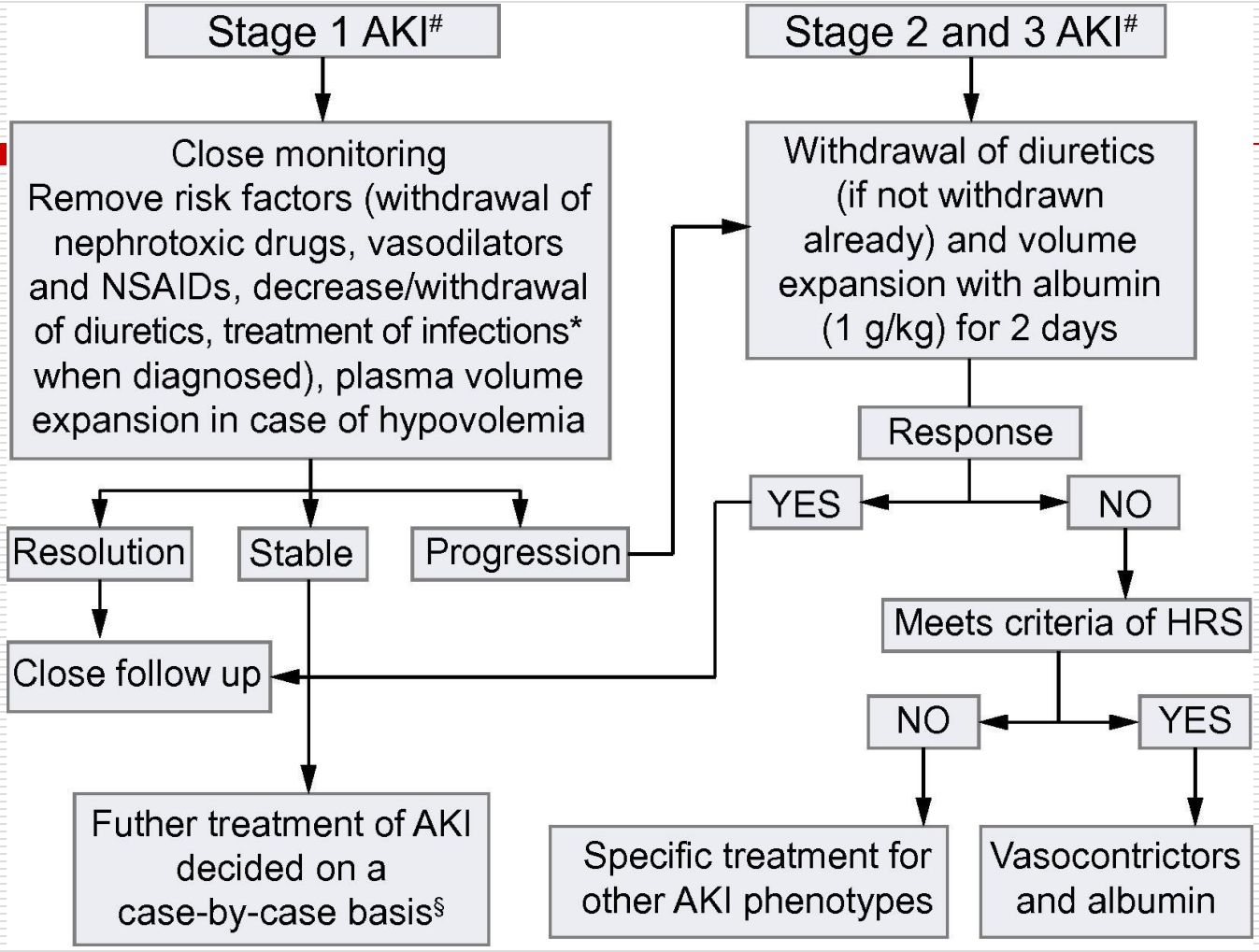
Patients at risk				
- Parenchymal nephropathy	41	36	31	29
- Hypovolemia	149	98	70	62
- Infection	213	96	65	53
- HRS	60	24	16	7

