Update on strategies to reduce contrast induced nephropathy: What works and what doesn’t

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A brief history of contrast media

- Werner Forssmann
  - Cath in 1928
  - First attempt at atrial injection 1931
- 1924- Femoral angiography - Barney Brooks

Complications associated with iodinated contrast

- Contrast induced kidney injury
  - Anaphylactoid reactions
  - Delayed reaction
    - T cell mediated
    - IL-2 exposure

How do you define CIN?

- Traditional definition,
  - Rise in serum creatinine > 0.5 mg/dl
- European Society of Urogenital Radiology
  - Increase in SCr by >0.5 mg/dl or >25% within 3 days without an alternative etiology

Why does contrast cause AKI?

- Hemodynamic effects-
  - Vasodilation followed by vasoconstriction (NO mediated)
- Increased oxidative stress
- Direct Tubular cell toxicity
  - Free iodine mediated
Independent factors associated with CIN

<table>
<thead>
<tr>
<th>Name</th>
<th>Odds Ratio (95% CI)</th>
<th>P – Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine Clearance &lt;30 mL/min&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.1 (2.1, 4.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Low BMI &lt;18&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.3 (1.2, 9)</td>
<td>0.024</td>
</tr>
<tr>
<td>High BMI &gt;30&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.3 (1.5, 12.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Pre Anemia&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.1 (1.6, 2.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.8 (1.4, 2.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prior Ccr&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.7 (1.3, 2.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>COPD&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.7 (0.5, 0.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Prior PCI&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.4 (1.1, 1.7)</td>
<td>0.013</td>
</tr>
<tr>
<td>Prior CABG&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.7 (0.5, 0.9)</td>
<td>0.012</td>
</tr>
<tr>
<td>Critical Limb Ischemia&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.6 (1.2, 2.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prior Pericarditis&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.8 (1.2, 2.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>Status – Urgent&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3 (2.4, 3.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Status – Emergent&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7.7 (4.9, 12.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Contrast/CCC Ratio &gt; 3&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.4 (1.1, 1.8)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Model Assessment Measure
Hosmer-Lemeshow P-Value: 0.487; Area Under the ROC Curve (AUC): 0.786

<sup>a</sup> Reference is Creatinine clearance >60mL/min
<sup>b</sup> Reference is Normal BMI (18 ≤ BMI ≤ 30)
<sup>c</sup> Reference is Elective
<sup>d</sup> Reference is Contrast/CCC ratio ≤ 3

Cost Implications of CI-AKI

Average cost of CI-AKI ~ $8900

What does not prevent CI-AKI?

- Hemodynamic model
  - Fenoldopam (dopamine A-1 receptor agonist)
  - Dopamine
- Oxidative injury model
  - N-Acetyl cysteine
  - Poor renal bioavailability (30% with IV)
  - Vitamin C

How to prevent CIN?

- Identify the high risk patient
- Hydrate prior to and after the procedure
- Prophylactic therapy
  - Statins
- Minimize contrast medium use
- Type of contrast media

Why saline hydration works?

- Increased GFR
- Decreased contrast concentration in the filtrate
- Decreased oxygen consumption in the medulla due to decrease need for sodium reabsorption
- Decreased oxidative stress
- Increased catalase and superoxide dismutase
- Decreased endogenous vasoconstrictors
  - Angiotensin, vasopressin
What hydration to use?

**NaHCO3**

Meier et al. BMC Med, 2009

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CIN Rate by Percentage of Pre-Hydration

2014: BMC PVI procedure sites with greater than 55% post-procedure serum creatinine, n=29

Steep slope shows reduction in CIN from 7% to 1%

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CIN Rate by Percentage of Hydration

2014: BMC PVI procedure sites with greater than 55% post-procedure serum creatinine, n=29

Sites with high pre-hydration rates also have high post-hydration rates

Steeper slope means that pre-hydration was more important and there is little post-hydration

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Role for Statins in preventing CIN

Li, PLOS one, 2012

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Rosuvastatin for CIN (PRATO-ACS)

ORcrude (95% CI): 0.41 (0.22 - 0.74)

ORadjusted (95% CI): 0.38 (0.20 – 0.71)

NNT = 12

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Reduce contrast volume

- Contrast media induced injury appears to be directly related to the concentration of contrast media in the glomerular filtrate and eventually in the renal tubules.
  - More contrast injected = higher contrast concentration in tubule
  - Less glomeruli (CKD)=higher contrast concentration in tubule
  - Less glomerular filtrate (Dehydration) = higher contrast concentration in tubule
Minimising contrast volume

• A general principal of as low as reasonably possible should be employed for contrast use

• A ratio of contrast volume/GFR of 2 or less should be considered the ideal dose for a procedure and all attempts should be made to avoid exceeding a dose of 3 X contrast volume/GFR.

• The contrast thresholds (2X GFR and 3X GFR) will be calculated and acknowledged by the team prior to starting the procedure.

Conclusion

• CI-AKI is an uncommon and mostly but not completely, preventable

• Prevention prior to the procedure
  – Identify the high risk patient
  – Preload all patients with statins
  – Ensure adequate hydration, avoid prolonged NPO
  – Stop all nephrotoxic drugs prior (eg NSAIIDs, Aminoglycosides etc)
  – Use the least amount of contrast
  – Use CO2 liberally for those with GFR< 30.