AKI in Rhabdomyolysis, Major Surgery and Trauma

Barts Health NHS
NHS Trust

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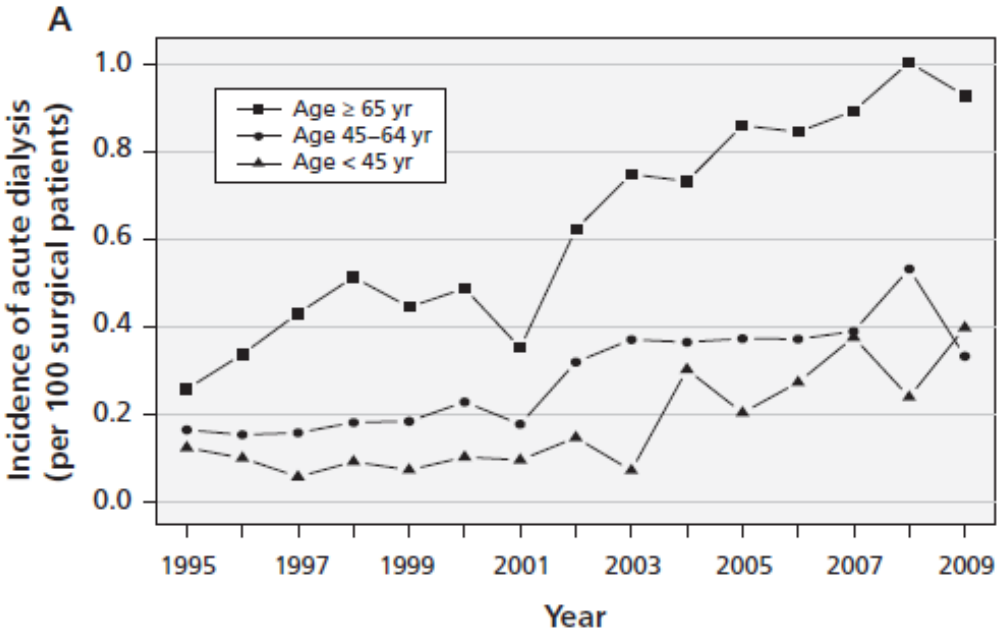
Overview

