CITIZENS HOSPITAL
Hyderabad
Defining Healthcare

Acute Kidney Injury

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Topics covered:

- Definitions
- Pathophysiology in brief
- Special investigations
- Preventive strategies
- Approach

Definition

" Abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes"

> 30 definitions available in literature

NCEPOD Findings & Recommendations :

FINDINGS:

- 50% of cases with AKI documented as cause of death received satisfactory or good care
- 30% of cases inadequately investigated and managed
- 20% of post-admission AKI is predictable and avoidable (or hospital acquired AKI = HAAKI)

Recommendations:

- All emergency admissions should have electrolytes checked on admission and appropriately thereafter
- All acute admissions should receive adequate senior reviews, with consultant review within 12 hours of admission
- Implementation of ***NICE guidance CG50***

Why ?

- Associated with increased hospital stay, morbidity/ mortality , cost
- Preventable if detected & preventive measures taken
- Protocols should be implemented from ER level
- Reversible if identified & treated on time

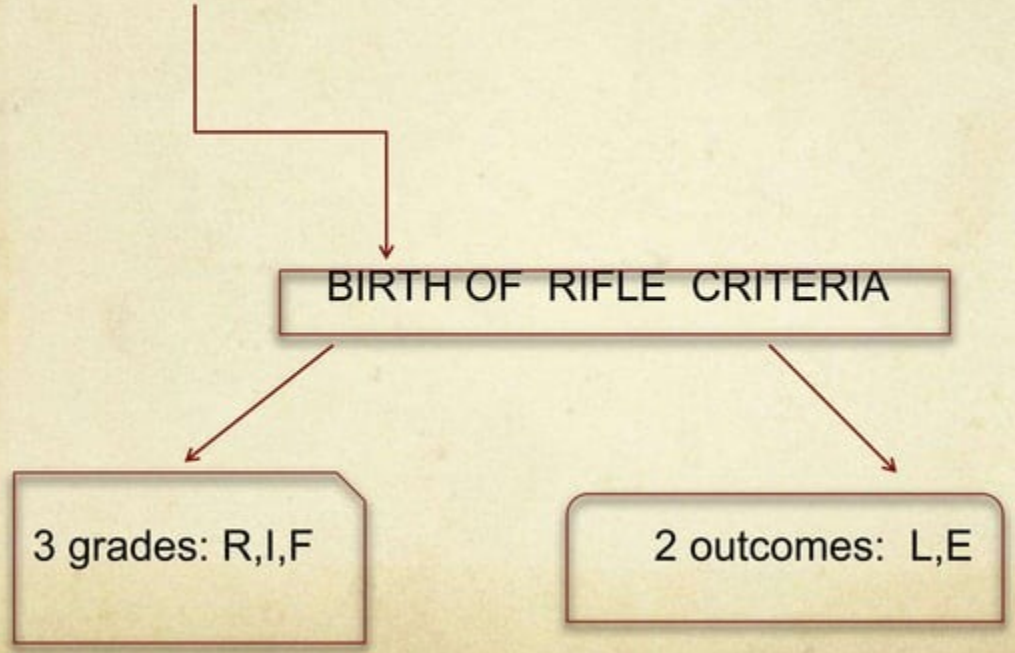
Epidemiology:

- ≈ 10 % in hospitalized patients
- ≈70% in critically ill patients
- 5-6% ICU patients require RRT



Beginning of definitions:

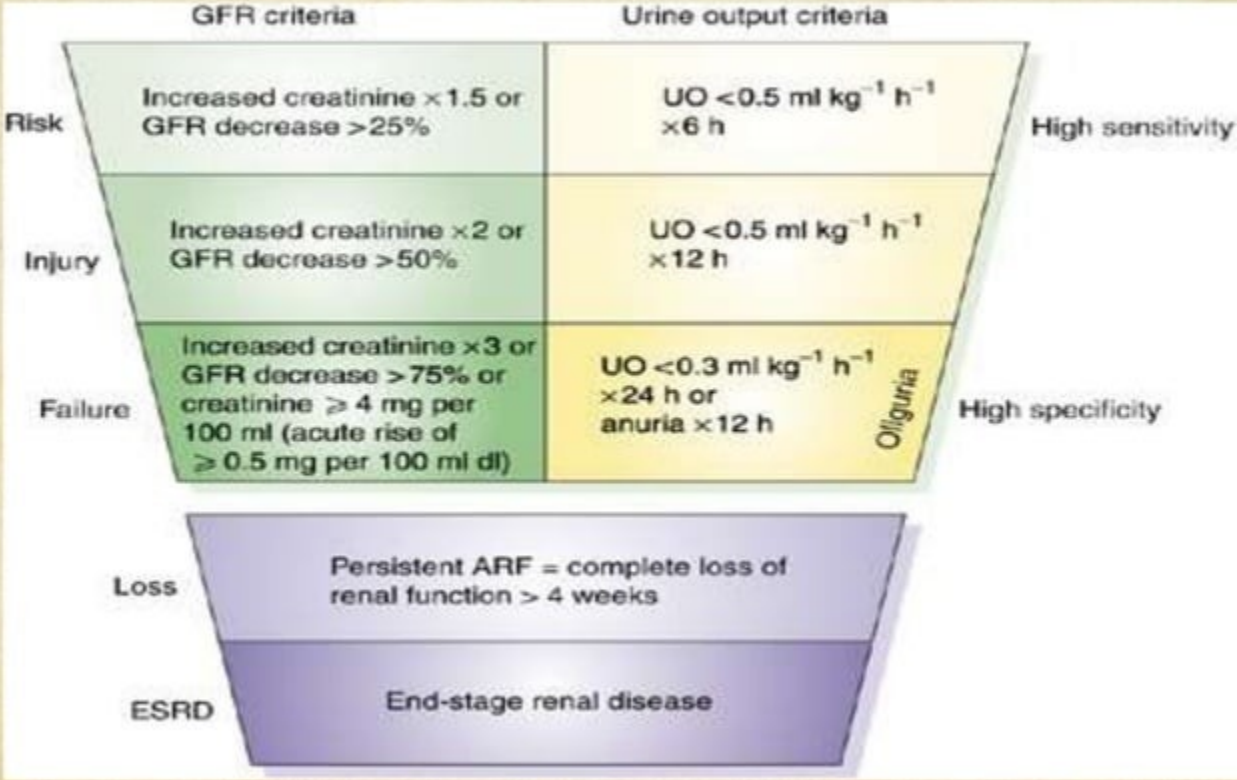
- ***ADQI (2002)***: To create consensus & evidence based guidelines for prevention & treatment of AKI



RIFLE criteria for diagnosis of AKI based on The "Acute Dialysis Quality Initiative" (2002):

	Increase in S_{Cr}	Urine output
Risk of renal injury	0.3 mg/dl increase	< 0.5 ml/kg/hr for > 6 h
Injury to the kidney	2 X baseline	< 0.5 ml/kg/hr for >12h
Failure of kidney function	3 X baseline OR > 0.5 mg/dl increase if S_{Cr} >=4 mg/dl	Anuria for >12 h
Loss of kidney function	Persistent renal failure for > 4 weeks	
End-stage disease	Persistent renal failure for > 3 months	

Am J Kidney Dis. 2005 Dec;46(6):1038-48


GFR criteria
Urine output criteria
Risk
Increased creatinine ×1.5 or GFR decrease >25%
UO <0.5 ml kg⁻¹ h⁻¹ ×6 h
High sensitivity
Injury
Increased creatinine ×2 or GFR decrease >50%
UO <0.5 ml kg⁻¹ h⁻¹ ×12 h
Failure
Increased creatinine ×3 or GFR decrease >75% or creatinine ≥ 4 mg per 100 ml (acute rise of ≥ 0.5 mg per 100 ml dl)
UO <0.3 ml kg⁻¹ h⁻¹ ×24 h or anuria ×12 h
Oliguria
High specificity
Loss
Persistent ARF = complete loss of renal function > 4 weeks
ESRD
End-stage renal disease

