

Contrast Induced - Acute Kidney Injury (CI-AKI)

Dr Andy Lewington
**Consultant in Renal Medicine/
Honorary Clinical Associate Professor**
Leeds Teaching Hospitals Trust

Declaration of Interest

- AbbVie – Advisory Board for Melanocortin therapy for AKI, Honoraria for Lectures
- AM Pharma – Advisory Board
- Alere – Honoraria for chairing meeting
- Bioporto – Advisory Board for NGAL
- Fresenius – Honoraria for lecture at ICS
- Baxter – Honoraria for lecturing on IV Fluids



Leeds Teaching Hospitals/University of Leeds



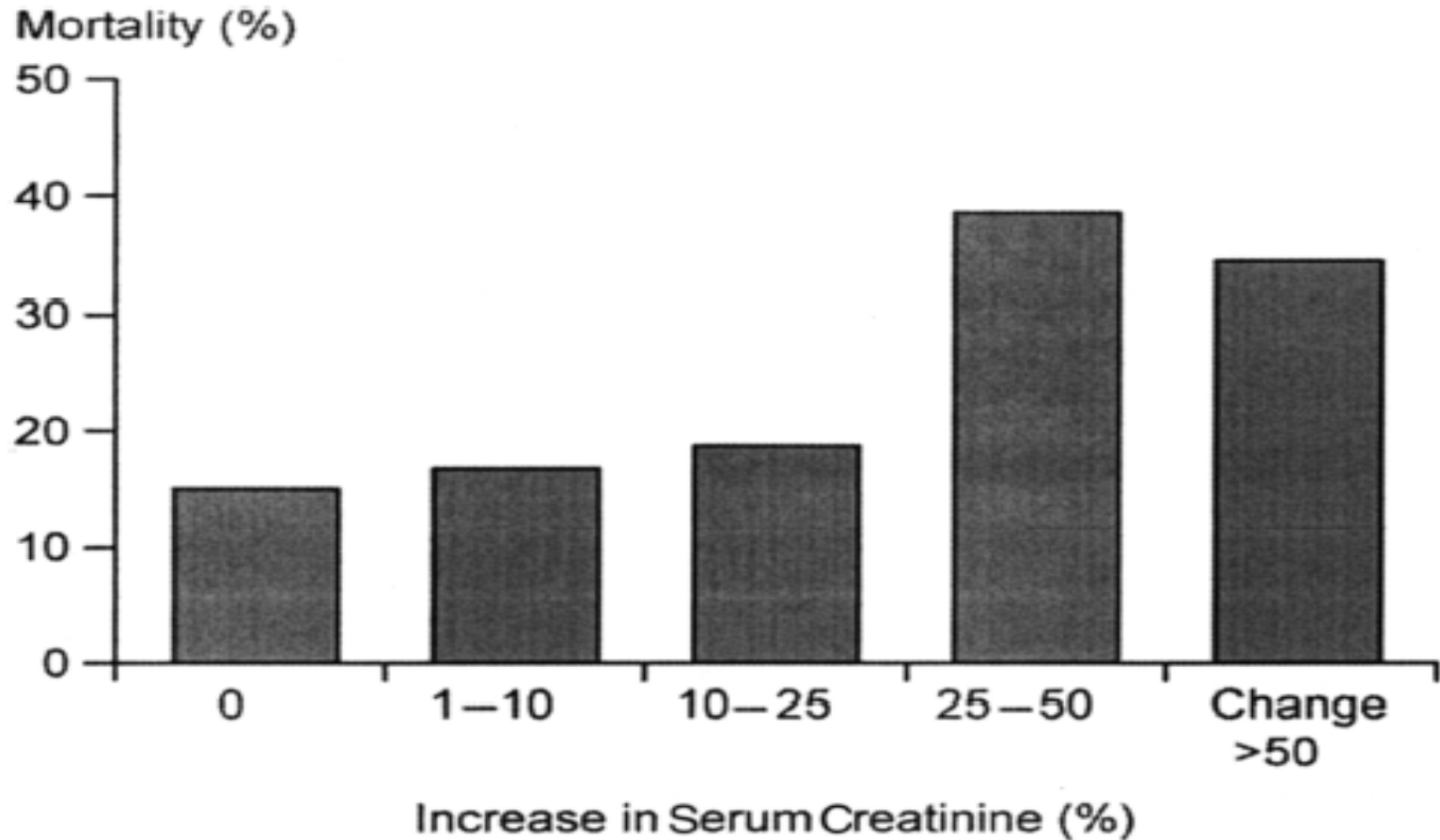
Outline

- Definitions
- Pathophysiology
- Prevention
- Guidelines

Why is this Important?

Outcomes

Change in Serum Creatinine and Mortality in CIN



McCullough et al (Am J Cardiol 2006;98[suppl]:5K-13K)

Future hospital: Caring for medical patients

Executive summary and
full recommendations
September 2013

Hospital population

- 25% of general population > 60yrs
- >85yrs age group will double in next 20 years
- 37% rise in admissions over last 10 years
- 66% of patients admitted > 65yrs
- 25% of patients have dementia
- Patients > 85yrs account for 22% of bed days in NHS

Hospital Population

- Many patients have
 - multiple co-morbidities
 - more complex management issues
 - decreased functional reserve
 - Cardiac
 - Respiratory
 - Kidney
 - polypharmacy – e-prescribing

‘The use of intravascular contrast agents has increased dramatically in recent years’

RCR 2014

Definition

- Contrast induced nephropathy (CIN)
 - Acute renal failure 2° /2 intravascular iodinated contrast media
 - Increase in serum creatinine (SCr) by
 - 44 μ mol/L (0.5mg/dl) or
 - increase of least 25% from baseline SCr

Definition

- occurs within 3 days of receiving contrast
- usually non-oliguric
- SCr peaks at 4 - 5 days
- recovery to baseline by 7-10 days
- differential diagnosis includes renal atheroembolism
 - difficult to differentiate
 - recovery less likely

Epidemiology of CIN following Percutaneous Coronary Intervention

- ranges 1 – 20%
- incidence increases following emergency PCI
- associated with poorer outcomes even in patients with normal baseline kidney function

