Randomized clinical trial to compare the nephrotoxic effects of iso-osmolar vs. low-osmolar contrast medium in patients with impaired renal function undergoing PCI

**CONTRAST**

(Contrast media and NephroToxicity following coronary Revascularization by Angioplasty)

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Patients with chronic renal failure (CRF) have an increased incidence of coronary artery disease.

In these high risk patients, PCI is often complex and associated with increased application of contrast medium.

However, patients with CRF are at increased risk for contrast medium induced nephropathy (CIN) that is associated with adverse outcomes.

Therefore, a strategy to reliably decrease the occurrence of CIN following PCI in these high risk patients is warranted.
To compare nephrotoxicity between the iso-osmolar contrast medium IODIXANOL and the low-osmolar contrast medium IOMEPROL in patients with impaired renal function undergoing PCI.
Patient selection

Inclusion criteria

- Indication for coronary angiography with intention for PCI
- Chronic renal failure (eGFR\(^1\) ≤ 60 ml/min or S-creatinine ≥ 1.5 mg/dl)
- Age ≥ 18 years, no pregnancy
- Informed, written consent

Exclusion criteria

- Prior hemodialysis
- Cardiogenic shock
- Concurrent intake of nephrotoxic medication (e.g. metformin, NSAID, aminoglycosides, etc.) ≤ 48h prior contrast exposure
- Prior kidney transplantation
- Contra-indications for the use of Iodixanol or Iomeprol
- Prior or planned intravascular administration of iodine-containing contrast medium at least 7 days before or after catheterization

\(^{1}\) estimated glomerular filtration rate (eGFR) calculated according to MDRD formula (Levey et al., Ann Int Med 1999)
Primary endpoint:
Rise of S-creatinine as a measure of contrast medium induced nephrotoxicity during hospitalization for PCI

Secondary endpoints:
- Duration of hospitalization
- Incidence of severe acute kidney failure (creatinine increase by more than 1mg/dl and/or dialysis)
- Reassessment of the primary endpoint 6 months after PCI
- Mortality within 12 months
- Cardiovascular events within 12 months (death, myocardial infarction, TLR)
Study flow chart

975 pts. with renal failure undergoing coronary angiography

477 pts. received Iodixanol
- 315 pts. did not undergo PCI
- 162 pts. underwent PCI
  - Included in analysis

498 pts. received Iomeprol
- 162 pts. underwent PCI
  - Included in analysis
- 336 pts. did not undergo PCI
### Baseline characteristics – renal function

<table>
<thead>
<tr>
<th></th>
<th>Iodixanol 320</th>
<th>Iomeprol 350</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-creatinine prior PCI</td>
<td>1.36 ± 0.51</td>
<td>1.37 ± 0.33</td>
<td>.74</td>
</tr>
<tr>
<td>S-urea prior PCI</td>
<td>55.6 ± 23.7</td>
<td>57.8 ± 27.4</td>
<td>.44</td>
</tr>
<tr>
<td>eGFR prior PCI</td>
<td>46.4 ± 9.3</td>
<td>47.1 ± 9.0</td>
<td>.44</td>
</tr>
</tbody>
</table>

S-creatinine [mg/ml]; S-urea [mg/ml]; eGFR [ml/min/1.73m²]
## Results – renal function post PCI

<table>
<thead>
<tr>
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<th>Iodixanol 320</th>
<th>Iomeprol 350</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. S-creatinine post PCI</td>
<td>1.55 ± 0.58</td>
<td>1.59 ± 0.48</td>
<td>.51</td>
</tr>
<tr>
<td>Max. S-urea post PCI</td>
<td>59.4 ± 30.8</td>
<td>61.2 ± 30.0</td>
<td>.59</td>
</tr>
</tbody>
</table>

S-creatinine [mg/ml]; S-urea [mg/ml]
Results – renal function post PCI

Maximal rise in S-creatinine post PCI [mg/dl]

P = 0.53

<table>
<thead>
<tr>
<th></th>
<th>Iodixanol</th>
<th>Iomeprol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal</td>
<td>0.19</td>
<td>0.21</td>
</tr>
</tbody>
</table>


Contrast-induced nephropathy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Iodixanol</th>
<th>Iomeprol</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ S-Crea ≥ 0.5 or Δ S-Crea ≥ 25%</td>
<td>22.2%</td>
<td>27.7%</td>
<td>0.25</td>
</tr>
<tr>
<td>Δ S-Crea ≥ 1.0</td>
<td>6.2%</td>
<td>3.7%</td>
<td>0.30</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1.9%</td>
<td>0.6%</td>
<td>0.31</td>
</tr>
</tbody>
</table>
Subgroup analysis: eGFR and contrast volume

**Iodixanol** better  **Iomeprol** better

\[ \Delta S - \text{creatinine} \]

- eGFR [ml/min/1.73m²]; contrast volume [ml]
- eGFR \( \leq 50 \) vs. > 50
- contrast volume \( \leq 340 \) vs. > 340

\[ -0.4 \quad -0.2 \quad 0.0 \quad 0.2 \quad 0.4 \]
Subgroup analysis: diabetes

\[ \Delta S - \text{creatinine} \]

Iodixanol better    Iomeprol better

- No diabetes, \( n=203 \)
- Diabetes, \( n=121 \)
- NIDDM, \( n=76 \)
- IDDM, \( n=45 \)
<table>
<thead>
<tr>
<th>Event</th>
<th>Iodixanol 320</th>
<th>Iomeprol 350</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target lesion revasc., %</td>
<td>2.5</td>
<td>2.5</td>
<td>1.00</td>
</tr>
<tr>
<td>Myocardial infarction, %</td>
<td>3.7</td>
<td>4.3</td>
<td>.77</td>
</tr>
<tr>
<td>Stent thrombosis, %</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Death, %</td>
<td>1.2</td>
<td>1.8</td>
<td>.65</td>
</tr>
<tr>
<td>MACE, %</td>
<td>6.2</td>
<td>6.8</td>
<td>.82</td>
</tr>
</tbody>
</table>
Conclusion

In patients with impaired renal function undergoing PCI following appropriate i.v. hydration, the iso-osmolar contrast medium Iodixanol revealed similar nephrotoxicity compared to the low-osmolar contrast medium Iomeprol.