Definition of Acute Kidney Injury (AKI) based on "Acute Kidney Injury Network" (2004):

Stage	Increase in Serum Creatinine	Urine Output
1	1.5-2 times baseline **OR** 0.3 mg/dl increase from baseline	<0.5 ml/kg/h for >6 h
2	2-3 times baseline	<0.5 ml/kg/h for >12 h
3	3 times baseline **OR** 0.5 mg/dl increase if baseline>4mg/dl **OR** Any RRT given	<0.3 ml/kg/h for >24 h **OR** Anuria for >12 h

RIFLE *vs* AKIN:

- RIFLE: 7 days, AKIN: 48 hours
- AKIN doesn't entertain GFR
- In AKIN: patient investigated after volume resuscitation and ruling out post renal obstruction
- Can determine outcome in RIFLE

KDIGO definition (2012)

AKI is defined as any of the following :

- Increase in Creat by > 0.3 mg/dl (X26.5 mol/l) within 48 hours; or
- Increase in Creat to > 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume < 0.5 ml/kg/h for 6 hours

KDIGO staging:

Stage	Serum creatinine	Urine output
1	1.5-1.9× baseline OR >0.3 mg% ↑	<0.5 ml/kg/hr for 6-12 hrs
2	2-2.9× baseline	<0.5 ml/kg/hr > 12 hrs
3	3 times baseline OR RRT OR < 18 yrs, GFR < 35 ml/min for 1.73 m^2	<0.3 ml/kg/hr > 24 hrs OR Anuria > 12 hrs

Risk index for developing AKI in the peri-operative patient

RISK FACTORS
Age >56
Male
Active Congestive cardiac failure
Presence of ascites
Hypertension
Emergency Surgery
Intra-peritoneal surgery
pre-renal dysfunction
Diabetes Mellitus

Table 4: Other risk factors for AKI

PATIENT FACTORS	ANAESTHETIC FACTORS	SURGICAL FACTORS
Age	Peri-operative hypotension	Prolonged surgery
Gender	Blood product administration	Major surgery
Co-morbidities	Drugs	Cardiothoracic surgery
Hypovolaemia		Transplant surgery
Sepsis		Immunosuppressant therapy
		Aortic clamping
		Significant 3rd space losses

Pathophysiology:

- Endothelial injury
- Nephrotoxins
- Deranged autoregulation
- Inflammatory mediators

Prerenal Azotemia :

- **Intravascular volume depletion**

  bleeding, GI loss, Renal loss, Skin loss, Third space loss

- **Decreased cardiac output**

  CHF

- **Renal vasoconstriction**

  Liver Disease, Sepsis, Hypercalcemia

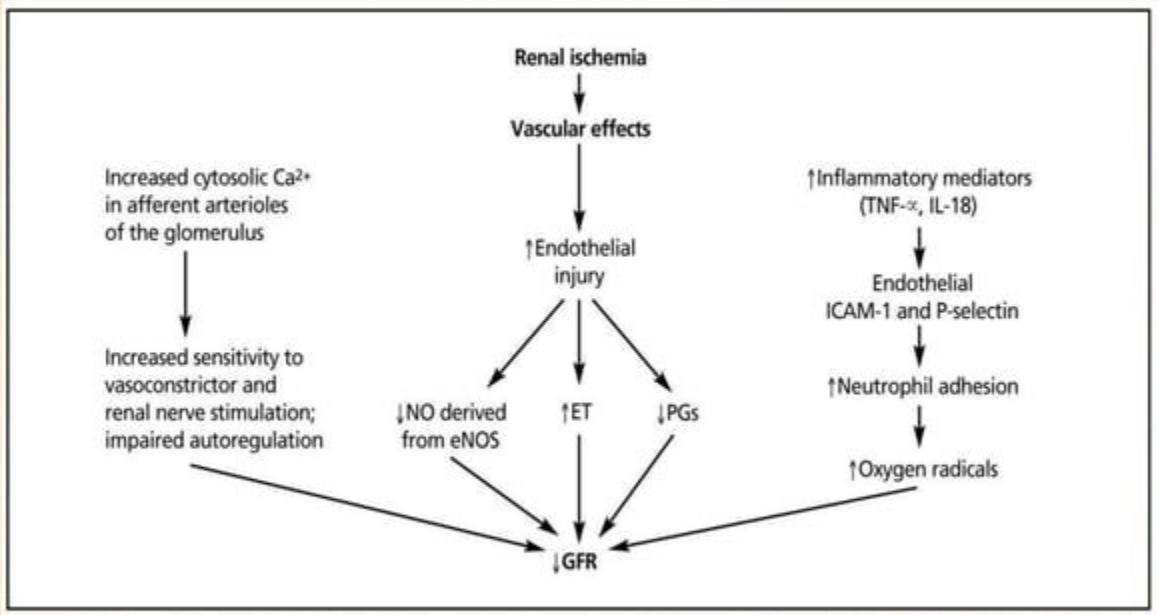
- **Pharmacologic impairment of autoregulation and GFR in specific settings**