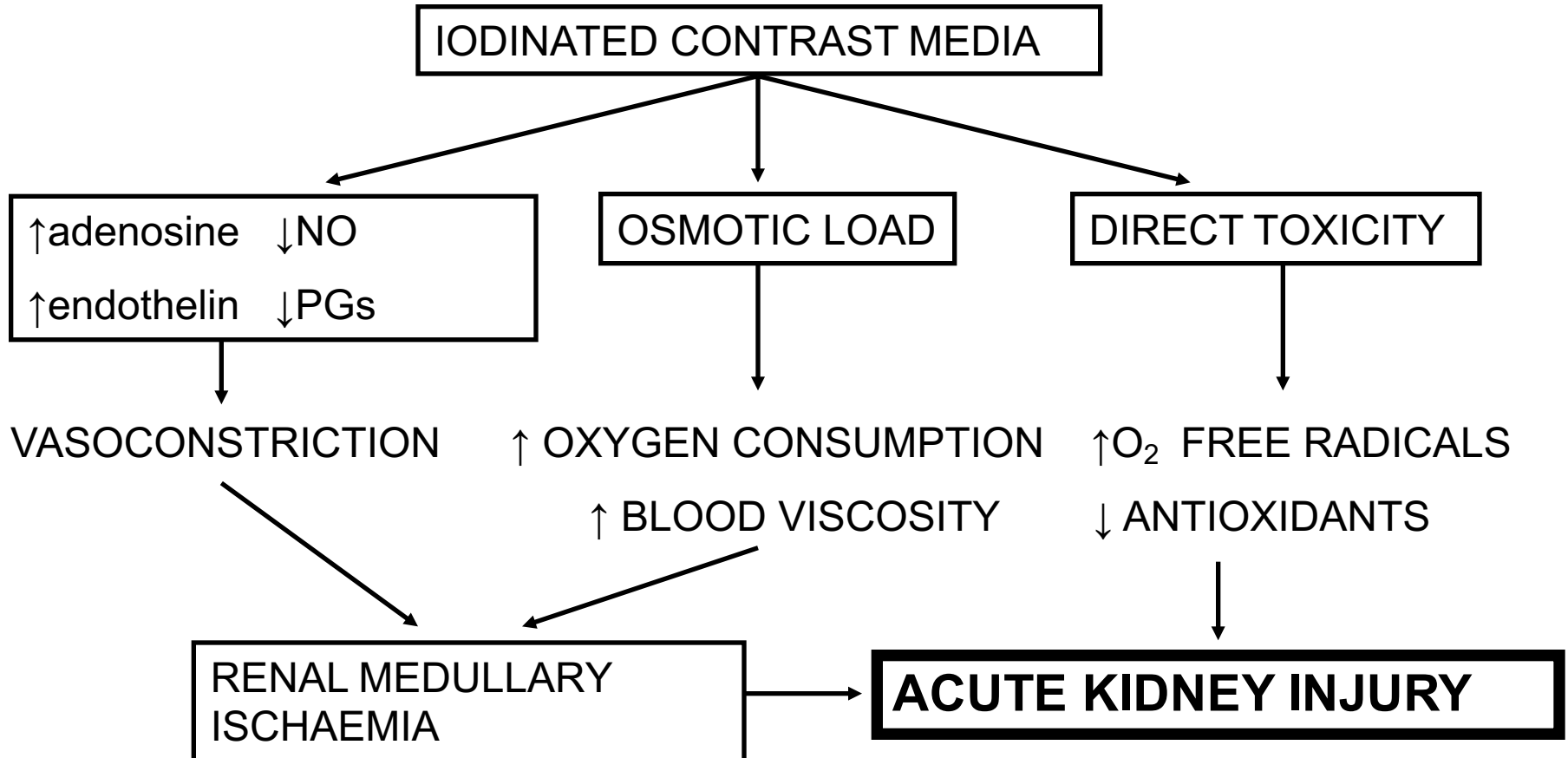
Lindsay et al. Catheter Cardiovasc Interv
2003;59:338-43

New definition

- Kidney Disease: Improving Global Outcomes (KDIGO)
 - Contrast induced - acute kidney injury (CI-AKI)

