Protecting The Kidneys From Contrast  
“To CIN or not to CIN”

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The Issues

- What IS contrast-induced nephropathy?
  - How do we measure it?
  - Change in serum creatinine? Decrease in GFR? Other measure?

- Who is at risk?

- What can we do to minimize the risk?

- How do we follow up these patients?
Problems with the Literature

- Few studies address emergent imaging
  - Most studies are in outpatients undergoing elective procedures, particularly cardiac angiography
- Inclusion criteria vary between studies
- Definition of acute kidney injury varies between studies
- Variable doses and regimens of interventions used
Risk Factors for CI N

- Not modifiable
  - Chronic kidney disease*
  - Shock/hypotension
  - Diabetes
  - Age ≥ 70 years
  - Congestive heart failure

- Modifiable
  - Type of imaging procedure performed
  - Type of contrast used**
  - Dose of contrast used**
  - Hydration status
  - Concomitant nephrotoxic agents
  - Recent contrast administration

** Most important risk factor
So, Which Patients Do We Worry About?

- First, need to assess renal function
- What should we use…
  - Serum creatinine?
  - Glomerular filtration rate?
  - Creatinine clearance?
  - eGFR?
  - Something else?
Is the Serum Creatinine a Good Measure of Renal Function?

  - N = 765, needing CT scans
  - 14% CrCl < 60 ml/min; 40% had serum Cr < 1.5
  - Using CrCl of ≥ 60 ml/min as adequate renal function, looked at correlation of serum creatinine

<table>
<thead>
<tr>
<th>sCr</th>
<th>Sensitivity for eGFR &lt; 60</th>
<th>Specificity for eGFR &lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8 mg/dl</td>
<td>45%</td>
<td>99.9%</td>
</tr>
<tr>
<td>1.5 mg/dl</td>
<td>60%</td>
<td>98%</td>
</tr>
<tr>
<td>1.2 mg/dl</td>
<td>81%</td>
<td>88%</td>
</tr>
<tr>
<td>1.0 mg/dl</td>
<td>91%</td>
<td>70%</td>
</tr>
</tbody>
</table>
The Cr is > 1.5 and/or the eGFR is < 60…

Now What?

- Minimize the risk
  - Consider using alternative imaging methods (e.g. ultrasound, MRI or a noncontrast CT a viable alternative?)
  - If CT with contrast unavoidable
    - Use low or iso-osmolar nonionic contrast agents
    - Consider using lower doses of contrast
  - Avoid NSAIDs or other nephrotoxic drugs
  - Assure adequate hydration
What About Giving Fluids?

- Adequate hydration most important factor in preventing CI N
- How should the fluids be given?
  - Oral or IV?
- What fluids should we use?
  - 0.5 NS? NS? Isotonic sodium bicarbonate?
Normal Saline or 0.5 Normal?

- Studies addressing this typically include all patients (normal and decreased renal function)
- Overall data shows normal saline more beneficial
- Most benefit seen in diabetics and those receiving high (> 250 ml) doses of contrast
- Benefit decreases in those with more chronic renal dysfunction
IV Bicarbonate?

- Hogan SE, Am Heart J 2008
  - Meta-analysis of 7 RCT; N = 1,307 patients
    - Moderate heterogeneity between studies
  - Compared prehydration with NS vs. sodium bicarbonate
  - Relative risk of CN 0.37 in bicarbonate group
  - No statistically significant impact on...
    - Need for hemodialysis
    - Mortality
Fluids: Bottom Line

- IV more effective than oral
- Normal saline better than 0.5 normal saline
- Isotonic sodium bicarbonate probably best
  - No real downside; may be some benefit
- After procedure, goal is urine output of 150 ml / hour for 6-12 hours
- Diuretics and mannitol NOT effective in preventing CI N - do not use
IV Fluids: Bottom Line

- Isotonic saline
  - Start at 1 ml/kg/hr at least 2 and preferably 6-12 hours before; continue 6-12 hours after contrast
IV Fluids: Bottom Line

- Isotonic bicarbonate
  - 3 amps bicarbonate in 850 ml sterile water (equals 150 mEq sodium/liter)
  - 1.5 amps bicarbonate in one liter 0.5 NS (equals 152 mEq sodium/liter)
- Risk of error in preparation a concern
- Bolus 3 mL/kg for one hour before; continue at rate of 1mL/kg/hr for 6 hours after procedure
N-acetylcysteine