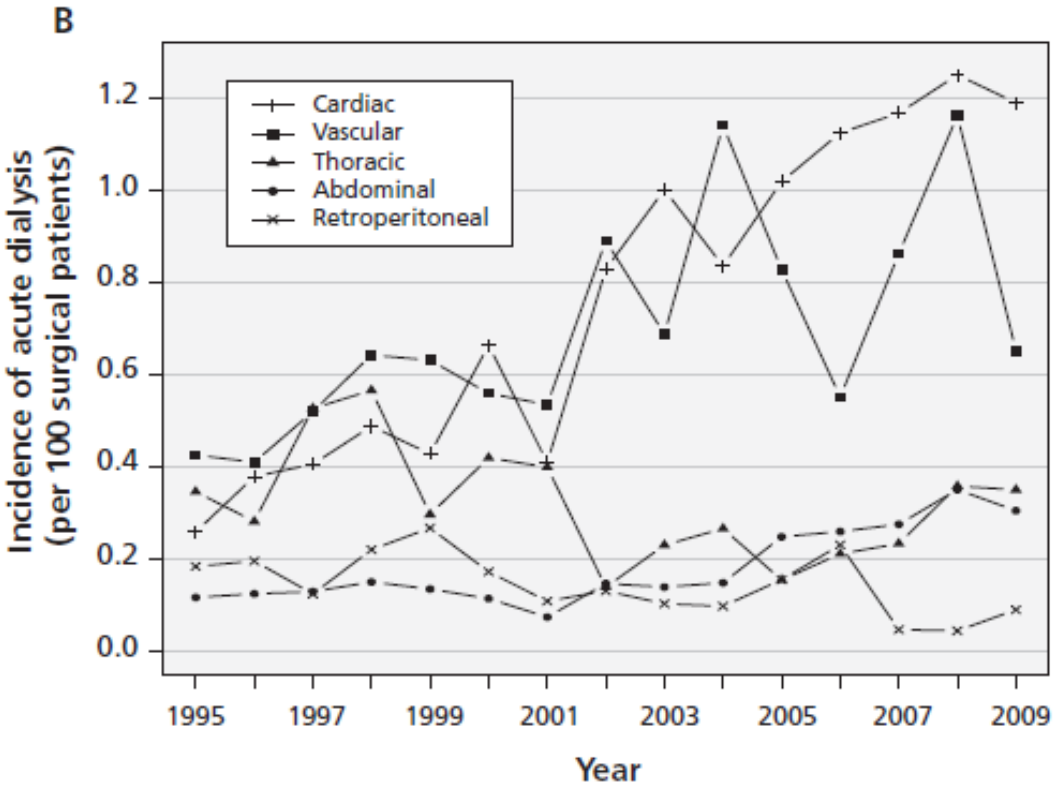
Major Surgery

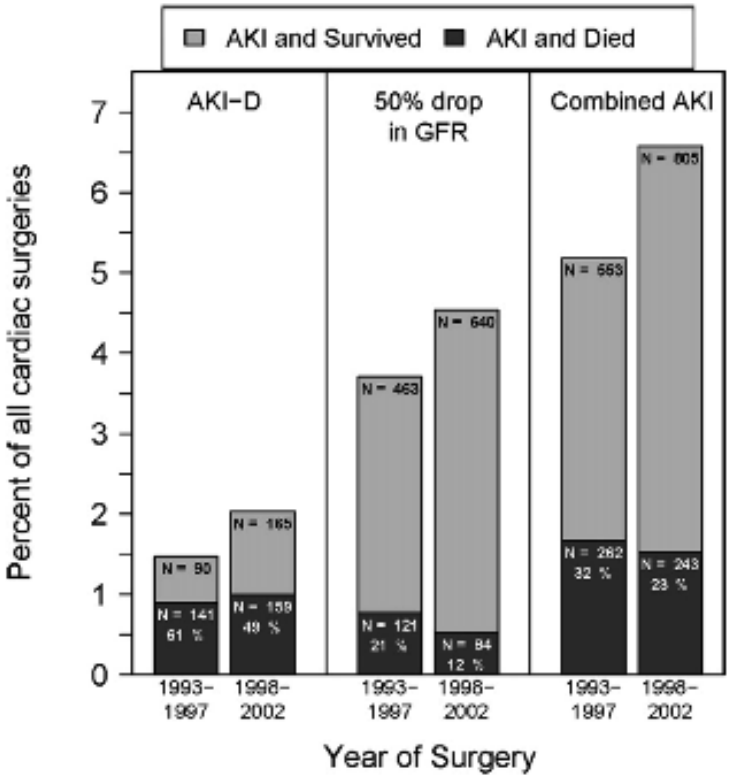
- Surgery and AKI
  - The need for acute dialysis is increasing in all age groups following major surgery[1]



[1]Siddiqui CMAJ 2012

Specific Types of Surgery





[1]Siddiqui CMAJ 2012

[2]Thakar AJKD 2007

Preventing AKI after Surgery

- LAKIN
  - Internet
  - App

London Acute Kidney Injury Network

www.londonaki.net

- Peri-operative guidelines for management of AKI
- Peri operative optimisation of DO_2I

Does perioperative hemodynamic optimization protect renal function in surgical patients? A meta-analytic study

Nicola Brienza, MD, PhD; Maria Teresa Giglio, MD; Massimo Marucci, MD; Tommaso Fiore, MD

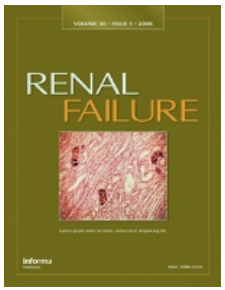
Crit Care Med 2009 Vol. 37, No. 6

YES!

