Risk Assessment and Prevention of Contrast-Induced Nephropathy in Patients Undergoing Coronary Angiography

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Key words: contrast-induced nephropathy, ascorbic acid, coronary angiography, risk assessment and prevention

(Intern Med 51: 519-521, 2012)
(DOI: 10.2169/internalmedicine.51.6875)

Contrast-induced nephropathy (CIN) is one of the most important clinical complications associated with coronary diagnostic and interventional procedures, accounting for 10% of all causes of hospital-acquired renal failure (1, 2). Its development is associated with increased morbidity and mortality, including the need for transient dialysis and/or extended hospitalization, and can lead to chronic end-stage renal disease (1, 3, 4). A number of risk factors for the development of CIN have been reported. The Mehran CIN-Risk score was proposed as a simple risk score to be readily applied by clinicians to assess the individual risk for CIN development following percutaneous coronary intervention (Table 1) (5, 6). This score includes 8 clinical and procedural variables, as listed in Table 1, and has been validated for the prediction after non-urgent percutaneous coronary intervention in patients undergoing angioplasty. Risk assessment by scoring was proven to successfully predict CIN and to stratify patients for poor clinical outcomes both in the short- and long-term follow-up (7). In addition, choice of contrast media (8), urgent interventions, and patient dehydration are involved in other specific risk factors (9). The superiority of low-osmolar over high-osmolar contrast medium is generally accepted, in particular, in patients with chronic renal insufficiency because high-osmolar contrast media was shown to have direct nephrotoxicity (10). Dehydration is also widely believed to be a risk factor based on clinical experience, but there are few trials demonstrating this risk (11).

To date, many prophylactic strategies have been investigated extensively. The recent guidelines have been proposed the following strategies to prevent CIN (11).

[1] Hydration with intravenous infusion (12)
A recommended regime is 1.0-1.5 ml/kg/h for at least 6 hours before and after contrast medium administration for normal saline (sodium chloride), or 3 ml/kg/h for 1 hour before followed by 1 ml/kg/h for 6 hours after for sodium bicarbonate.

[2] Use of low or iso-osmolar contrast medium and the lowest dose for at-risk patients.

[3] Patients taking metformin
1) Patients with eGFR equal to or greater than 60 ml/min/1.73 m² can continue to take metformin normally.
2) Patients with eGFR 30-59 ml/min/1.73 m²:
   a) Patients receiving intravenous contrast medium with eGFR equal to or greater than 45 ml/min/1.73 m² can continue to take metformin normally.
   b) Patients receiving intra-arterial contrast medium, and those receiving intravenous contrast medium with an eGFR of between 30 and 44 ml/min/1.73 m², should stop metformin 48 hours before contrast medium and should only restart metformin 48 hours after contrast medium if renal function has not deteriorated.
3) Patients with eGFR of less than 30 ml/min/1.73 m², or with a concomitant illness causing reduced liver function or hypoxia. Metformin is contraindicated and iodine-based contrast media should be avoided.
4) Emergency patients. Metformin should be stopped from the time of contrast medium administration. After the procedure, the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

The nephrotoxic drugs could be withdrawn after discussing the relative benefits and harms.

[5] Pharmacological prophylaxis

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Received for publication November 4, 2011; Accepted for publication November 23, 2011

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Table 1. Mehran Risk Scores and Prediction of Contrast-Induced Nephropathy (CIN)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Integer Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>5</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>5</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>5</td>
</tr>
<tr>
<td>Age &gt;75 yrs</td>
<td>4</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
</tr>
<tr>
<td>Contrast media volume</td>
<td>1 for each 100 cc</td>
</tr>
<tr>
<td>eGFR &lt;20 mL/min/1.73 m²</td>
<td>6</td>
</tr>
<tr>
<td>eGFR 20–40 mL/min/1.73 m²</td>
<td>4</td>
</tr>
<tr>
<td>eGFR 40–60 mL/min/1.73 m²</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sum of Risk Score</th>
<th>Risk of CIN</th>
<th>Risk of Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5</td>
<td>7.5 %</td>
<td>0.04 %</td>
</tr>
<tr>
<td>6 - 10</td>
<td>14.0 %</td>
<td>0.12 %</td>
</tr>
<tr>
<td>11 - 16</td>
<td>26.1 %</td>
<td>1.09 %</td>
</tr>
<tr>
<td>&gt; 16</td>
<td>57.3 %</td>
<td>12.8 %</td>
</tr>
</tbody>
</table>

Hypotension means systolic blood pressure <80 mmHg; Anemia, hematocrit <39% for men and <35% for women, and eGFR, estimated glomerular filtration rate.

Actually, no drugs have been approved for the prevention of CIN because none of the pharmacological manipulations have been shown to offer consistent protection. A number of trials using different agents have been tested and published. These agents include N-acetylcysteine, ascorbic acid, atrial natriuretic peptide (ANP), L-arginine, fenoldopam, dopamine, calcium channel blockers, prostaglandin E₁, furosemide, mannitol, endothelin receptor antagonist and statin, but the evidence is limited at best. Some studies reported preferable effects, but then subsequent studies reported conflicting results. Above all, considerable attention has been paid to N-acetylcysteine. In addition to the preferable results, there are other specific reasons in consideration that N-acetylcysteine is reasonably priced and safe, and it can be available for both oral and intravenous administration.

Recently, the meta-analysis of prophylaxis using high-dose statin for the prevention of CIN has been reported, indicating the support of the effectiveness of periprocedural short-term treatment with high-dose statin (13, 14). Further prospective clinical trials will be necessary to reflect these results as the guidelines.

In the issue of Internal Medicine, Zhou and Chen (15) report that short-term pretreatment with high-dose ascorbic acid did not prevent renal function deterioration in patients with chronic renal insufficiency although ascorbic acid treatment did not develop any adverse effects and appeared to attenuate worsening renal function compared with control. Ascorbic acid is cheap and considered safe orally and intravenously, and may be beneficial because of its antioxidant activity which is similar to N-acetylcysteine. This study demonstrated the conflicting results from the previous report by Spargias et al (16). However, there are several differences between the two studies in dosage used and the route of administration of ascorbic acid, severity of renal insufficiency, the size of study group, and so forth. The studies following Spargias et al to test the effects of ascorbic acid on CIN did not obtain as many beneficial results as their study (17, 18). Additionally, one study regarding comparisons between the effects of N-acetylcysteine and ascorbic acid on preventing CIN suggests that N-acetylcysteine is more beneficial than ascorbic acid (19). Taken together, currently, there is no reliable evidence to recommend the use of ascorbic acid for preventing CIN in at-risk patients.

In terms of ANP, we have previously reported the significantly beneficial effects on preventing the development of renal dysfunction in the patients with chronic renal insufficiency (20) compared with the previous study (21), and we believe that such successful results contribute to the lower dose of ANP and infusion for 48-hours after the procedure in addition to the 4- to 6-hour infusion before the procedure.

Immediately after angiography, hemodialysis is often performed to remove the contrast medium in patients with advanced renal dysfunction, but in the study of Morcos et al, hemodialysis did not protect against CIN (22). Therefore, the guideline does not recommend it (11).

The authors state that they have no Conflict of Interest (COI).

References