  ACE inhibitors, ARBs, NSAIDS, Aminoglycosides

Renal causes:

- Tubule: ATN (ischemic, toxins)
- Interstitium: AIN (Drug, infection, neoplasm)
- Glomerulus: AGN(primary, infection, rheumatologic, vasculitis)
- Vasculature: Embolic, livedo reticularis, eosinophiluria, hypocomplementemia

Mechanisms of acute kidney injury: a molecular viewpoint.



Lattanzio M R , and Kopyt N P J Am Osteopath Assoc 2009;109:13-19

Published by American Osteopathic Association

THE JOURNAL of the AMERICAN OSTEOPATHIC ASSOCIATION

General guidelines for differentiating the etiology of acute kidney injury (ie, prerenal vs renal) using laboratory studies.

Indices	Prerenal	Renal
Blood urea nitrogen to creatinine ratio	>20	<20
Fraction of filtered sodium, %	<1	>2
Fractional excretion of urea, %	<35	>35
Urine osmolality, mOsm/L	>500	<400
Urine sediment, cast type	bland, hyaline	granular
Urine sodium, mEq/L	<20	>40

Lattanzio M R , and Kopyt N P J Am Osteopath Assoc 2009;109:13-19

Published by American Osteopathic Association

THE JOURNAL of the AMERICAN OSTEOPATHIC ASSOCIATION

Urine analysis :

- Unremarkable in pre and post renal causes
- Differentiates ATN vs. AIN. vs. AGN
  - Muddy brown casts in ATN
  - WBC casts in AIN
  - RBC casts in AGN

Can creatinine increase in absence of AKI?

- Inhibition of tubular secretion of creatinine: Trimethoprim, Cimetidine, Probenecid
- False elevation due to interference in lab: Fluocytosine, Ascorbic acid

NEW MARKERS OF AKI

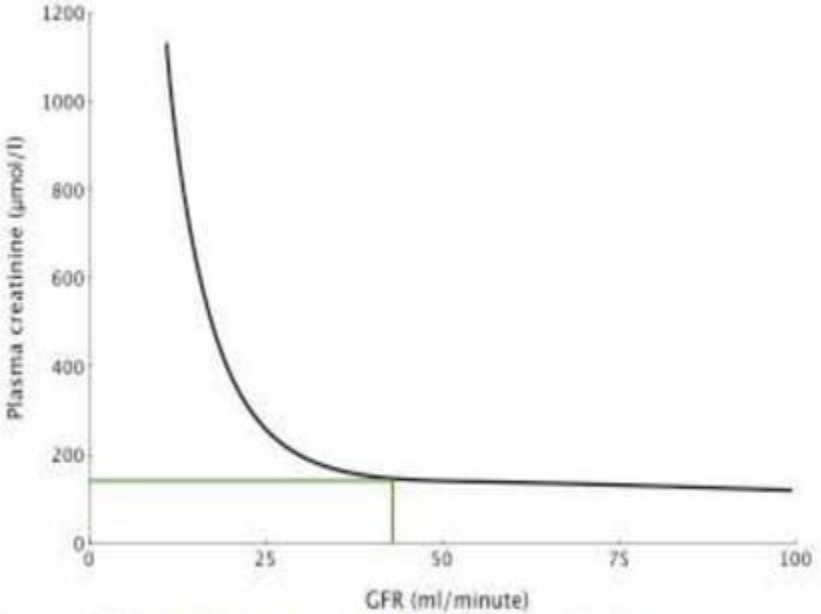


Figure 1: Relationship between plasma creatinine and GFR

NGAL:

- Expressed in proximal and distal nephron
- Binds and transports iron-carrying molecules
- Role in injury and repair
- Rises very early (hours) after injury in animals, confirmed in children having CPB

Range:

- <20 ng/ml: considered normal
- >1200 ng/ml: HIGH

Nephrology (Carlton). 2010 Jun;15(4):419-28. doi: 10.1111/j.1440-1797.2010.01317.x.

Full Text Online WILEY ONLINE LIBRARY

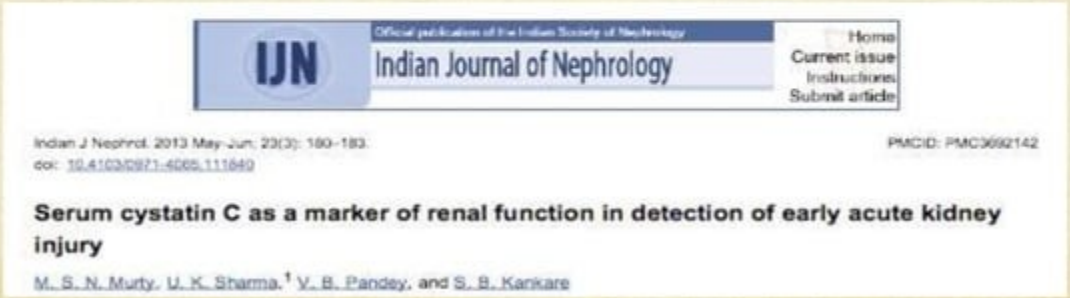
Review: neutrophil gelatinase-associated lipocalin: a troponin-like biomarker for human acute kidney injury.

Devarajan P.

process. However, given the complexity of AKI, additional biomarkers (perhaps a panel of plasma and urinary biomarkers) may eventually need to be developed and validated for optimal progress to occur.

Cystatin C

- Better marker in early detection
- Not affected by age, gender, muscle mass, ethnicity
- Normal level: 0.5-1 mg/L
- Almost 100 times costly, compared to creatinine



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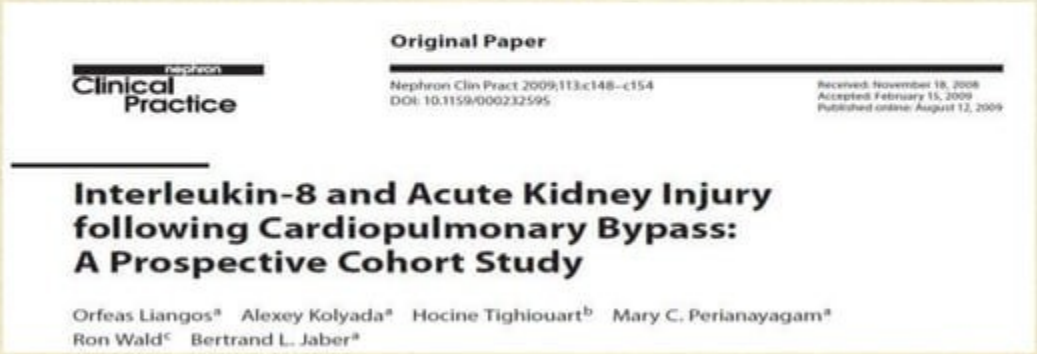
Indian J Nephrol. 2013 May-Jun; 23(3): 180–183.
doi: 10.4103/0971-4065.111849
PMCID: PMC3692142

Serum cystatin C as a marker of renal function in detection of early acute kidney injury