Trauma

Confusing literature

- Bagshaw S. *A multi center evaluation of early AKI in critically ill trauma patents.* Renal Failure 2008
- Yuan F. *Natural history and impact of AKI in patients who have had an RTA.* Clinical Nephrology 2009
- Livia K. *AKI after Trauma.* Indian J CCM 2010
- Gomes E. *AKI in severe trauma*. Scandinavian J TREM 2010



A Multi-Center Evaluation of Early Acute Kidney Injury in Critically Ill Trauma Patients

2008, Vol. 30, No. 6 , Pages 581-589

Sean M. Bagshaw[1†], Carol George[2], R.T. Noel Gibney[1] and Rinaldo Bellomo[3]

- 9449 critically ill trauma patients
- AKI 18.1%
- Mortality 16.7% v 7.8%
  - Older,
  - female OR 1.6
  - co-morbidities OR 2.7
- AKI as independent risk of mortality
  - Risk OR 1.68
  - Injury OR 1.88
  - Failure OR 2.29

Clin Nephrol. 2009 Jun;71(6):669-79.

Natural history and impact on outcomes of acute kidney injury in patients with road traffic injury.

Yuan F, Hou FF, Wu Q, Chen PY, Xie D, Zhang X.

1Division of Nephrology, Nanfang Hospital, and 2Department of Biostatistics, Southern Medical University, Guangzhou, P.R. China.

- 3945 patients who had been in an RTA in Guangzhou, China
- AKI in 423 (10.7%)
  - RRT in 59 (13.9%)
- Vasopressors and high does loop diuretics were risk factors for AKI
- Mortality
  - No AKI 7.1%
  - Risk 37.4%
  - Injury 52.9%
  - Failure 79.2%
- 77.5% of AKI survivors had 'normal' renal function on d/c
  - No long term f/u

Research Article 2010

IJCCM Indian Journal of Critical Care Medicine
Official Publication of Indian Society of Critical Care Medicine

Acute kidney injury after trauma: Prevalence, clinical characteristics and RIFLE classification

Krasnalhia Lívia S. de Abreu[1], Geraldo B. Silva Júnior[1], Adller G. C. Barreto[1], Fernanda M. Melo[1], Bárbara B. Oliveira[1], Rosa M. S. Mota[2], Natália A. Rocha[1], Sônia L. Silva[1,3], Sônia M. H. A. Araújo[1], Elizabeth F. Daher[1]

Brazil

- 129 patients – 80% male – mean age: 32m / 22w
- 55 AKI
  - More Abdominal trauma
  - Less brain trauma
  - 19 RRT
  - Longer ICU and hospital stay
  - 50 had rhabdomyolysis
- Mortality was 95.3% for all trauma patients!

Gomes et al. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2010, 18:1
http://www.sjtrem.com/content/18/1/1

ORIGINAL RESEARCH Open Access

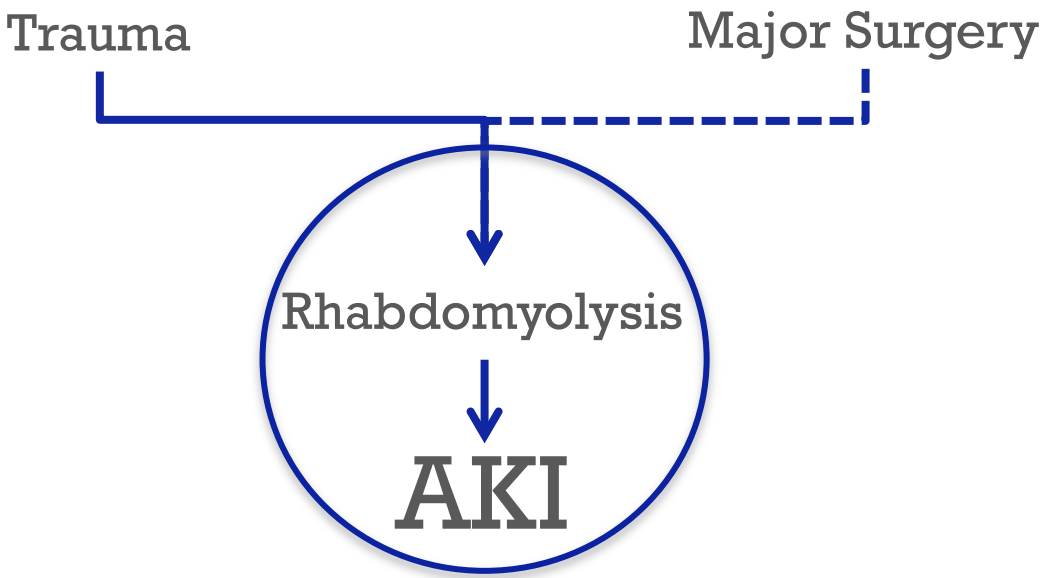
Acute kidney injury in severe trauma assessed by RIFLE criteria: a common feature without implications on mortality?

