Contrast-Induced Acute Kidney Injury

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Outline

• Etiology of acute kidney injury (AKI)
• Pathophysiology and outcomes
• Approach to prevention
• Selection of contrast
• IV Fluid
• N-Acetylcysteine
• Summary
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HART AKI™ (Acute Kidney Injury) Outcome Results

Multimarker Panel Done before Angiography

- Mix of acute & chronic patients referred cardiac cath (Casablanca) N=889
- Definition of AKI: Serum Cr ≥0.3 mg/dl or % increase of ≥50%, or oliguria of <0.5 mL/kg per hour for >6 hours within 7 days after contrast exposure
- Biomarkers: (↑) Blood Urea Nitrogen:Creatinine Ratio, C-Reactive Protein, Osteopontin (↓) CD5 Antigen-like, Factor VII
- Clinical Variables: (↑) Diabetes

An elevated score was predictive of Procedural AKI Odds Ratio = 9.87; p<0.001

Procedural AKI Risk Prediction
AUC = 0.816; p<0.001

Optimal Cutoff
3 Etiologies for AKI

1. Acute MI (or primary organ injured) itself
2. Iodinated Contrast
3. Athero-microembolism


Incidence of CI-AKI and new ESRD after coronary angiography with PCI according to baseline renal filtration function. Adapted with permission from Tsai et al. (2). ACC = American College of Cardiology; CI-AKI = contrast-induced acute kidney injury; ESRD = end-stage renal disease; GFR = glomerular filtration rate; PCI = percutaneous coronary intervention.
Figure 5. Risk of Death, Bleeding, and Myocardial Infarction in Patients With AKI and/or Dialysis
Outline

• Pathophysiology and outcomes
Markers of filtration indicate transient reductions in glomerular function, whereas cell damage markers indicate cellular injury, and the 2 together have a poorer prognosis than either alone. Not all of these markers have been validated for CI-AKI. Cell cycle arrest markers are TIMP2*IGFBP-7 (tissue inhibitor of metalloproteinase-2 and insulin-like growth factor binding protein-7). CI-AKI = contrast-induced acute kidney injury; GST = glutathione S-transferase; IL = interleukin; KIM = kidney injury molecule; L-FABP = L-type fatty-acid binding protein; NAG = N-acetyl-beta-D-glucosaminidase; NGAL = neutrophil gelatinase-associated lipocalin.
Major Adverse Renal and Cardiac Events After Coronary Angiography and Cardiac Surgery

MARCE = composite of renal replacement therapy, myocardial infarction, stroke, heart failure, renal/cardiac hospitalization, and death

Fig 1. Patient flow diagram. (ECMO = extracorporeal membrane oxygenation; REMPI = Regional Enterprise Master Patient Index; TQI = Texas Quality Initiative.)

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Trans-Radial Coronary Angiography/PCI

Figure 1. Overall percentage of transradial PCI procedures between 2007 and 2012 and PubMed search results on TRA between 1991 and 2008. The overall percentage of F-PCI performed in the United States began to demonstrate an upswing around 2009 (A). There has been an increased number of hits in literature searches on radial access (B), demonstrating the initial enthusiasm period that lasted until the introduction of vascular closure devices, followed by a period of renewed enthusiasm and rapid growth from 2004 to 2008.

Improve Renal Blood Flow
Reduce Extravasation into Peritubular Space
Attenuate Inflammation/Oxidation
Reduce Direct Cellular Toxicity in Nephron

1) Improve Renal Blood Flow
   - Pre-procedure IV NS or NaHCO3
2) Minimize Contrast Volume

1) Reduce Tubular and Peritubular Contrast Stasis with Post-procedure IV NS or NaHCO3
2) Antioxidant Tubular Protection with NAC or Ascorbic acid

1) Anticipate Volume Overload in ESRD and Dialyze Same Day
2) Pre-emptive Hemofiltration for Near Dialysis CKD Patients Before and After PCI

Attempted Preventive Strategies
Trends in the Incidence of Acute Kidney Injury in Patients Hospitalized With Acute Myocardial Infarction

Cerner Db, N=31,532, had 2 or more Cr measures, AKIN used

Figure 2. Unadjusted trends in the incidence of acute kidney injury (AKI).
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Review

Effects of Intra-Arterial and Intravenous Iso-Osmolar Contrast Medium (Iodixanol) on the Risk of Contrast-Induced Acute Kidney Injury: A Meta-Analysis