- Issues with the studies
  - Most used oral preparation a day or two in advance of contrast – not applicable to ED
  - Doses varied / patients included varied
  - Most well known study is the ACT trial
    - Acetylcysteine for the prevention of Contrast-induced Nephropathy
Oral N-acetylcysteine

- ACT Trial
  - N = 2,308 patients undergoing angiography
  - “High risk” patients – at least one of: Age > 70 years, chronic kidney disease, diabetes mellitus, CHF or LVEF < 45%, or shock
  - Received either 1200 mg NAC twice daily or placebo on the day before and after angiography
  - AKI defined as ≥ 25% increase in serum Cr 48-96 hours after angiography
  - Found no difference: 12.7% in both groups
Oral N-acetylcysteine

- Criticisms of the ACT Trial
  - Only 367 patients had a serum Cr ≥ 1.5 mg/dL
    - Majority of patients had only mild CKD (GFR 45-60 mL/min/1.73m2) – how much risk of AKI in these patients?
  - Study may have been underpowered to exclude benefit in highest risk patients
  - Baseline Cr within 3 months of procedure – not right before
  - High osmolal contrast used in 20%
IV N-acetylcysteine

Issues with the studies

Okay, so what about the use of NAC in “emergent” cases?

A few studies looked at IV NAC

Doses and administration varied
IV N-acetylcysteine – A “Nay”

- Webb JG; Am Heart J 2004
  - N = 487, mean baseline Cr 1.6 mg/dL
  - Isotonic saline – 200 mL before procedure, 1.5 mL/kg/hr for 6 hours after
  - IV NAC 500 mg immediately before procedure
  - No benefit
  - What might be some problems with this study?
IV N-acetylcysteine – “Aye”??

  - N = 354 AMI patients
  - Different doses of NAC (1200 mg vs. 600 mg IV, then same oral dose twice daily for two days) vs. placebo
  - AKI: Placebo = 33%, low dose = 15%, high dose = 8%
- Issues
  - Included all patients, even those with normal Cr (in whom risk is already low)
  - High rate of medical complications confounding data
Baker CS, J Am Coll Cardiol 2003

- N = 80, mean baseline Cr 1.8 mg/dL
- Compared isotonic saline (1 mL/kg/hr for 12 hours pre- and post-contrast) to IV NAC (150 mg/kg prior, then 50 mg/kg over 4 hours after)
- AKI: NAC = 5%, saline = 20%
- 7% anaphylactoid reactions
IV N-acetylcysteine: Bottom Line

- Data unclear on efficacy when used in emergency situation
- Possibly useful... high risk patients?
- Beware of possible anaphylactoid reactions
- Guidelines contradictory in recommendations
  - Up To Date: No; unproven benefit, risk of anaphylactoid reactions
  - Society for Cardiovascular Angiography: Yes, oral
Possibly Beneficial Therapies

- Prostaglandin E1
  - Hypotension
- Aminophylline / theophylline
  - Arrhythmogenic
- Ascorbic acid – jury’s out
- Statins – maybe... await more data
Not Proven Beneficial

- Angiotension II
- Fenoldopam
- Dopamine
- Calcium channel blocker
- Adenosine
- Endothelin antagonists
What About Follow Up?

- Patients at high risk should get creatinine rechecked in 48 hours
- Patients not at high risk don’t need follow up
Preventing CIN: The Bottom Line

- Identify the patients at risk
  - Cr ≥ 1.5 and/or eGFR ≤ 60 ml/1.73m²
  - Know the additional risk factors
    - Diabetes, hypotension/shock, age > 70, CHF
Preventing CIN: The Bottom Line

- Optimize the basics
  - Consider other imaging modalities (US, MRI, non-contrast CT)
  - If CT unavoidable
    - Avoid high osmolar agents
    - Use low doses of contrast
- Avoid agents toxic to the kidneys
  - NSAIDs
  - Aminoglycosides
  - Diuretics (unless necessary to manage patient)
Preventing Cl N: The Bottom Line

- Assure adequate hydration with IV fluids
  - At minimum, normal saline
  - Isotonic sodium bicarbonate may be better
- NAC not proven effective
  - But consider in high risk patients
- Insufficient data at this point to recommend statins, ascorbic acid, or other agents
Thank You For Your Attention!

Any Questions?