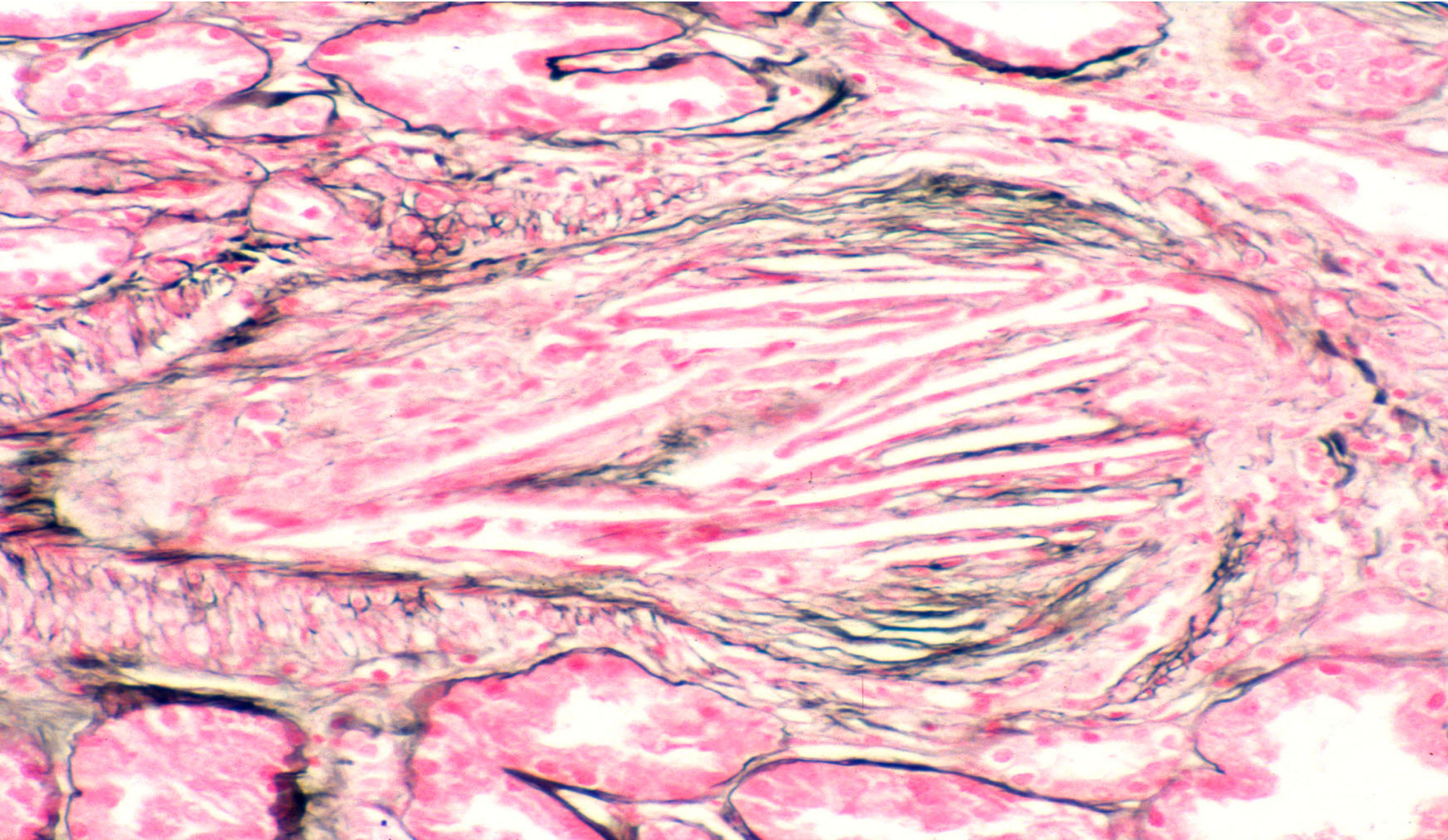
Pathophysiology

Pathophysiology





Cholesterol embolisation



Prevention of CI-AKI

Prevention

- evaluate risk factors
- consider whether study is appropriate
- consider the type of contrast media
- consider the dose of contrast media
- ensure adequate hydration/volume expansion
- avoid nephrotoxic medications

Risk Factors

Risk Factors for CI-AKI

- Non Modifiable
 - age > 75 years
 - chronic kidney disease (CKD)
 - eGFR < 40 ml/min/1.73m²
 - acute kidney injury
 - liver disease
 - cardiac failure

Risk Factors for CI-AKI

- Modifiable
 - nephrotoxic drugs
 - sepsis
 - hypovolaemia
 - intra-arterial
 - high-dose/multiple contrast studies
 - type of contrast media

Iodinated contrast

Type of Contrast Media

- high osmolality (ionic monomeric)
 - 1000-1800 mOsm/Kg
- low osmolality (non-ionic monomeric)
 - 600-800 mOsm/Kg
- iso-osmolar (non-ionic dimeric)
 - 290 mOsm/Kg

Type of Contrast Media

- *Aspelin NEJM 2003; 348: 491-9*
- iso-osmolar (non-ionic dimeric)
 - Iodixonal 290 mOsm/Kg
 - beneficial in patients with
 - Diabetes and CKD (Cr 132-308 μ mo/L)
 - Iodixanol vs Iohexol for angiography
 - CIN 3.1% vs 26.2%