Ernestina Gomes[1], Rui Antunes[1*], Cláudia Dias[2], Rui Araújo[1], Altamiro Costa-Pereira[3]

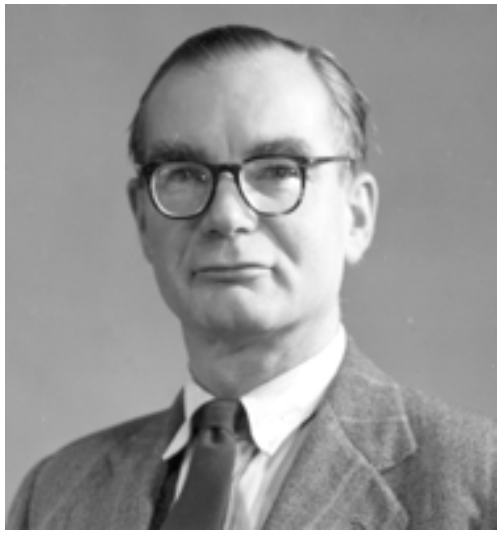
Portugal

- 436 patients – 80% male – median age 37
- AKI : no AKI was a 50:50 split
  - None underwent RRT
  - Mortality ~20% in all groups
- AKI
  - Longer ICU stay (significantly so if AKI 3)
  - Longer stay in hospital
  - Lower early mortality (<2days)
    - Probably due to increase in severe head injury in no AKI group

Overview



London 1940 – 1941



Prof. Eric Bywaters (1910-2003)

Hammersmith Hospital

Case Report

- Patient had been buried for several hours
- On admission …. he looks good apart from swelling of the limb
- His blood pressure falls
- Signs of renal damage soon appear
- The urine contains albumin and dark brown granular casts

BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 22 1941

CRUSH INJURIES WITH IMPAIRMENT OF RENAL FUNCTION

BY

E. G. L. BYWATERS, M.B., B.S., M.R.C.P.

Beit Memorial Fellow

AND

D. BEALL, Ph.D.Toronto

(From the Departments of Medicine and Pathology, British Postgraduate Medical School)

[WITH SPECIAL PLATE]

Amongst air-raid casualties seen at this hospital have been four cases of crush injury of the limbs which, because of the general similarity of their clinical course, were thought to represent a specific and hitherto unreported syndrome, and one which has been and will be seen elsewhere during the war. Such a condition may have been observed in civil practice, but we have been unable to find any account of it in the literature. The cases are of interest on account of the problem propounded by both pathogenesis and treatment. The picture presented by these four cases, and substantiated by others, is briefly as follows:

The patient has been buried for several hours with pressure on a limb. On admission he looks in good condition except for swelling of the limb, some local anaesthesia, and wheals. The haemoglobin, however, is raised, and a few hours later, despite vasoconstriction, made manifest by pallor, coldness, and sweating, the blood pressure falls. This is restored to pre-shock level by (often multiple) transfusions of serum, plasma, or, occasionally, blood. Anxiety may now arise concerning the circulation in the injured limb, which may show diminution of arterial pulsation distally, accompanied by all the changes of incipient gangrene. Signs of renal damage soon appear, and progress even though the crushed limb be amputated. The urinary output, initially small, owing perhaps to the severity of the shock, diminishes further. The urine contains albumin and many dark brown or black granular casts. These later decrease in number. The patient is alternately drowsy and anxiously aware of the severity of his illness. Slight generalized oedema, thirst, and incessant vomiting develop, and the blood pressure often remains slightly raised. The blood urea and potassium, raised at an early stage, become progressively higher, and death occurs comparatively suddenly, frequently within a week. Necropsy reveals necrosis of muscle and, in the renal tubules, degenerative changes and casts containing brown pigment.

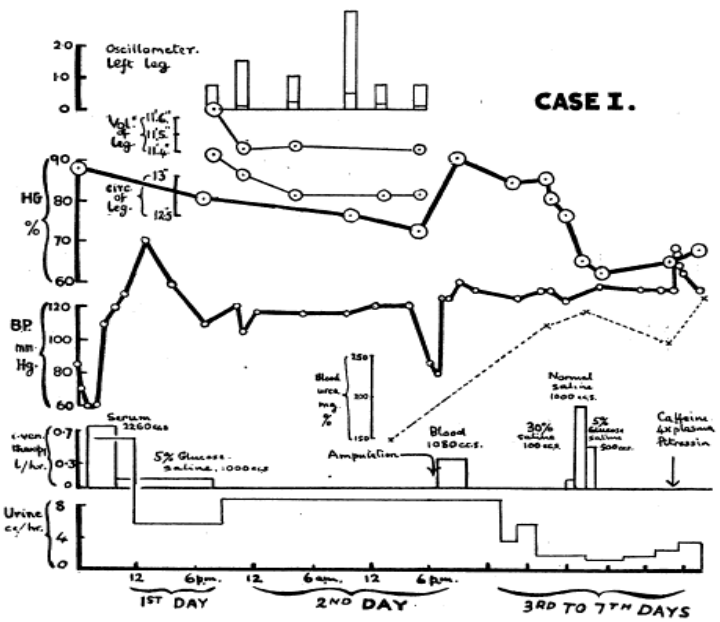


CHART I.—Case I.

Case I

A female aged 17 had been buried for nine hours with heavy masonry lying across the left leg. On admission she showed slight bruises generally, and multiple superficial abrasions below the left knee. The leg was swollen and sensation was impaired at the ankle, where all power and movement were lost. Other limbs appeared undamaged. The skin was pallid and clammy; the blood pressure was 85/70 mm. Hg. The clinical course is shown on Chart I. Recalcified plasma–saline (Clegg and Dible, 1940) (subsequently referred to as "serum"), followed by 5% glucose–saline,

Pathophysiology of Rhabdomyolysis

- Rhabdomyolysis – 'the dissolution of striped (skeletal) muscle'
  - Direct sarcolemmic injury
    - Trauma
    - Ischaemia reperfusion and inflammation
  - Depletion of ATP within the myocyte
    - Unregulated intracellular Ca^{2+} increase
    - Destruction of myofibrillar, cyctoskeletal and membrane proteins
  - Release of muscle cell contents
    - myoglobin

Myoglobin and AKI

- Myoglobin
  - Iron and O_2 binding protein
  - 17.8 kDa
  - Freely filtered at the glomerulus
  - Tubular epithelial cells metabolise it
  - Appears in urine when concentration is >0.5-1.5mg/dL
  - Urine becomes red when concentration is >100mg/dL
  - Myoglobinuria only occurs in the context of rhabdomyolysis