Peter A. McCullough\textsuperscript{a}  Jeremiah R. Brown\textsuperscript{b}

\textsuperscript{a}St. John Providence Health System, Providence Hospital and Medical Centers, Providence Park Clinical Research, Providence Park Heart Institute, Detroit and Novi, Mich., and
\textsuperscript{b}Dartmouth Institute for Health Policy and Clinical Practice, and Section of Cardiology, Department of Medicine, Dartmouth Medical School, Lebanon, N.H., USA
25 Intra-arterial Trials: CI-AKI Pre-Specified Endpoint

<table>
<thead>
<tr>
<th>Study, year</th>
<th>IOCM</th>
<th>LOCM</th>
<th>Rel. Wt.</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspelin [26] (NEPHRIC), 2003</td>
<td>64</td>
<td>65</td>
<td>5.49</td>
<td>0.115 (0.027–0.493)</td>
</tr>
<tr>
<td>Hill [27], 1994</td>
<td>101</td>
<td>99</td>
<td>2.32</td>
<td>0.198 (0.010–4.074)</td>
</tr>
<tr>
<td>Sinha [28], 2004</td>
<td>35</td>
<td>35</td>
<td>5.47</td>
<td>0.222 (0.051–0.956)</td>
</tr>
<tr>
<td>Wessely [32], 2009</td>
<td>162</td>
<td>162</td>
<td>8.88</td>
<td>0.801 (0.548–1.173)</td>
</tr>
<tr>
<td>Hardiek [15], 2008</td>
<td>54</td>
<td>48</td>
<td>3.82</td>
<td>0.183 (0.023–1.475)</td>
</tr>
<tr>
<td>Laskey [33], 2009</td>
<td>215</td>
<td>203</td>
<td>8.43</td>
<td>1.143 (0.652–2.005)</td>
</tr>
<tr>
<td>Solomon [16] (CARE), 2007</td>
<td>210</td>
<td>204</td>
<td>7.64</td>
<td>1.523 (0.674–3.439)</td>
</tr>
<tr>
<td>Juergens [35], 2009</td>
<td>91</td>
<td>100</td>
<td>8.62</td>
<td>1.196 (0.733–1.951)</td>
</tr>
<tr>
<td>Li [36], 2008</td>
<td>44</td>
<td>43</td>
<td>4.03</td>
<td>0.090 (0.012–0.659)</td>
</tr>
<tr>
<td>Nie [37], 2008</td>
<td>106</td>
<td>102</td>
<td>6.63</td>
<td>0.352 (0.116–1.066)</td>
</tr>
<tr>
<td>Han [25] (abstract), 2010</td>
<td>828</td>
<td>828</td>
<td>8.86</td>
<td>0.122 (0.082–0.493)</td>
</tr>
<tr>
<td>Hernández [38], 2009</td>
<td>118</td>
<td>132</td>
<td>6.11</td>
<td>0.115 (0.027–0.180)</td>
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<tr>
<td>Rudnick [14] (VALOR), 2008</td>
<td>156</td>
<td>143</td>
<td>8.80</td>
<td>0.301 (0.085–1.063)</td>
</tr>
<tr>
<td>Jo [39] (RECOVER), 2006</td>
<td>140</td>
<td>135</td>
<td>6.96</td>
<td>0.916 (0.603–1.391)</td>
</tr>
<tr>
<td>Mehran [40] (ICON), 2009</td>
<td>72</td>
<td>74</td>
<td>7.95</td>
<td>0.404 (0.147–1.114)</td>
</tr>
</tbody>
</table>

**Fig. 2.** Meta-analysis of the incidence of CI-AKI (defined as ≥0.5 mg/dl increase in sCr from baseline) in trials reporting this outcome comparing IA iodixanol (IOCM) with LOCM.
Major Findings

- Pain, warmth, discomfort occur with cerebral and peripheral injections
- Iodixanol associated with ~90% reduction in symptoms compared to LOCM agents
The effect of major adverse renal cardiovascular event (MARCE) incidence, procedure volume, and unit cost on the hospital savings resulting from contrast media use in inpatient angioplasty

Eric Keuffel, Peter A. McCullough, Thomas M. Todoran, Emmanouil S. Brilakis, Swetha R. Palli, Michael P. Ryan, and Candace Gunnarsson

Major Findings

- MARCE events occur in 5-10% of cases
- Iodixanol-only strategy would result in substantial cost savings to health systems

MARCE events were defined as a composite of renal failure with dialysis, AKI with and without dialysis, acute myocardial infarction, angina, stent occlusion/thrombosis, stroke, transient ischemic attack, or death occurring during the inpatient visit.
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Methods
Sliding Scale Hydration Protocol

