Patients treated by the interventional cardiologist are now older and more frequently have coexistent renal insufficiency than in the past. Exacerbation of renal function can be a serious, morbidity complication of cardiac catheterization or intervention and efforts to avoid this untoward event are important to acknowledge.

The incidence of contrast-induced nephropathy (CIN) ranges from 2% in patients with normal baseline renal function to as high as 20% to 30% in patients with a baseline creatinine >2 mg/dL.3 The most commonly used definition of CIN is an absolute rise in serum creatinine (SCr) of 0.5 mg/dL or a 25% increase from the baseline value, assessed within 48 hours after the procedure.3

Risk Assessment
Most CIN risk factors can be accessed from clinical history, physical examination, and common laboratory tests. Preexisting chronic kidney disease is probably the most important preprocedural risk factor for CIN. Because an estimated glomerular filtration rate <60 mL/min per 1.73 m² is a major risk factor for CIN,4 the baseline estimated glomerular filtration rate should be determined before any procedure in which contrast is administered. Other independent predictors for CIN include the presence of diabetes mellitus, volume depletion, the use of nephrotoxic drugs, hypotension, age >75 years, advanced heart failure, left ventricular systolic function <45%, and anemia.5,6 Different scoring schemes have been proposed to predict the risk for CIN, but none has been adequately validated. When at-risk patients are identified, various measures can be offered to reduce CIN occurrence.

Before the Procedure
Withdrawal of Potentially Nephrotoxic Medications
Patients should be advised to withhold all nonessential medications that may be nephrotoxic for 24 hours before the procedure (Table). Although there has been controversy as to whether angiotensin-converting enzyme inhibitors or angiotensin receptor blockers may predispose to nephrotoxicity, a recent study demonstrated no such effect.7 Accordingly, it is reasonable to continue angiotensin-converting enzyme inhibitors or angiotensin receptor blockers if patients are already taking these drugs.

Pharmacological Strategies
N-acetylcysteine was considered a renal protective agent against CIN in the past. However, recent studies have failed to demonstrate a benefit.8 Thus, current guidelines of both the American Heart Association and the European Society of Cardiology do not recommend the use of N-acetylcysteine to prevent CIN in patients undergoing angiographic procedures.9,10

Because of their anti-inflammatory and antithrombotic effects in preservation of endothelial function at the level of the glomerulus, statins seem to play a role in CIN prevention. Several studies have shown the efficacy of short-term, high-dose statins in reducing the incidence of CIN in patients undergoing cardiac catheterization.11,12 Thus, the implementation of high-dose statin before coronary angiography should be considered as an additional preventive measure in patients without contraindications.

Pre Hydration
Hydration before cardiac catheterization is by far the most effective prophylactic intervention. Hydration ensures adequate renal blood flow and acts to dilute contrast media (CM) in both blood and tubular filtrate. The oral route of fluid administration may be acceptable if adequate intake is assured. However, in moderate- or high-risk patients, especially those with preexisting chronic kidney disease, intravenous hydration is preferred over oral hydration because it ensures delivery of an appropriate volume and has proven efficacy.13 There are limited data on the most appropriate choice of intravenous fluid, but most evidence indicates that isotonic crystalloid (saline or bicarbonate solution) is more effective than half-normal saline.14 The ongoing Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial, which aims to compare the effectiveness of intravenous isotonic sodium bicarbonate with isotonic sodium chloride for the prevention of CIN, may help to clarify optimal therapy.15

There is no evidence to determine the optimal rate and duration of infusion. No specific fluid volume or length of treatment has been verified. The American Heart Association guidelines recommend isotonic saline infusion at a rate of 1 to 1.5 mL/kg per hour for 3 to 12 hours before the procedure and continuing 6 to 24 hours after the procedure, whereas the European Society of Cardiology guidelines recommend saline infusion at a rate of 1 to 1.5 mL/kg per hour for 12 hours before and up to 24 hours after the procedure.9,10
Throughout the Procedure

Choice of Contrast Media

Initially, developed CM was hyperosmolar and potentially nephrotoxic; now this type of contrast is used rarely. Newer agents, including nonionic low-osmolar and iso-osmolar CM, are now readily available. Comparative studies of low-osmolar and iso-osmolar agents have produced variable and sometimes contradictory results. Thus, current data are insufficient to justify specific recommendation about the preferred use of either low- or iso-osmolar CM.

Minimizing Contrast Media Volume

The correlation between the volume of CM and the risk of CIN is well documented. Consequently, minimizing the CM volume is a important measure to prevent CIN. A specific method for quantifying the maximum safe volume of CM has been proposed by Laskey et al., who demonstrated that a ratio of the volume of CM:creatinine clearance >3.7 associates strongly with the risk of developing CIN in patients undergoing coronary angiography. Staged procedure should be considered when contrast volume exceeds 3.7× of creatinine clearance as recommended by both the European Society of Cardiology guidelines and the consensus statement from the Society for Cardiovascular Angiography and Interventions. Because previous CM exposure within 72 hours is a risk factor for CIN, it is reasonable to perform the staged procedure at least 3 days later in patients without clinical indications for emergent coronary angiography.