Volume expansion

Volume expansion

- haemodynamic effects
 - ↑ RBF
 - ↑ medullary bloodflow
 - vasa recta supplying medulla are very sensitive to vasopressin
 - suppresses vasopressin release
 - vasa recta vasodilate
- tubular pressure effects
 - dilutes contrast media
 - ↓ viscosity

Volume expansion

- *Solomon NEJM 1994; 331: 1416-1420*
 - 78 patients, mean Cr 186 μ mol/L
 - iv 0.45% saline
 - 1 ml/kg/h, 12hr pre-and post angiography
 - better protection when given alone rather than with furosemide or mannitol

Volume expansion

- *Mueller Arch Int Med 2002; 162: 329-36*
 - 1620 patients (20% with mild CKD)
 - iv 0.9% saline superior to 0.45% saline

Volume expansion

- *Merten G JAMA 2004; 291: 2328-2334*
 - RCT, 119 patients
 - mean Cr 150 μ mol/L
 - 0.9% saline vs isotonic sodium bicarbonate
 - 3ml/kg/hr 1 hr pre-procedure followed for 6 hrs post-procedure
 - CIN 2% (bicarbonate) vs 14% (0.9% saline)
 - protection from oxidant injury through alterations in pH

Pharmacological Prevention of CI-AKI

Fenoldopam

- selective dopamine-1 receptor agonist
 - increases cortical and medullary renal blood flow
 - 6x more potent than dopamine
 - increases GFR, induces diuresis
 - administered intravenously
 - risk of hypotension, regular monitoring
- 2 conflicting studies
 - most recent negative study JAMA 2003

N-acetylcysteine

- *Tepel NEJM 2000; 343: 180-184*
 - RCT
 - 83 patients
 - mean Cr 216 (30% DM)
 - CT with LOCM
 - NAC 600 mg PO bd pre-and post-procedure and 0.45% saline vs placebo and 0.45% saline
 - CIN 2% vs 21%
 - minimal side-effects

N- acetylcysteine

- antioxidant properties
- induces glutathione production
 - role in cellular defence
- inactivates hydroxyl radicals
- stabilises nitric oxide
 - forming a more potent vasodilator
- ameliorates renal vasoconstriction

N-acetylcysteine

- *Pannu KI 2004; 65: 1366-1374*
 - meta-analysis
 - 15 studies
 - 3 additional negative studies included contributing 271 patients
 - in one study - majority of patients had normal renal function
 - two studies were abstracts
 - benefit of borderline statistical significance

ACT Trial

- Randomised acetylcysteine for contrast – induced nephropathy trial (ACT)
- Coronary or peripheral angiography
- N=2308
- No beneficial effect on incidence of CIN

Circulation 2011;124:1250-1259

Haemofiltration

- “The Prevention of Radiocontrast-Agent-Induced Nephropathy by Haemofiltration”

Marenzi G NEJM 2003; 349: 1333-40

- RCT, 114 patients (CrCl 26 ml/min)
- coronary interventions, LOCM (large vol)
- haemofiltration 4-8 hrs pre and 18-24 hrs post procedure vs hydration (N/S 1ml/kg/hr)
- ↓ RCIN incidence 5% vs 50%
- ↓ in-hospital events 9% vs 52%
- ↓ in-hospital mortality 2% vs 14%
- ↓ 1 yr mortality 10% vs 30%

Haemofiltration

- points to consider
 - haemofiltration lowers creatinine concentration
 - no information regarding atheroembolism
 - use of heparin and role in attenuating
 - acute inflammation
 - ischaemia-reperfusion injury
 - role of ICU care
 - logistics
 - high-risk patients, multiple interventions
 - treated patients with higher baseline Cr experienced the greatest positive effect – long-term survival

Avoidance of Nephrotoxins

Nephrotoxic Drugs

- Aminoglycosides
 - proximal tubule cell toxicity
- Amphotericin B
 - lipid formulations preferred
- NSAIDS