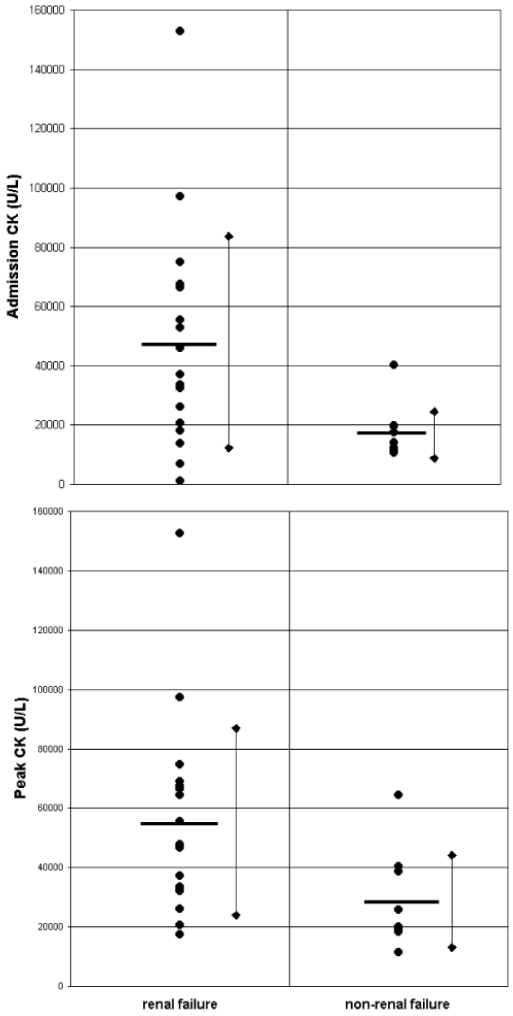
Myoglobin and AKI

- The toxic effects of myoglobin……
  - Intra renal vasoconstriction
    - Tx A2
    - Endothelin 1
    - TNF α
  - Direct and ischaemic tubular injury
    - Heme
    - Free radicals
      - Fe^{3+}
  - Tubular obstruction
    - Tamm-Horsfall protein
    - Acidic urine

- Hypovolaemia
- RAS

Biochemical Markers of Muscle injury and AKI

- Serum Creatinine
  - Cannot predict progression to AKI or its severity on admission
  - No correlation to CK levels
- Serum Creatine Kinase
  - Sensitive indicator of muscle damage
    - >1000 (>5000)
    - Severe >10,000 (>15,000)
  - Peak CK and admission CK correlates to development of AKI*
- Urine
  - Myoglobin
  - Uric acid
  - Creatine / creatinine ratio



Brancaccio et al Clin Chem Lab Med 2010
de Meijer et al ICM 2003

Serum Myglobin?

Journal of Critical Care
2010

Peak value of blood myoglobin predicts acute renal failure induced by rhabdomyolysis

Shunji Kasaoka MD*, Masaki Todani MD, Tadashi Kaneko MD, Yoshikatsu Kawamura MD, Yasutaka Oda MD, Ryosuke Tsuruta MD, Tsuyoshi Maekawa MD

CK remains at higher levels for longer periods than Myoglobin (hence why it is widely used)

- Conclusions
  - Peak CK does not predict AKI
  - Admission myoglobin does not predict AKI
  - Peak myoglobin does predict AKI
    - Check every 12 to 24 hours to find the peak
    - Does not predict / change the outcome
  - Perhaps monitoring rate of clearance may be of use in directing therapy

Basic Epidemiology

Depends on the definition of Rhabdomyolysis and ARF / AKI

- 7-10% of AKI in USA is caused by Rhabdomyolysis
- 13-50% Incidence of AKI in Rhabdomyolysis
- AKI more common in those who had had trauma and drugs / alcohol than trauma alone
- Mortality
  - Rhabdomyolysis from limb ischaemia + AKI 32% mortality
  - In ICU 59% with AKI; 22% without AKI
- Most patients with AKI recover renal function

Bosch et al NEJM 2009

Categories of Rhabdomyolysis

Bosch et al NEJM 2009

- Trauma
- Exertion
- Muscle hypoxia
- Genetic defects
  - Mitochondrial diseases; lipid and glucose metabolic disorders
- Infections
  - Influenza A, coxsakie, EBV, Strep, clostridium
- Body temperature changes
  - Malignant hyperthermia, hypothermia
- Metabolic and electrolyte disorders
- Drugs and toxins
  - Statins, heroin, alcohol
- Idiopathic