Martin-Llahi et al, *Gastroenterology* 2011

Causes & Outcomes of Renal Failure



Martin-Llahi et al, *Gastroenterology* 2011


Stage 1 AKI#
Stage 2 and 3 AKI#
Close monitoring
Remove risk factors (withdrawal of nephrotoxic drugs, vasodilators and NSAIDs, decrease/withdrawal of diuretics, treatment of infections* when diagnosed), plasma volume expansion in case of hypovolemia
Withdrawal of diuretics (if not withdrawn already) and volume expansion with albumin (1 g/kg) for 2 days
Response
YES
NO
Resolution
Stable
Progression
Close follow up
Meets criteria of HRS
NO
YES
Futher treatment of AKI decided on a case-by-case basis§
Specific treatment for other AKI phenotypes
Vasocontrictors and albumin

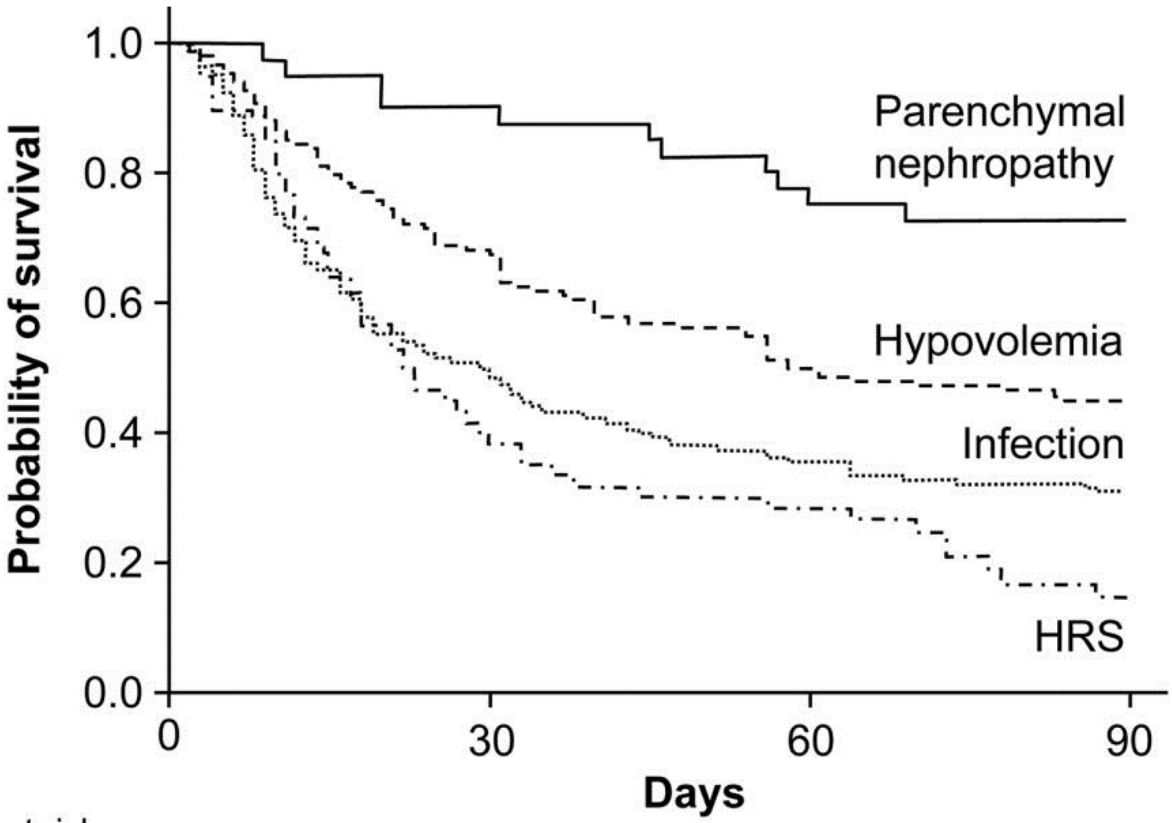
Acute Kidney Injury in Cirrhosis

Nearly 50% of patients with cirrhosis develop AKI