M. S. N. Murty, U. K. Sharma,[1] V. B. Pandey, and S. B. Kankare

IL-18:

- Role in inflammation, activating macrophages and mediates ischemic renal injury
- IL-18 antiserum to animals protects against ischemic AKI
- Studied in several human models



Original Paper

Nephron Clinical Practice

Nephron Clin Pract 2009;113:c148–c154
DOI: 10.1159/000232595

Received: November 18, 2008
Accepted: February 15, 2009
Published online: August 12, 2009

Interleukin-8 and Acute Kidney Injury following Cardiopulmonary Bypass: A Prospective Cohort Study

Orfeas Liangos[a] Alexey Kolyada[a] Hocine Tighiouart[b] Mary C. Perianayagam[a] Ron Wald[c] Bertrand L. Jaber[a]

KIM-1:

- Epithelial transmembrane protein, ?cell-cell interaction.
- Appears to have strong relationship with severity of renal injury

Nephrol Dial Transplant (2009) 1 of 4
doi: 10.1093/ndt/gfp010

NDT
Nephrology Dialysis Transplantation

Editorial Comment

Kidney injury molecule-1 (KIM-1): a urinary biomarker and much more

Joseph V. Bonventre[1]

Initial assessment:

- History
- Medications including contrast
- RFT, CUE
- Volume status
- Color of urine
- ABG
- Imaging

Preventive strategies?

Role of ANP analogues in AKI?

- 61 patients in 2 cardiothoracic ICU with post-op AKI assigned to receive recombinent ANP (50ng/kg/min) or placebo

- The need for RRT before day 21 after development of AKI was significantly lower in ANP group (21% vs 47%)

- The need for RRT or death after day 21 was significantly lower in ANP group (28% vs 57%)

Crit Care Med. 2004 Jun;32(6):1310-5

Diuretic in AKI!

- Converts oliguric AKI into non-oliguric
- Psychological relief
- Better in volume resuscitated patients
- Not associated with improved survival or early recovery

Is there a role for Fenoldopam in prevention or treatment of AKI in ICU setting?

- Dopamine-1 receptor agonist, lack of Dopamine-2, and alpha-1 receptor effect, make it a potentially safer drug than Dopamine!
- Reduces in hospital mortality and the need for RRT in AKI
- Reverses renal hypoperfusion more effectively than renal dose Dopamine
- Studied in cardiothoracic ICU patients, awaiting more powered trials in other groups!

J Cardiothorac Vasc Anesth. 2008 Feb;22(1):23-6.
J Cardiothorac Vasc Anesth. 2007 Dec;21(6):847-50
Am J Kidney Dis. 2007 Jan;40(1):56-68
Crit Care Med. 2006 Mar;34(3):707-14

AKI Care Bundle

Institute in all patients with a 1.5 X rise in creatinine or oliguria (<0.5mls/kg/hr) for >6 hours

This is a Medical Emergency

Full set of physiological observations
Assess for signs of shock/hypoperfusion
If MEWS triggering give oxygen, begin resuscitation and contact critical care outreach team

Fluid therapy in AKI

Assess heart rate, blood pressure, jugular venous pressure, capillary refill (should be <3 sec), conscious level.
If hypovolaemic give bolus fluids (e.g. 250-500mls) until volume replete with regular review of response.
Middle grade review if >2 litres filling in oliguria.
If the patient is euvolaemic give maintenenance fluids (estimated output plus 500mls) and set daily fluid target.

Monitoring in AKI

Do arterial blood gas and lactate if venous bicarbonate is low or evidence of severe sepsis or hypoperfusion.
Consider insertion of urinary catheter and measurement of hourly urine volumes.
Measure urea, creatinine, bone, other electrolytes and venous bicarbonate at least daily while creatinine rising.
Measure daily weights, keep a fluid chart and perform a minimum of 4 hourly observations.
Perform regular fluid assessments and check for signs of uraemia.

