A Propensity-Matched Study of the Association of Contrast Media Administration with Acute Kidney Injury (AKI) in ICU patients

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A propensity-matched study of the association of contrast media administration with acute kidney injury (AKI) in critically ill patients

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Gail Walker, PhD

June 17, 2016
What is Acute Kidney Injury (AKI)?

AKI is defined as **any** of the following:

- Increase in Serum Creatinine (SCr) by 0.3 mg/dl (26.5 lmol/l) within 48 hours; or

- Increase in SCr to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or

- Urine volume ≤ 0.5 ml/kg/h for 6 hours.
## Criteria

<table>
<thead>
<tr>
<th>GFR criteria</th>
<th>UO criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 1 (Risk)</strong></td>
<td></td>
</tr>
<tr>
<td>Increased creatinine x1.5 or</td>
<td>UO &lt;0.5 ml/kg/h x 6 hours</td>
</tr>
<tr>
<td>Increased by 0.3 mg/dL within</td>
<td></td>
</tr>
<tr>
<td>48 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Stage 2 (Injury)</strong></td>
<td></td>
</tr>
<tr>
<td>Increased creatinine x2 (consider possible Renal Replacement Therapy)</td>
<td>UO &lt;0.5 ml/kg/h x 12 hours</td>
</tr>
<tr>
<td><strong>Stage 3 (Failure)</strong></td>
<td></td>
</tr>
<tr>
<td>Increased creatinine x3 or SCr ≥4 mg/dl</td>
<td>UO &lt;0.3 ml/kg/h x 24 hours or anuria x 12 hours</td>
</tr>
</tbody>
</table>

AKI occurs in more than 50% of all ICU patients.

Worsening AKI is associated with increased mortality.
Contrast and AKI

Risk of contrast induced nephropathy in the critically ill: a prospective, case matched study


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Andrew A Quartin (aquartin@med.miami.edu)

Frequency of Acute Kidney Injury Following Intravenous Contrast Medium Administration: A Systematic Review and Meta-Analysis

**Data preparation**

**BHSF IT data warehouse**

- **ICU**
  - Dates
  - Discharge location
  - APACHE score

- **Hospital**
  - Patient demog.
  - Dates
  - Discharge location

- **ICD9 diagnoses**
  - Primary
  - 2dry + POA

- **Labs**
  - Creatinine

- **ICD9 procedures**
  - Dialysis
  - Imaging

- **Charges**
  - Contrast

**KDIGO Creatinine Criteria**

<table>
<thead>
<tr>
<th>AKI stage</th>
<th>eGFR</th>
<th>CKD stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≥ 90</td>
<td>1 Normal</td>
</tr>
<tr>
<td>1 Risk</td>
<td>60-89</td>
<td>2 Mild</td>
</tr>
<tr>
<td>2 Injury</td>
<td>30-59</td>
<td>3A-B Moderate</td>
</tr>
<tr>
<td>3 Failure</td>
<td>15-29</td>
<td>4 Severe</td>
</tr>
<tr>
<td>Dialysis</td>
<td>&lt;15</td>
<td>5 Very severe</td>
</tr>
</tbody>
</table>

KDIGO Creatinine Criteria:

- < 1.5 × baseline \* and increase < 0.3 within 48 hrs
- (1.5 to 1.9) × baseline or increase ≥ 0.3 within 48 hrs
- (2.0 to 2.9) × baseline
- ≥ 3.0 × baseline or ≥4.0 mg/dL or initiation of renal replacement rx
Analysis sets

20,408 hospitalizations 2010-2014 with a single ICU stay ≥ 1 day & no prior hospitalization < 30 days

Exclusions
- LOS > 30 days
- Discharged AMA or transfer
- Discrepant ICU and hospital data
- Missing APACHE or creatinine data
- ≥ 4 contrast
- 1st contrast ≥ 2 days post admit