Treatment of AKI caused by Rhabdomyolysis

- Cause*
  - Fasciotomy (Trauma)
- Fluids
  - Early
  - Diuretics
- Alkalisation of the urine
  - Bicarbonate
- Extracorporeal removal of myoglobin
  - High volume HF
  - Super high flux HD

Fluid Therapy

- Where is the best place to find data……

J Am Soc Nephrol 15: 1862–1867, 2004

Early and Vigorous Fluid Resuscitation Prevents Acute Renal Failure in the Crush Victims of Catastrophic Earthquakes

The American Journal of Emergency Medicine

2011

Prophylactic fluid therapy in crushed victims of Bam earthquake☆

Najafi Iraj[a,b], Safari Saeed[a,b,c,*], Hosseini Mostafa[d], Sanadgol Houshang[e], Sharifi Ali[b], Rashid Farokhi Farin[f], Seirafian Shiva[g], Mooraki Ahmad[h], Hamidreza Samimagham[i], Vahid Pourfarziani[j], Atabak Shahnaz[k], Osareh Shahrzad[l], Boroumand Behrooz[h]

Fluid Therapy

A brief summary of the main messages from both papers

- Worse the injury / time spent under rubble, the worse the AKI ($p<0.05$)
- The earlier fluids are given (i.e. on scene) the better the outcome ($p<0.001$) – (debatable, but within 24 hours is a must)
- The more fluids per day given the better the outcome ($p<0.005$)
  - 6L in severe (CK>15,000)
  - 3L in moderate (CK >5000)
- Alkalisation of the urine
  - Alkaline Mannitol diuresis (resource issue)

- Other literature suggests 12 to 24L of fluid in a day but <3L in a day causes an upsurge in the cases of AKI

Beware early high volume fluids in haemorrhagic trauma

Extracorporeal Myoglobin Removal

- High volume HF[1] with a large Filter (1.9m^2)
  - Pore size ~50kDa
  - Blood flows >300mL/min and high exchange rate
  - Efficiency
    - 300ml/min blood and 60mL / 70kg patient / hr (4.2L exchange)
      - i.e. ~70mL/min exchange ~23% clearance

- High Flux / Super High Flux Haemodialysis[1]
  - Pore size 30-60kDa (conventional HD <15kDa)
  - Efficiency
    - High flux dialysis ~50% clearance

[1]Ling et al J of Injury 2010, Naka et al Critical Care 2005
[2]Basnayake et al NEJM 2009 (letter)

Prevention of AKI caused by rhabdomyolysis – translational research

PNAS

Acetaminophen inhibits hemoprotein-catalyzed lipid peroxidation and attenuates rhabdomyolysis-induced renal failure

Olivier Boutaud[a,1,2], Kevin P. Moore[b,1], Brandon J. Reeder[c], David Harry[b], Alexander J. Howie[b], Shuhe Wang[a], Clare K. Carney[d], Tina S. Masterson[a], Taneem Amin[a], David W. Wright[d], Michael T. Wilson[c], John A. Oates[a,e], and L. Jackson Roberts II[a,e]

2010

Acetaminophen-induced rhabdomyolysis

Allergy **54**, 1999 / 1114–1123 | 1115

D.A. Moneret-Vautrin*, M. Morisset, J.C. Humbert, E. Beaudouin, N. Tupin, L. Plantier

Conclusions

- AKI is common following major surgery
  - There are simple measures and easily available guidance to help prevent this throughout the peri-operative period
- AKI is common following major trauma
  - These are a different epidemiological group to routine AKI patients
    - though the risk factors remain the same
  - AKI has an impact on mortality
- AKI following rhabdomyolysis is rare
  - Early fluid resuscitation
    - high in / high out and keep the urine pH>6
  - Can consider renal replacement therapy for myoglobin removal
  - Should we give paracetamol early?