Investigation of AKI

Investigate the cause of all AKI unless multi-organ failure or obvious precipitant
Urine dipstick. If proteinuria is present perform urgent spot urine protein creatinine ratio (PCR).
USS should be performed within 24 hours unless AKI cause is obvious or AKI is recovering or within 6 hours if obstruction with infection (pyonephrosis) is suspected.
Check liver function (hepatorenal), CRP and CK (rhabdomyolysis). If platelets low do blood film/LDH/Bili/retics (HUS/TTP). If PCR high, consider urgent Bence Jones protein & serum free light chains.

Supportive AKI care

Treat sepsis - in severe sepsis intravenous antibiotics should be administered within 1 hour of recognition.
Stop NSAID/ACE/ARB/metformin/K-sparing diuretics and review all drug dosages.
Give proton pump inhibitor and perform dietetic assessment.
Stop anti-hypertensives if relative hypotension. If hypovolaemic consider stopping diuretics.
Avoid radiological contrast if possible. If given follow prophylaxis protocol.

Causes Think 'STOP AKI'

Sepsis and hypoperfusion, **T**oxicity (drugs/contrast), **O**bstruction, **P**arenchymal kidney disease (acute GN)

website: www.londonaki.net
email: info@londonaki.net

http://londonaki.net/

- 1.5 × creatinine or oliguria > 6 hrs: Medical emergency
- Fluids
- Monitoring
- Investigate

"***STOP AKI***": ***S***epsis & hypoperfusion, ***T***oxicity, ***O***bstruction, **P**arenchymal kidney disease

NAC:

- Efficacy proven in CIN
- Not an alternative to IV hydration
- Protocols to be circulated to ER & Radiology department
- Should be given pre-exposure and to be continued
- Oral NAC had less bioavailability than IV

N acetyl cysteine

Intravenous N-Acetylcysteine for Prevention of Contrast-Induced Nephropathy: A Meta-Analysis of Randomized, Controlled Trials

Zikai Sun[1], Qiang Fu[1], Longxing Cao[1], Wen Jin[2], LingLing Cheng[1], Zhiliang Li[1]*

1 Cardiovascular Department, Zhujiang Hospital, Southern Medical University, Guangdong Province, China, 2 Cardiovascular Department, Guangdong No.2 Provincial People's Hospital, Guangdong, China

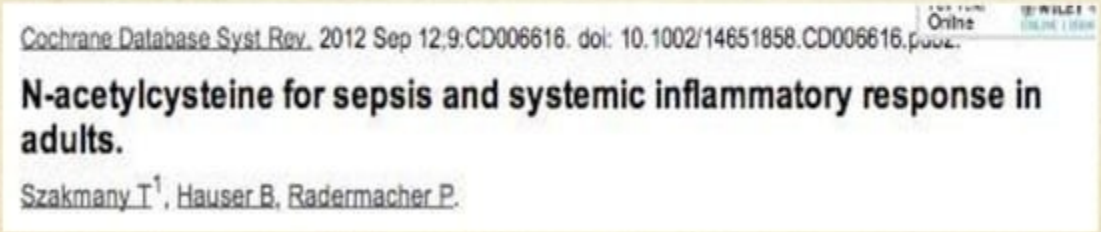
- MEDLINE, OVID,EMBASE
- Web of Science, Cochrane Central Register of Controlled Trials
- Conference proceedings from major cardiology and nephrology meetings
- Primary outcome: ***CIN***
- Secondary outcomes : renal failure requiring dialysis, mortality, length of hospitalization

Results:

- Too inconsistent at present to warrant a conclusion on efficacy
- Large, well designed trials required

NAC & SEPSIS!

- Ineffective in reducing mortality & complications
- Can be harmful, even if started early



Cochrane Database Syst Rev. 2012 Sep 12;9:CD006616. doi: 10.1002/14651858.CD006616.pub2.

Online

N-acetylcysteine for sepsis and systemic inflammatory response in adults.

Szakmany T[1], Hauser B, Radermacher P.