After the Procedure

Post Hydration

As noted previously, current guidelines recommend continuation of hydration after the completion of the procedure. The exact duration differs with a range of 6 to 24 hours.

SCr Monitoring

The definition of CIN is based on the rise of SCr and decline in the estimated glomerular filtration rate. The timing of SCr measurement after the procedure is of paramount importance. If it is measured too early, the rise in SCr may be missed. On the contrary, if it is measured too late, it may unnecessarily prolong hospitalization. Although the trajectory of the rise in SCr commonly peaks at 48 to 96 hours after contrast exposure, it is not necessary to monitor the SCr until it peaks. In fact, nearly all patients who develop serious renal failure experience a rise in SCr >0.5 mg/dL at 24 hours. Moreover, patients whose SCr levels rise <0.5 mg/dL at 24 hours are unlikely to incur any adverse renal outcomes and may be considered for discharge without further SCr monitoring. Based on the current evidence, it is appropriate to monitor SCr at 24 hours after contrast administration.

When CIN Occurs

If CIN develops despite preventive measures, continue to withhold nephrotoxic medications, maintain adequate hydration status, and monitor electrolytes. Early nephrology consultation is warranted.

Novel Preventive Measures

Hydration Optimization Guided by Left Ventricular End-Diastolic Pressure

As mentioned above, little is known about the optimal rate and duration of fluid administration around the time of CM exposure. Underhydration increases the risk of CIN, whereas overhydration aggravates pulmonary congestion especially in those with preexisting chronic kidney disease or left ventricular dysfunction. The Prevention of Contrast Renal Injury With Different Hydration Strategies (POSEIDON) trial describes left ventricular end-diastolic pressure as a tool to guide the rate of fluid administration. The left ventricular end-diastolic pressure is measured by placing a pigtail catheter in the midcavity of the left ventricle before the administration of CM. This randomized controlled trial demonstrated that left ventricular end-diastolic pressure–guided volume expansion in at-risk patients was safe and resulted in larger volume expansion and a significant reduction in the incidence of CIN from 16.3% in the control group to 6.7% in the left ventricular end-diastolic pressure–guided group.

Furosemide With Matched Hydration

Theoretically, furosemide should protect the kidney from CIN by reducing CM-related outer medullary hypoxia and decreasing the concentration and the transit time of CM in kidneys. Furosemide, however, has been shown to have deleterious effect in kidneys after CM exposure. This untoward effect may be related to the use of high-dose furosemide without matched hydration that results in volume depletion.

To avoid hypovolemia, a novel approach is developed, in which high-risk patients for CIN receive 250 mL of isotonic saline infusion for >30 minutes (or ≤150 mL in those with left ventricular dysfunction), followed by intravenous administration of furosemide (0.25 mg/kg) to achieve an optimal urine flow of ≥300 mL/h. Cardiac catheterization is performed as soon as the target urine output is reached. Hourly urine output is measured with the same amount of fluid being replaced intravenously for 4 hours post the procedure. The benefits of this approach for CIN prevention were demonstrated by a randomized controlled trial. According to the European Society of Cardiology guidelines, this treatment is rated as a class IIb recommendation for patients at a high risk of CIN.

Novel Devices in Reducing Contrast Media Volume

Automated contrast injectors are developed to reduce the amount of CM delivery. Automated contrast injectors are

### Table. Nephrotoxic Medications

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal anti-inflammatory</td>
<td>Ibuprofen, Diclofenac, Celecoxib</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Antifungals</td>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Antivirals</td>
<td>Acyclovir, Ganciclovir, Tenofovir</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Cyclosporine, Tacrolimus</td>
</tr>
<tr>
<td>Antineoplastic</td>
<td>Cisplatin, Ifosfamide</td>
</tr>
</tbody>
</table>

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more commonly used in computed tomography, but now some injectors are capable of injecting CM for other angiographic procedures as well. A recent meta-analysis27 that included studies comparing the amount of CM volume delivery between automated contrast injectors and manual manifold injection demonstrated a decrease of contrast volume delivery by 45 mL/case and significant reduction in CIN incidence. Another novel technique, the coronary sinus contrast removal system, may also reduce the volume delivery of CM. Several studies reported this innovative technique to be safe and feasible.28,29 However, trials are needed to validate the potential clinical benefits of this approach.

Conclusions

CIN remains a notable cause of morbidity and mortality after invasive cardiac procedures. Preexisting chronic kidney disease is one of the most important risk factors in CIN prediction. Special precautions should be taken when patients with estimated glomerular filtration rate <60 mL/kg per 1.73 m² receive CIN. Current preventive measures mainly focus on appropriate hydration, the withdrawal of nephrotoxic agents, and minimizing of contrast load. Novel interventions are being developed to further mitigate the risk of CIN.

Disclosures

None.

References


Keywords: creatinine ■ furosemide ■ hypovolemia ■ renal insufficiency ■ ventricular dysfunction, left
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