Potential Nephrotoxic Drugs

Angiotensin converting enzyme inhibitors

- ACE-inhibitors

- Angiotensin II causes efferent arteriolar vasoconstriction
- Role in CI-AKI uncertain
- Conflicting results from a number of studies

Guidelines

- RA/BCIS/RCR
 - Joint guideline www.renal.org
- NICE AKI CG 169
 - CI-AKI
- Royal College of Radiologists
 - draft 2014

Clinical Practice Guidelines Committee

Introduction

Chair: Dr Andy Lewington, Andrew.lewington@leedsth.nhs.uk.

The Clinical Practice Guidelines Committee was established by the UK Renal Association (RA) to prepare guidelines for the management of patients with renal disease and help identify the data to be collected by the Renal Registry.

The RA has produced guidance on best practice in the management of patients with kidney disease since 1995. The RA Clinical Practice Guidelines are not funded by any external organisation, commercial company or charity.

In 2013 it was agreed that for appropriate topics The Renal Association would produce joint adult and paediatric guidelines with the British Association for Paediatric Nephrology .

NICE Accreditation

The National Institute for Health and Care Excellence (NICE) has accredited the process used by The Renal Association to produce its Clinical Practice Guidelines. Accreditation is valid for 5 years from 9 November 2010.

Accreditation helps health and social care professionals identify the most robustly produced guidance available, enabling them to deliver high quality care.

More information on accreditation can be viewed at <http://www.nice.org.uk/accreditation>



Clinical Practice Guidelines Committee

Introduction

Chair: Dr Andy Lewington, Andrew.lewington@leedsth.nhs.uk.

The Clinical Practice Guidelines Committee was established by the UK Renal Association (RA) to prepare guidelines for the management of patients with renal disease and help identify the data to be collected by the Renal Registry.

The RA has produced guidance on best practice in the management of patients with kidney disease since 1995. The RA Clinical Practice Guidelines are not funded by any external organisation, commercial company or charity.

In 2013 it was agreed that for appropriate topics The Renal Association would produce joint adult and paediatric guidelines with the British Association for Paediatric Nephrology .

NICE Accreditation

The National Institute for Health and Care Excellence (NICE) has accredited the process used by The Renal Association to produce its Clinical Practice Guidelines. Accreditation is valid for 5 years from 9 November 2010.

Accreditation helps health and social care professionals identify the most robustly produced guidance available, enabling them to deliver high quality care.

More information on accreditation can be viewed at <http://www.nice.org.uk/accreditation>



Prevention of Contrast Induced Acute Kidney Injury (CI-AKI)

**Renal Association,
British Cardiovascular Intervention Society
and
The Royal College of Radiologists**

Dr Andrew Lewington (RA)

Dr Robert MacTier (RA)

Dr Richard Hoefield (RA)

Dr Mark Downes (RCR)

Dr Andrew Sutton (BCIS)

Dr David Smith (BCIS)

Guideline 3.1 – Strategies to Prevent CI-AKI

- We suggest that unenhanced scanning or alternative imaging techniques should be considered in patients with risk factors for developing CI-AKI. (Not Graded)

Guideline 3.2 – Strategies to Prevent CI-AKI

- We recommend intravenous volume expansion with 0.9% sodium chloride or isotonic sodium bicarbonate in patients identified as high risk of CI-AKI (Grade 1A)

Guideline 3.4 – Strategies to Prevent CI-AKI

- We recommend that there is no convincing benefit for prescribing oral or intravenous N-acetylcysteine or any other pharmacological agents to prevent CI-AKI. (Grade 1A)

Acute kidney injury: prevention, detection and management up to the point of renal replacement therapy (CG169)

- **Guidance from the National Institute for Health and Care Excellence**
 - **August 2013**

Thousands dying of thirst on NHS: Watchdog forced to issue guidelines on giving patients water