Erythropoeitin in AKI:

Moore and Bellomo *Annals of Intensive Care* 2011, 1:3
http://www.annalsofintensivecare.com/content/1/1/3

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Erythropoietin (EPO) in acute kidney injury

Elizabeth Moore, Rinaldo Bellomo*

- EPO- TBI trial :NCT00987454
- EPO-AKI is a sub study of the above trial
- AKI defined as per RIFLE
- HOW??! INDUCES HSP70 & prevents APOPTOSIS
- At present studied in cardiac surgery patients & heterogenous MICU patients
- Results awaited

Liver dysfunction & AKI:

- Volume responsive AKI
- Volume unresponsive AKI (ATN)
- HRS

- IV Albumin 40-60 GM/ day × 3-4 days: CIRRHOSIS

Management:

- Identify the cause
- Fluid optimization
- Vasopressor/ Vasodilators
- Management of hyperkalemia
- Management of acidosis, RRT
- CCB(in animals), Antidotes

Perioperative management:

- EUVOLEMIA!!
- IV volume replacement (WHICH, HOW MUCH ?)
- Acid base balance
- Avoid nephrotoxic drugs
- Foley's
- MAP, CVP, Cardiac output
- Vasopressors
- Anticipation

Why aggressive in AKI ?

Blood Purif. 2008;26(5):407-16.

Design and challenges of the Randomized Evaluation of Normal versus Augmented Level Replacement Therapy (RENAL) Trial: high-dose versus standard-dose hemofiltration in acute renal failure.

RENAL Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Goldsmith D, Myburgh J, Norton R, Scheinkestel C.

Long-Term Survival and Dialysis Dependency Following Acute Kidney Injury in Intensive Care: Extended Follow-up of a Randomized Controlled Trial

Martin Gallagher[1,2]*, Alan Cass[1,3], Rinaldo Bellomo[4], Simon Finfer[1,2], David Gattas[1,5], Joanne Lee[1], Serigne Lo[1], Shay McGuinness[6], John Myburgh[1,7], Rachael Parke[6], Dorrilyn Rajbhandari[1], for the POST-RENAL Study Investigators and the ANZICS Clinical Trials Group*

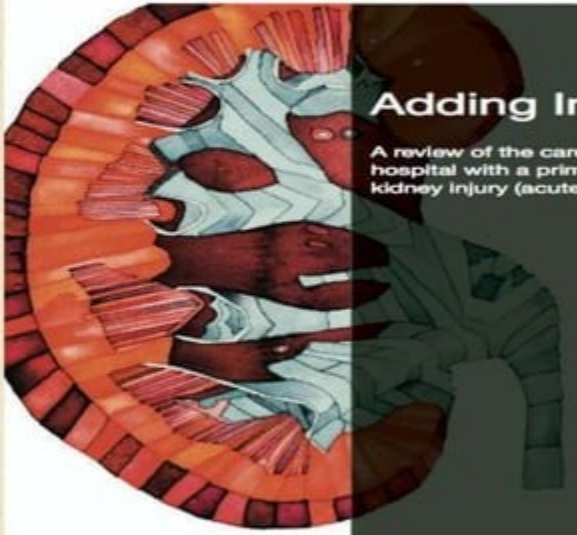
1 The George Institute for Global Health, Sydney, Australia, 2 University of Sydney, Sydney, Australia, 3 Menzies School of Health Research, Darwin, Australia, 4 Austin Hospital, Heidelberg, Australia, 5 Royal Prince Alfred Hospital, Camperdown, Australia, 6 Auckland City Hospital, Auckland, New Zealand, 7 St. George Clinical School, University of New South Wales, Sydney, Australia

PLoS Med. Feb 2014; 11(2): e1001601.

- Survivors of RENAL study followed upto 4 years/ death
- Survivors had heavy burden of proteinuria
- Increased frequency of RRT
- Costly affair, poor quality of life

Further reading:





Adding Insult to Injury

A review of the care of patients who died in hospital with a primary diagnosis of acute kidney injury (acute renal failure).

NCEPOD

NICE National Institute for Health and Care Excellence

Acutely ill patients in hospital

Recognition of and response to acute illness in adults in hospital

Issued: July 2007

NICE clinical guideline 50
guidance.nice.org.uk/cg50








it's tea time!