Future analysis
- AKI Stage 3 on admit
- CKD 3-5 on admit (N=6,033)

8,394

14,461

20,408

3,051 Contrast
5,343 No contrast

15,957
### Contrast, AKI and hospital death

#### Worsening AKI vs. Stable AKI vs. All

<table>
<thead>
<tr>
<th></th>
<th>Worsening AKI</th>
<th>Stable AKI</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Contrast</td>
<td>670</td>
<td>22.0</td>
<td>2,381</td>
</tr>
<tr>
<td>No contrast</td>
<td>1,075</td>
<td>20.1</td>
<td>4,268</td>
</tr>
<tr>
<td>All</td>
<td>1,745</td>
<td>20.8</td>
<td>6,649</td>
</tr>
</tbody>
</table>

#### Died vs. Alive vs. All

<table>
<thead>
<tr>
<th></th>
<th>Died</th>
<th>Alive</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Worsening AKI</td>
<td>291</td>
<td>16.7</td>
<td>4,381</td>
</tr>
<tr>
<td>Stable AKI</td>
<td>253</td>
<td>3.8</td>
<td>4,268</td>
</tr>
<tr>
<td>All</td>
<td>544</td>
<td>6.5</td>
<td>7,850</td>
</tr>
</tbody>
</table>
36.3% of study cases had contrast (3051 / 8394)
- 47.9% of patients hospitalized for cardiovascular disease (975 / 2037)
- 35.4% of diabetic patients (822 / 2321)
- 28.5% of patients with renal comorbidity (74 / 260)
- 8.0% of patients hospitalized for endocrine, metabolic or immune disorders (35 / 438)

Is contrast associated with AKI and hospital mortality after adjusting for factors that influence its use?
Method—propensity score matching

- Propensity score (PS)
  - Predicted probability of receiving contrast ......
  - ...... from regression model of contrast use (Y/N) in relation to many factors
  - Used to match contrast cases to similar cases in the larger no-contrast pool
  - Enables estimation of the relative risk of worsening AKI in matched sample

- PS model covariates
  - Age, gender, race, BMI
  - 12 categories of primary diagnosis; 7 categories on ICU admit
  - 13 comorbidities
  - Severity scores: APS, APACHE, predicted ICU and hospital mortality

- Matching criteria
  - Propensity scores of matched pairs within $20\% \times \sigma_{PS}$
  - Same reference AKI stage

- Implemented in R MatchIt package (Ho et al. 2011)

Did we get a good match?
Graphical summary of pre and post match balance

2,749 (90%) of 3,051 contrast cases were matched
**Results**

**Unadjusted**

- 8,394 cases
  - 36.3% contrast
  - 20.8% worsening AKI
  - 6.5% died in hospital
  - 22.0 vs. 20.1% by contrast
  - 16.7 vs. 3.8% by worsening AKI

*RR of worsening AKI due to contrast*  
1.09 (95% CI: 1.0—1.2), p=0.047

*RR of death due to worsening AKI*  
4.4 (95% CI: 3.7—5.1), p<0.001

**Propensity matched**

- 5,498 cases
  - 50.0% contrast
  - 20.4% worsening AKI
  - 6.7% died in hospital
  - 21.5 vs. 19.3% by contrast
  - 17.1 vs. 4.0% by worsening AKI

*RR of worsening AKI due to contrast*  
1.11 (95% CI: 1.0—1.2), p=0.048

*RR of death due to worsening AKI*  
4.3 (95% CI: 3.5—5.2), p<0.001

*RR: Relative risk*
Does contrast affect the pattern of worsening AKI?