- Tens of thousands dying in hospital from kidney failure linked to dehydration
- NHS officials calculate up to 42,000 deaths a year could be avoided
- NICE issuing guidelines to help staff prevent deaths from condition
- Estimated a fifth of patients attending A&E every year suffer from the illness

By SOPHIE BORLAND

PUBLISHED: 00:00, 28 August 2013 | UPDATED: 01:41, 28 August 2013

[f](#) Share [t](#) Tweet [g+](#) +1 [s](#) Share | **301** shares

[d](#) **273** View comments

Tens of thousands of patients are dying needlessly in hospital every year from kidney failure linked to dehydration, NHS officials have revealed.

They calculate that up to 42,000 deaths a year would be avoided if staff ensured patients had enough to drink and carried out simple tests.

NICE, the NHS watchdog, is today issuing guidelines to staff to help them prevent deaths from the condition – known as acute kidney injury – which is common in the elderly and patients with heart disease, diabetes and blood infections.

Site Web

[f](#) Like MailOnline [t](#) Follow @DailyMailUK

Risk of CI - AKI

- Assessing risk factors in adults having iodinated contrast
 - eGFR must be checked within 3 months
 - Be aware of risk factors
 - Discuss risk with patients
- Ensure that risk assessment does not delay emergency imaging

Risk of CI-AKI

- age ≥ 75 years
- eGFR < 40 ml/min/1.73 m²
- heart failure
- renal transplant
- hypovolaemia
- increasing volume of contrast agent
- intra-arterial administration of contrast agent

Preventing CI -AKI

- Offer iv volume expansion to adults having iodinated contrast agents if
 - they are at increased risk of contrast-induced acute kidney injury because of risk factors
 - they have an acute illness.
- Offer either
 - isotonic sodium bicarbonate or 0.9% sodium chloride

Preventing CI -AKI

- Consider temporarily stopping ACE inhibitors and ARBs in adults having
 - iodinated contrast agents if they have chronic kidney disease with an eGFR < 40ml/min/1.73m²

Referral to Nephrology

- Discuss care with a nephrology team before offering iodinated contrast agent to adults with contraindications to iv fluids if
 - they are at increased risk of contrast-induced acute kidney injury, or
 - they have an acute illness, or
 - they are on renal replacement therapy

Royal College of Radiologists

Standards for Intravascular Contrast Administration to Adult Patients – 3rd Edition (Draft)

- Accepts term CI-AKI
- Recognises all contrast agents are nephrotoxic in the presence of reduced kidney function
- Non emergency patients
 - eGFR available within 3 months
- Acute illness or CKD
 - Cr within 7 days

Gadolinium Based Contrast Agents

- administration in patients with severely reduced kidney function rarely results in
 - nephrogenic systemic fibrosis
 - deposition of connective tissue in skin resulting in joint contractures and other organ systems
 - manifestation up to many years post exposure

Gadolinium Based Contrast Agents

- European Medicines Agency
 - High risk
 - Omniscan
 - Magnevist
 - Optimark
 - Low risk
 - Doleram
 - Prohance
 - Gadovist

RCR

- eGFR < 30 ml/min/1.73m² or AKI
 - high risk agent contraindicated
 - medium or low risk agent can be used
 - lowest dose possible
 - < 0.1 mmol/kg
 - do not repeat in 7 days
 - avoid in AKI while Cr still rising
 - if already on HD – commence within 24 hrs following administration

Subclinical AKI

Subclinical AKI

- recent demonstration of tubular damage as evidenced by biomarkers without rise in serum creatinine
- associated with worse renal and overall outcomes

Subclinical AKI due to iodine-based contrast media

Ronco C et al

Eur Radiol Aug 16 2012

Subclinical AKI

- for many years we have considered the kidneys as rather forgiving organs
- we must consider the consequences of any kidney injury in terms of future risk
- more elderly population
- complex disease
- multiple medications
- Increased demands on renal reserve

'Kidneys are for Life'

Thank you