Causes

- Pre-renal
- Renal
- Post-renal

Causes & Outcomes of Renal Failure



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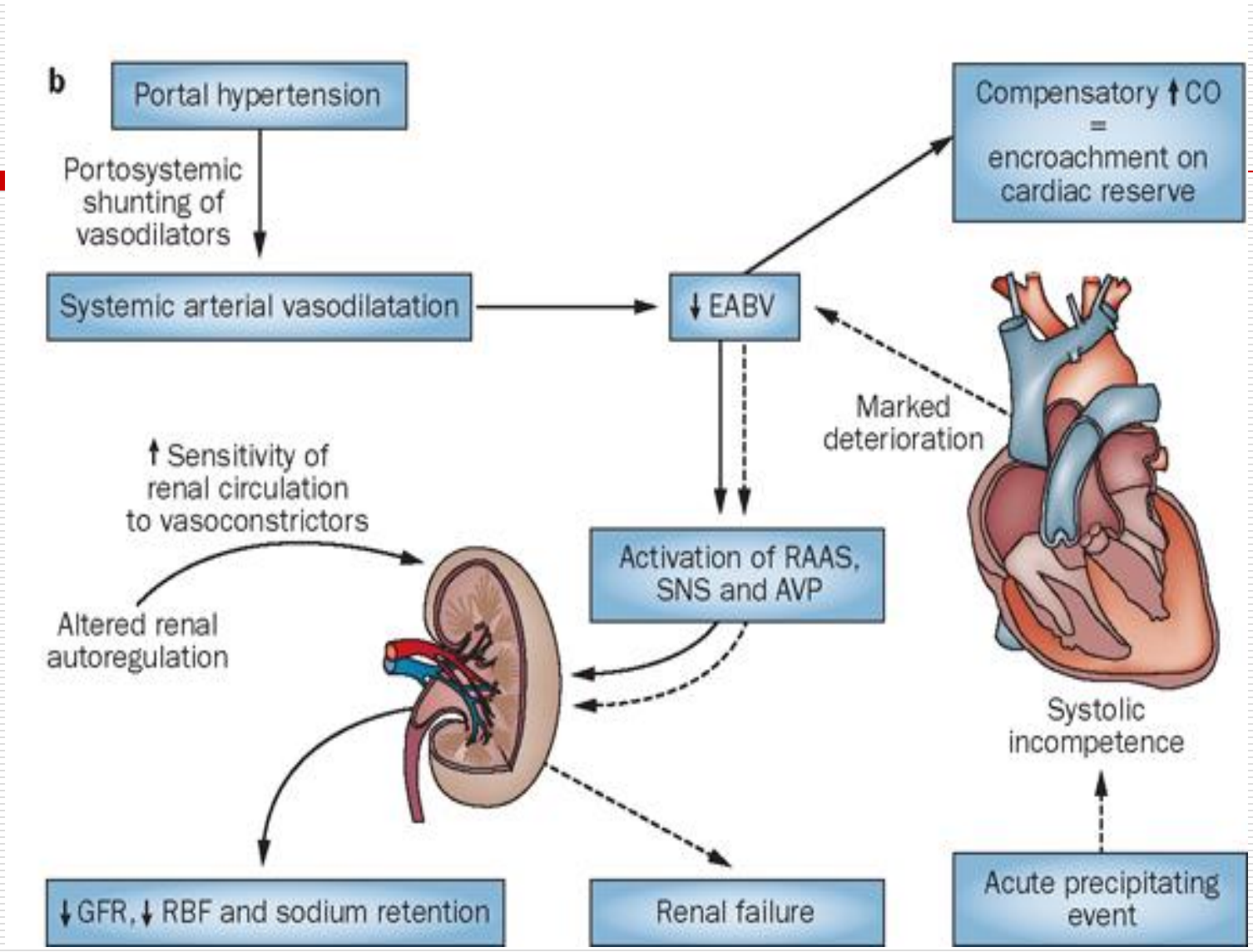
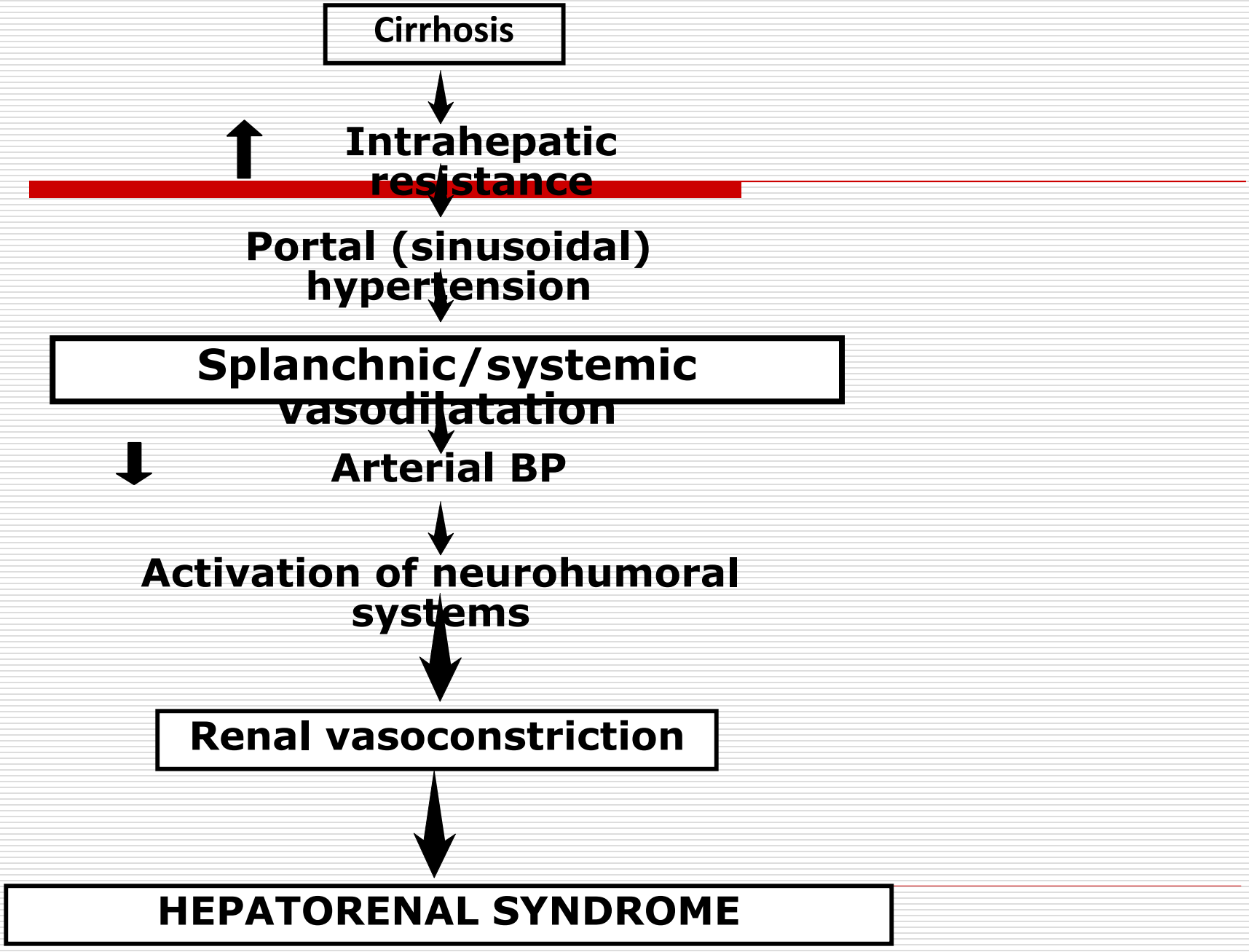
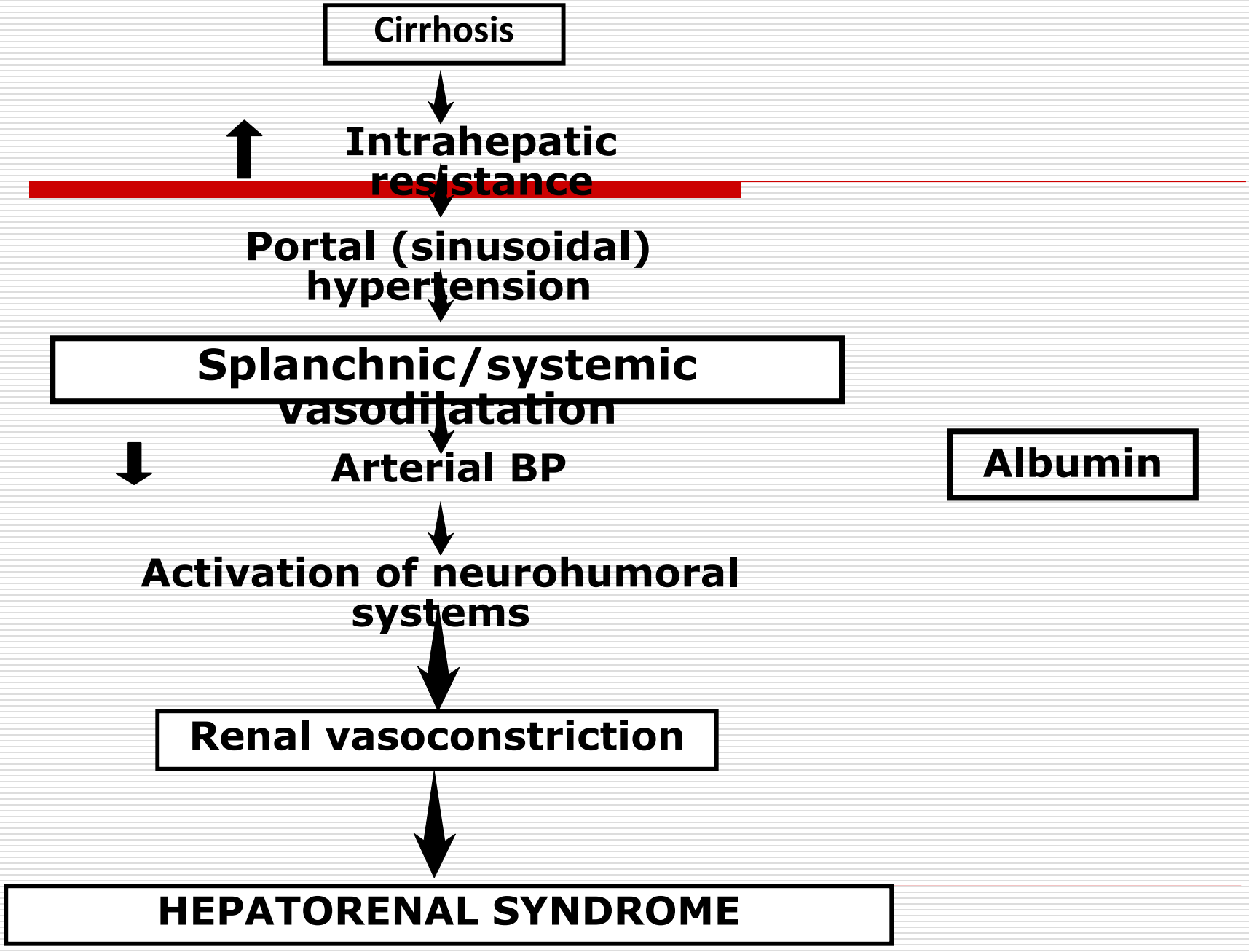