- 1,122 (20.4%) patients developed worsening AKI
- 803 (71.6%) of these patients recovered

**If not contrast, what?**

Baptist Health South Florida
Research & Grants
Elevating care through discovery
Factors associated with worsening AKI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contrast</td>
<td>1.17</td>
<td>1.02 to 1.34</td>
<td>0.023</td>
</tr>
<tr>
<td>Age, per 15 years</td>
<td>1.15</td>
<td>1.07 to 1.24</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male vs female</td>
<td>1.21</td>
<td>1.05 to 1.39</td>
<td>0.007</td>
</tr>
<tr>
<td>Black vs White, White Hispanic or Other</td>
<td>1.29</td>
<td>1.04 to 1.59</td>
<td>0.021</td>
</tr>
<tr>
<td>BMI ≥ 30 (obese/morbidly obese) vs &lt;30</td>
<td>1.14</td>
<td>0.98 to 1.33</td>
<td>0.096</td>
</tr>
</tbody>
</table>

Primary diagnosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>—</td>
<td>reference</td>
<td>—</td>
</tr>
<tr>
<td>Cerebrovascular or peripheral vascular</td>
<td>0.91</td>
<td>0.72 to 1.14</td>
<td>0.401</td>
</tr>
<tr>
<td>Digestive</td>
<td>1.34</td>
<td>1.05 to 1.30</td>
<td>0.019</td>
</tr>
<tr>
<td>Respiratory (parenchymal or airway)</td>
<td>1.56</td>
<td>1.25 to 1.94</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>1.40</td>
<td>1.03 to 1.90</td>
<td>0.032</td>
</tr>
<tr>
<td>Injury/poisoning</td>
<td>1.21</td>
<td>0.90 to 1.64</td>
<td>0.214</td>
</tr>
<tr>
<td>Sepsis and other infections</td>
<td>2.35</td>
<td>1.78 to 3.11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Endocrine/metabolic/immune</td>
<td>2.08</td>
<td>1.17 to 3.70</td>
<td>0.012</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>1.21</td>
<td>0.62 to 2.38</td>
<td>0.576</td>
</tr>
<tr>
<td>Other</td>
<td>1.45</td>
<td>1.06 to 1.97</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Comorbidity

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>1.13</td>
<td>0.97 to 1.32</td>
<td>0.129</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.37</td>
<td>1.18 to 1.60</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CPD</td>
<td>1.23</td>
<td>1.05 to 1.44</td>
<td>0.004</td>
</tr>
<tr>
<td>CHF</td>
<td>1.62</td>
<td>1.37 to 1.93</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Vascular</td>
<td>1.20</td>
<td>0.98 to 1.47</td>
<td>0.084</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.08</td>
<td>0.85 to 1.35</td>
<td>0.536</td>
</tr>
<tr>
<td>Liver</td>
<td>1.80</td>
<td>1.42 to 2.28</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Renal</td>
<td>5.83</td>
<td>4.02 to 8.47</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
APACHE as a predictor of AKI

- 4,725 patients admitted to ICU within 1 day of hospital admit
- Predicted probability at age 65 by gender, race, BMI and APACHE score

90th percentile APACHE (73)
- Black male, obese
- Black female, obese
- Black male
- White male, obese
- Black female
- White female, obese
- White male
- White female

Median APACHE (46)
- Black male, obese
- Black female, obese
- Black male
- White male, obese
- Black female
- White female, obese
- White male
- White female

10th percentile APACHE (27)
- Black male, obese
- Black female, obese
- Black male
- White male, obese
- Black female
- White female, obese
- White male
- White female
Analysis recap

- The BHSF IT data warehouse is an excellent resource for retrospective research studies.
- Time devoted to data cleaning and preparation always pays off and must be focused on a clear study objective and analysis plan.
- In absence of randomization, propensity score methods can reduce confounding in retrospective studies to establish valid comparison groups.
Clinical implications – So what?

• Contrary to current clinical belief, contrast should not be avoided when reasonably needed to treat critically ill patients

• Focus should be on prevention, reversal of renal ischemia, and maintenance of renal perfusion

• Prevent worsening AKI

• Implement KDIGO guidelines for early identification, early treatment and reversal of AKI