<table>
<thead>
<tr>
<th></th>
<th>LVEDP Guided Hydration</th>
<th>Standard Hydration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-procedure</strong></td>
<td>3 mL/kg x 1 hr</td>
<td>3 mL/kg x 1 hr</td>
</tr>
<tr>
<td><strong>During procedure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;13</td>
<td>5 mL/kg/hr</td>
<td>1.5 mL/kg/hr</td>
</tr>
<tr>
<td>13-18</td>
<td>3 mL/kg/hr</td>
<td></td>
</tr>
<tr>
<td>&gt;18</td>
<td>1.5 mL/kg/hr</td>
<td></td>
</tr>
<tr>
<td><strong>Post-procedure</strong></td>
<td>Continued x 4hrs</td>
<td>Continued x 4hrs</td>
</tr>
</tbody>
</table>

* For patients >100 kg, use 100 kg to calculate hydration rate

Maximal hydration rate: 500 mL/hr
Primary Endpoint
25% or 0.5 mg/dL increase in serum creatinine

\[ \downarrow 59\% \]

\[ \text{LVEDP guided} \]

\[ 6.7 \]

\[ \text{Control} \]

\[ 16.3 \]

\[ P=0.005 \]

RR (95% CI):
0.41 (0.22 – 0.79)

RD (95% CI):
-9.5% (-16.3 to -2.9)
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Does sodium bicarbonate or acetylcysteine prevent contrast induced harm? The PRESERVE Trial.

**Conclusions** Neither IV sodium bicarbonate or acetylcysteine has any effect at reducing contrast induced harm after angiography. No signal was seen at eGFR < 45.

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Peter A. McCullough, MD, MPH, James P. Choi, MD, Georges A. Feghali, MD, Jeffrey M. Schussler, MD, Robert M. Stoler, MD, Ravi C. Vallabahn, MD, Ankit Mehta, MD

CENTRAL ILLUSTRATION  Algorithm for the Prevention and Management of CI-AKI

Calculate estimated glomerular filtration rate (eGFR)
Assess Contrast-Induced Acute Kidney Injury (CI-AKI) risk

<table>
<thead>
<tr>
<th>eGFR &lt;30 ml/min/1.73 m²</th>
<th>eGFR 30-59 ml/min/1.73 m²</th>
<th>eGFR ≥60 ml/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Throughout:</strong></td>
<td><strong>Throughout:</strong></td>
<td><strong>Throughout:</strong></td>
</tr>
<tr>
<td>Good clinical practice as for eGFR &gt; 60 ml/min/1.73 m²</td>
<td>Good clinical practice as for eGFR &gt; 60 ml/min/1.73 m²</td>
<td>Good clinical practice: Discontinue metformin, other nephrotoxic drugs, RAAS inhibitors</td>
</tr>
<tr>
<td>Other strategies as for eGFR 30-59 ml/min/1.73 m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Before procedure:</strong></td>
<td><strong>Before procedure:</strong></td>
<td><strong>Before procedure:</strong></td>
</tr>
<tr>
<td>Consider hospital admission</td>
<td>Ensure statin use</td>
<td>Consider hospital admission</td>
</tr>
<tr>
<td>Nephrology consultation</td>
<td>Pre-procedure IV volume expansion**</td>
<td>Nephrology consultation</td>
</tr>
<tr>
<td>Dialysis planning*</td>
<td></td>
<td>Dialysis planning*</td>
</tr>
<tr>
<td>Same intravenous volume management as for eGFR 30-59 ml/min/1.73 m²</td>
<td></td>
<td>Same intravenous volume management as for eGFR 30-59 ml/min/1.73 m²</td>
</tr>
<tr>
<td><strong>During procedure:</strong></td>
<td><strong>During procedure:</strong></td>
<td><strong>During procedure:</strong></td>
</tr>
<tr>
<td>Iso-osmolar contrast (iodixanol)</td>
<td>LVEDP-guided intraprocedure + 4 hours post-procedure isotonic crystalloid management</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low-osmolar contrast</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iso-osmolar contrast (iodixanol) if ACS, CKD=DM, HF, TAVI</td>
<td></td>
</tr>
<tr>
<td></td>
<td>As low as reasonably achievable contrast volume</td>
<td></td>
</tr>
<tr>
<td><strong>Post procedure:</strong></td>
<td><strong>Post procedure:</strong></td>
<td><strong>Post procedure:</strong></td>
</tr>
<tr>
<td>Measure renal damage markers and daily serum creatinine</td>
<td></td>
<td>Ensure statin use</td>
</tr>
</tbody>
</table>

Conclusions

- Contrast-induced AKI occurs in ~15% at risk patients undergoing arterial administration and is associated with poor outcomes
- Contrast volume and type play a role
- Short-term volume expansion prior to exposure appears to be partially preventive
- NAC is not efficacious
- Future research is working towards non-contrast contrast agents and continues to pursue prophylactic, protective agents