Wong F. Nat Rev. Gastoenterol 2012


Cirrhosis
Intrahepatic resistance
Portal (sinusoidal) hypertension
Splanchnic/systemic vasodilatation
Arterial BP
Activation of neurohumoral systems
Renal vasoconstriction
HEPATORENAL SYNDROME


Cirrhosis
Intrahepatic resistance
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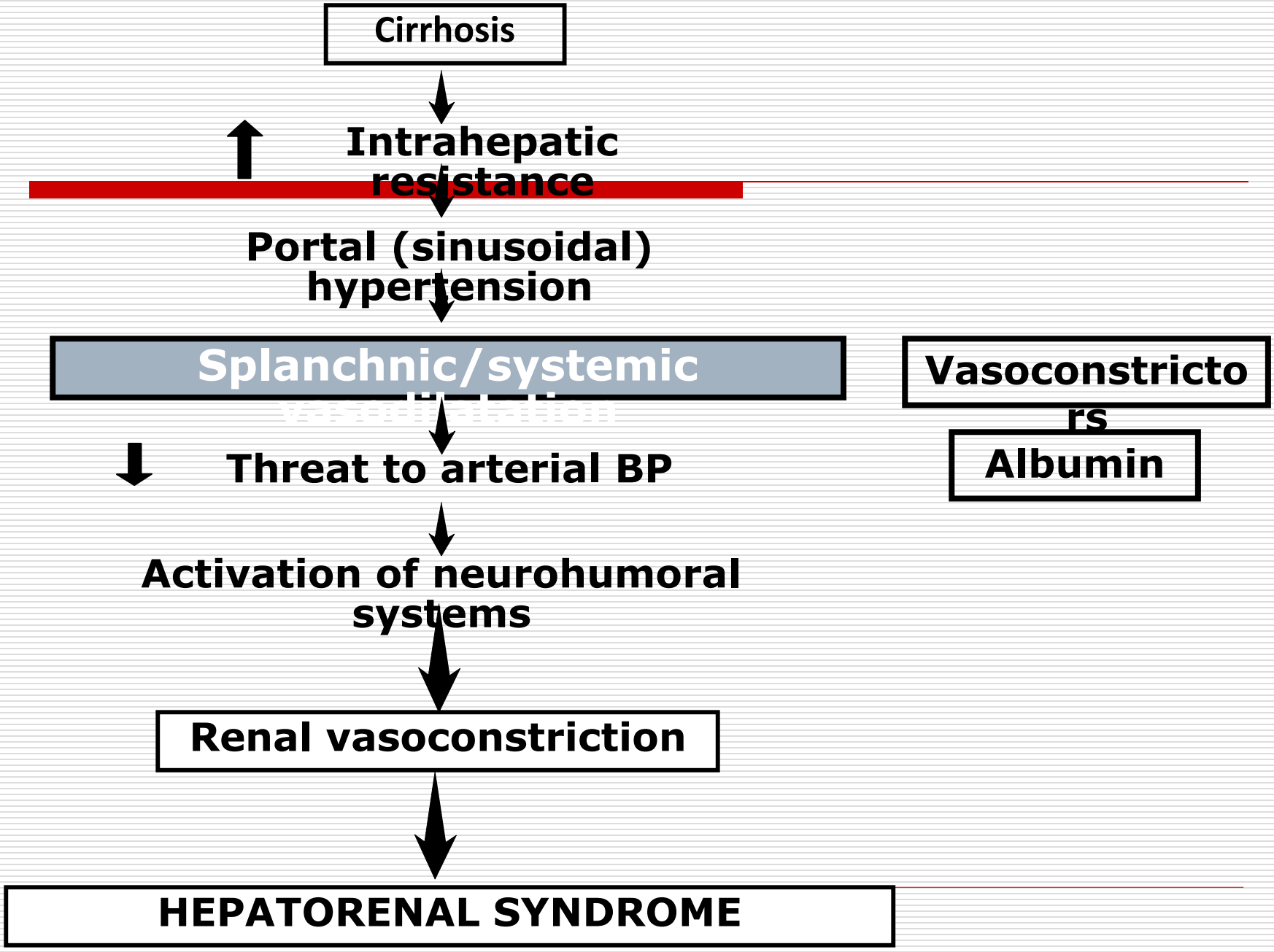
Arterial BP
Albumin
Activation of neurohumoral systems
Renal vasoconstriction
HEPATORENAL SYNDROME


Cirrhosis
Intrahepatic resistance
Portal (sinusoidal) hypertension
Splanchnic/systemic vasodilatation
Threat to arterial BP
Activation of neurohumoral systems
Renal vasoconstriction
HEPATORENAL SYNDROME
Vasoconstrictors
Albumin

ICU Management of HRS

1. Norepinephrine titrated to raise MAP >15
2. Octreotide and albumin used as adjuncts
3. Vasopressin has been used but in doses 10X septic shock doses. (Associated with complications)

Floor Management of HRS

1. Midodrine 7.5 mg PO TID, up to 15 mg PO TID
2. Octreotide 100 µg SC TID, up to 200 µg SC TID
3. Rapidly titrate to obtain increase in MAP ≥15 mmHg
4. Albumin (maintenance) 1 gm/kg/d X 48 hrs then 25-50 g/day
   - Discontinue if serum albumin >4.0 g/dL

Management of HRS

1. Stop treatment if no reduction in sCRE after 3 days or not <50% by day 7 of highest dose
   - ?Norepinephrine infusion if floor protocol fails
2. If response, continue until Cr <1.5 mg/dL or 14 days

HRS Prevention

Avoidance of nephrotoxins

IV diuretics only with peripheral edema + ascites

High volume paracentesis with SPA (8gm/liter removed)

Prophylactic antibiotics (quinolone) in high risk (low Na, increased creatinine, increased bilirubin with ascites albumin of < 1.5 gm/dl

Treatment of SBP

Summary

- HRS1 is a disease that has a high mortality
- If a liver transplant candidate, treatment is warranted (does not worsen outcomes)
- If not a transplant candidate, evaluate for reversible liver disease
- If no reversible liver disease, shared decision making regarding level of care
- Therapy is directed toward the pathophysiology of the syndrome

Case

Our patient developed progressive AKI

He was not a liver transplant candidate due to lack of abstinence – no RRT

He did not have acute hepatitis B – no RRT

He did have acute alcoholic hepatitis with a chance of reversibility – trial of RRT

Summary

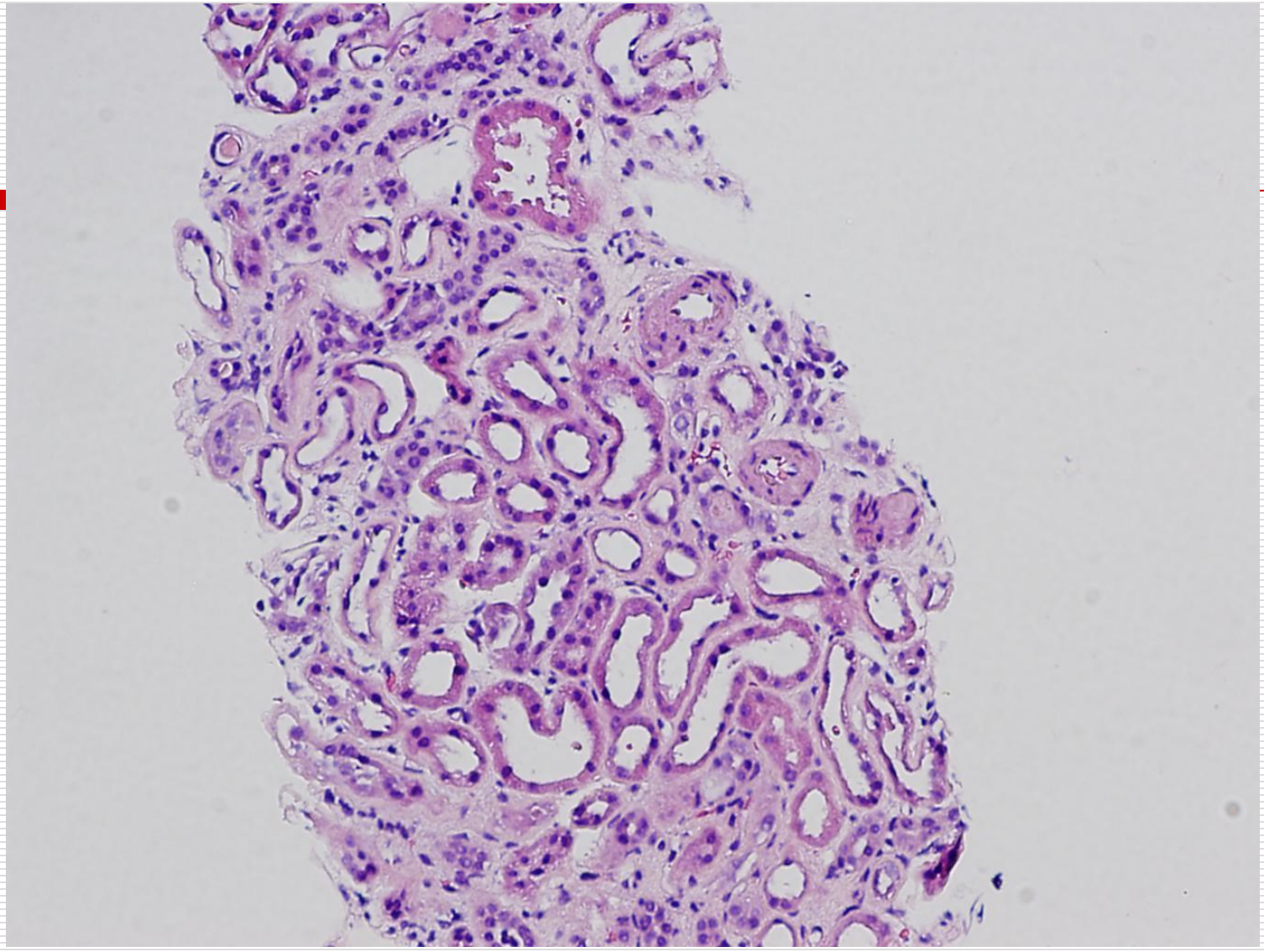
- HRS1 is a disease that has a high mortality
- If a liver transplant candidate, treatment is warranted (does not worsen outcomes)
- If not a transplant candidate, evaluate for reversible liver disease
- If no reversible liver disease, shared decision making regarding level of care
- Therapy is directed toward the pathophysiology of the syndrome

AKI Summary

Using a standard definition improves recognition

AKI leads to worse short term and long term outcomes

AKI is a predictor of severity of illness



ATN, H&E.